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The Challenges for Paediatric Respirologists

One of the challenges facing paediatric respirologists is the wide range of diseases from neonates to adolescents that come to us frequently. You will no doubt find support from the current issue.

Respiratory distress is very common in neonates, pre-terms or otherwise, and it is not surprising that respirologists are often called upon by our neonatologists. You will find a very helpful article by Dr. Steve Donn on the approach to neonatal respiratory distress other than respiratory distress syndrome.[1] For the treatment of respiratory distress, ventilators are often involved. Srisan and Meechaijaroenying[2] reported on the comparison of ventilator-associated pneumonia in children using disposable and non-disposable ventilator circuits, and it appeared that disposable circuits might not be cost-effective. For the older age group, asthma is the bread and butter for paediatric respirologists and eczema is very often associated with asthma. Hon *et al*.[3] reported a long-term follow-up detailing the association between asthma and eczema.

As 2018 approaches, I would like to wish all readers a very successful 2018.

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Review Article

Babies Who Don't Get Better: When It's Not Respiratory Distress Syndrome

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Abstract

Most preterm and late preterm infants who require mechanical ventilation for respiratory failure resolve their disease process and can be extubated. A small percentage, however, continues to exhibit respiratory failure and remain ventilator dependent. There are myriad conditions that the clinician needs to consider, some of which are treatable, but some of which are lethal. Strategies for diagnosis and management are discussed herein.

Keywords: Mechanical intubation, newborn, respiratory failure

Introduction

Respiratory failure is the most common problem facing the prematurely born infant. Morphological and anatomical lung abnormalities interfere with adequate pulmonary gas exchange and may lead to the need for mechanical intubation. It is widely recognized that the indications for intubation and mechanical ventilation include inadequate oxygenation and/or ventilation, apnea, airway obstruction, and the need for control of the airway. The goals of mechanical ventilation include assisting the baby to achieve adequate gas exchange, optimizing patient-ventilator interactions, minimizing lung injury, and enhancing patient comfort while decreasing the patient work of breathing.

A recent survey of European neonatal intensive care units by Van Kaam *et al*.[1] queried the reasons for mechanical ventilation in newborns [Table 1]. Although nearly half had respiratory distress syndrome, the remainder exhibited varying conditions including sepsis, congenital malformations, apnea, asphyxia, pneumonia, and others.

Fortunately, most babies improve and are able to be weaned from support. In the past decades, we have improved our understanding of the pathophysiology of these disorders. We have been provided with an expanding array of better technology and an expanded drug formulary. This population possesses the potential for growth, generation of new tissue, and the ability to heal, and it exhibits great plasticity. Yet, some babies get stuck. They may fail to wean, fail to grow, or fail to respond to treatment.

Physiologic Essentials for Extubation

A number of conditions must be achieved before a baby can be successfully extubated. First, there must be reliable respiratory spontaneous expiratory drive, the baby must display neuromuscular competence (the ability to transmit impulses from the respiratory center to the phrenic nerve and diaphragm), and there must be evidence of a reduced respiratory system load, characterized by the maintenance of oxygenation without intrinsic end-expiratory pressure, and adequate minute ventilation (tidal volume X frequency >240 mL/kg/min).[2]

Numerous impediments to weaning and successful extubation have been recognized [Table 2]. Each of these factors alone can increase the work of breathing and complicate the process. Some, such as anemia and electrolyte imbalances, are easily

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correctable, while others are more problematic. When these conditions have been adequately addressed, and the infant is still dependent on mechanical ventilation, the clinician must consider the possibility of an unusual underlying pathologic entity.[3]

Chronic Ventilator Dependence

From a diagnostic standpoint, it may be easiest to classify the underlying problem into one of four categories: primary pulmonary disease (affecting the airway, lung parenchyma, or both); neurologic disease (central or peripheral); myopathy; and metabolic disease.

Table 3 lists malformations of the tracheobronchial tree. These conditions can be diagnosed by imaging (plain or contrast radiography, computed tomography, or magnetic resonance imaging) or airway endoscopy. Most – but not all – are amenable to surgical intervention. The advent of detailed fetal imaging has led to the prenatal diagnosis in many instances, and delivery room intervention (i.e., tracheostomy and EXIT procedure) can be planned in advance.

Table 1: Reasons for ventilating newborns

Diagnosis	Percent
RDS	46
Sepsis	13
Malformations	7
Apnea	5
Asphyxia	5
Pneumonia	4
Surgery	4
Aspiration	3
Air leak	3
Patent ductus arteriosus	2
Other	8

From van Kaam *et al*.[1] RDS: Respiratory distress syndrome

Table 2: Impediments to successful weaning and extubation

Infection
Neurologic dysfunction
Neuromuscular incompetence
Inadequate caloric intake
Excessive fat or carbohydrate intake
Electrolyte imbalances
Metabolic alkalosis
Congestive heart failure
Anemia
Pharmacologic agents
Sedatives
Analgesics

Table 3: Malformations of the tracheobronchial tree

Tracheoesophageal fistula
Laryngotracheoesophageal cleft
CHAOS
Tracheal agenesis
Tracheal stenosis
Tracheo/bronchomalacia
Congenital bronchogenic cyst
Congenital lobar emphysema

CHAOS: Congenital high airway obstruction syndrome

Malformations of the distal lung parenchyma are shown in Table 4. These represent a spectrum from easily treatable to lethal, so it is incumbent on the clinician to make an expeditious diagnosis to institute appropriate therapy or to limit patient pain and discomfort through redirection of care. I will consider a few of these disorders with disparate prognoses to illustrate this point.[4-6]

Alveolar capillary dysplasia

This morphologic disorder was first described by Janney *et al*. in 1981.[7] There have been about 150 cases described in the medical literature, although the disease is probably much more prevalent. The exact etiology is unknown, but there are five reports of its occurrence in concordant siblings. Thus far, no karyotypic or cytogenetic abnormalities have been found.

It is believed to represent abnormal lung development during the pseudoglandular phase (4–16 weeks) and is characterized by arrested lung growth and development. The pulmonary veins adjacent to the pulmonary artery branches are displaced, and the arteries are also abnormal. The vessels share the arteriolar adventitia. The interlobular septa are abnormally broad with decreased numbers of capillaries, which fail to make contact with the alveolar epithelium. Thus, the blood-gas barrier is not formed normally, there is reduced pulmonary surface area, inadequate gas exchange, and pulmonary hypertension.

The usual clinical presentation is severe and intractable persistent pulmonary hypertension with unrelenting hypoxemia. Alveolar capillary dysplasia (ACD) occurs in term infants 90% of the time, often after normal Apgar scores. Half of the affected newborns present in the first 24 h. A later onset form has been reported, with signs appearing as late as 4–6 weeks. Pneumothorax is seen in half of the cases. Associated anomalies [Table 5] occur on 50%–65% of infants.

The chest radiograph in ACD may be initially unremarkable, or it may show mild haziness. Before 2000, more than 90% of cases were diagnosed by postmortem examination. Definitive diagnosis can be made by open lung biopsy.

ACD is a lethal disorder, with death occurring in the 1st day to weeks of age. There has been one reported survivor after lung transplant at 5 months of age.[8]

Surfactant protein deficiency diseases

Pulmonary surfactant is a complex mixture of phospholipids (90%) and proteins (10%). The first attempts at synthetic surfactant repletion in the 1960s, which failed, emphasized the importance of the surfactant-associated proteins.[9]

Table 4: Malformations of the distal lung parenchyma

Pulmonary agenesis/aplasia
Pulmonary hypoplasia
Congenital diaphragmatic hernia
Congenital bronchiolar cyst
Congenital pulmonary adenomatoid malformation
Bronchopulmonary sequestration
Alveolar capillary dysplasia
Congenital pulmonary lymphangiectasia
Interstitial lung disorders
Deficiency of surfactant-associated proteins
Thyroid transcription factor 1 deficiency
GM-CSF receptor deficiency
Cystic fibrosis
Alpha-1 antitrypsin deficiency
Pulmonary interstitial glycogenosis

GM-CSF: Granulocyte-macrophage colony-stimulating factor

Table 5: Alveolar capillary dysplasia: Associated anomalies

Gastrointestinal (40%)
Malrotation
Atresias
Hirschsprung's disease
Annular pancreas
Asplenia
Genitourinary (30%)
Uteropelvic obstruction
Bicornuate uterus
cryptorchidism
Posterior urethral valves
Hydronephrosis
Congenital heart disease (15%)
Musculoskeletal
Phocomelia
Developmental dysplasia of the hip

The proteins, SP-A, SP-B, SP-C, and SP-D, were named in order of their discovery. SP-A is a 35kD hydrophilic monomer, whose major functions are pathogen clearance, modulation of innate immunity, regulation of inflammation, and stabilization of tubular myelin. SP-B is an 8.7 kD amphipathic homodimer, whose functions include surface tension reduction, and surfactant organization and homeostasis. SP-C is a 3.7 kD hydrophobic monopolymer, with functions similar to SP-B. SP-D is a 37.7 kD hydrophilic dodecamer, whose functions include those ascribed to SP-A plus a role in surfactant metabolism.[9]

SP-B deficiency

SP-B was first characterized in 1987.[10] This protein consists of alpha-helices containing multiple amphipathic domains, allowing it to interact with phospholipid polar heads at the edge of the lipid bilayer. The amphipathic domains allow both hydrophobic and hydrophilic interactions, improving surfactant adsorption and reduction in alveolar surface tension. SP-B also aids in preventing alveolar collapse at end-expiration and facilitates recruitment during inspiration.

SP-B deficiency occurs in about 1 per million live births. Multiple different gene mutations, including nonsense, missense, frameshift, and splice site mutations have been identified. Infants with SP-B deficiency develop unresponsive respiratory failure, often resulting in unsuccessful extracorporeal membrane oxygenation therapy, and palliative care. The condition may show a temporary response to animal-derived surfactant administration but is uniformly lethal.[11]

SP-C deficiency

SP-C increases the fluidity of the surfactant phospholipid bilayer accounting for its role in reducing alveolar surface tension. Its deficiency has a high phenotypic variance. Missense, frameshift, insertion, deletion, and splice site mutations have all been identified. In fact, there have been more than 35 dominantly expressed mutations, of which 55% are spontaneous. SP-C deficiency may be diagnosed at any age from early infancy to adulthood. The clinical spectrum ranges from asymptomatic to chronic respiratory insufficiency, and significant disease progressing to death or the need for lung transplantation.[11] It has been postulated that the possible mechanism of disease is the misfolding of proproteins that inhibit protein trafficking and result in cellular stress, injury, and apoptosis. Histopathologic changes include alveolar proteinosis, interstitial pneumonitis, and disorganized lamellar bodies.

The diagnosis of either SP-B or SP-C deficiency can be made from a biochemical analysis of fluid obtained by tracheal aspiration. Genetic (DNA) sequencing can also be done (including ABCA3 mutations). Ultrastructural examination of lung biopsy specimens by electron microscopy can also be useful.

ABCA3 mutations

The exact frequency of ABCA3 mutations is unknown, but it may be the most common disorder of surfactant homeostasis. More than 70 recessive mutations have been identified in lethal RDS in newborns and chronic respiratory insufficiency in children. The precise role of ABCA3 in surfactant metabolism remains elusive. Surfactant isolated from bronchoalveolar lavage fluid from ABCA3-deficient infants has significantly decreased phosphatidylcholine and markedly reduced function, suggesting that the ABCA3 mutation mediates phosphatidylcholine transport into lamellar bodies (which appear small and dense on electron microscopy). The absence of ABCA3 may also affect the trafficking of SP-B and SP-C.[12]

Different classes of mutations that result in the absence, misrouting, or altered function of the ABCA3 protein likely lead to differences in the clinical expression of disease.

Interstitial Lung Diseases

Interstitial lung diseases (ILDs) refer to a group of pulmonary disorders involving both the airspaces and compartments of the

lung. They are relatively rare, but they can be associated with significant morbidity as well as mortality. A comprehensive review by Nogee was recently published and is highly recommended.[13]

Pulmonary Interstitial Glycogenosis

One of these entities is pulmonary interstitial glycogenosis (PIG), and because it is a nonlethal disorder, distinction of PIG from other lethal disorders is critical. The PIG was first described by Canakis *et al*. in 2002.[14] It is an atypical, noninfectious respiratory disorder, which may represent a possible developmental disorder of the lung. It should be distinguished from other forms of ILD, especially unusual interstitial pneumonitis, desquamative interstitial pneumonitis, and lymphoid interstitial pneumonitis.

On light microscopy, the lung tissue shows diffuse interstitial thickening, and the interalveolar septae are uniformly expanded by spindle type cells. Electron microscopy shows abnormalities of the interstitial cells, which have features of primitive mesenchymal cells, and they contain low contrast granular material suggestive of glycogen.

The clinical course of PIG is usually respiratory distress on the 1st day of life. Mechanical ventilation is generally required. The chest radiograph demonstrates large lung volumes, a coarse interstitial pattern, nonspecific haziness, and pneumothorax is common. The diagnosis can be confirmed by chest computed tomography or open lung biopsy.

In general, favorable outcomes have been reported for PIG. In the original series of Canakis *et al*., six of seven survived, and three had clinical resolution by the age of 6 years.[14] Thus, it is clear that this disorder must be distinguished from ACD and SP-B deficiency.

Neuromuscular Disorders

While it is beyond the scope of this review to present an in-depth discussion of all neuromuscular diseases that result in chronic respiratory insufficiency, several of the more common entities will be addressed. What these disorders have in common is a weakness of the respiratory muscles and the inability to compensate for increased respiratory loads. Airway clearance and recurrent pneumonia are also seen frequently. Ventilatory management of affected infants was recently reviewed by Alexiou and Piccione.[15]

Neonatal Onset Spinal Muscular Atrophy (Type 1, Werdnig–Hoffman Disease)

This lethal disorder is inherited as an autosomal recessive disease. It occurs in approximately 1/6000–1/10,000 live births and results from the absence of the SMN1 gene. Progressive destruction of the anterior horn cell leads to increasing weakness and loss of muscular function.[16]

Spinal Muscular Atrophy with Respiratory Distress, Type 1

This is another fatal infantile motor neuron disease. It causes diaphragmatic palsy, distal muscular weakness, muscle atrophy, sensory neuropathy, and autonomic nerve dysfunction. The IGHMBP2 gene has been implicated.[17]

Congenital Myopathies

This group of disorders includes diseases which primarily affect skeletal muscle fibers and are present at birth. An example is myotubular myopathy, an X-linked infantile myopathy. Muscle weakness and hypotonia, with resultant respiratory insufficiency, are the prominent findings. Affected fetuses may have reduced fetal movement, polyhydramnios (from a lack of swallowing), and thin ribs. After birth, there is severe hypotonia, muscle wasting, and generalized weakness. The majority of affected infants die in the 1st month of life. The diagnosis may be suspected by elevated muscle enzymes or abnormalities on electromyography, but only a muscle biopsy is confirmatory.[18]

Congenital muscular dystrophies

These are progressive disorders that lead to degeneration of muscle fibers. Congenital muscular dystrophy occurs in 0.68–2.5/100,000 live births. They are inherited as autosomal recessive diseases, although an autosomal dominant pattern has been reported. The specific type of muscular dystrophy can be determined by advanced diagnostic testing, including biochemical, genetic, and electromyographic.[18]

Congenital myasthenic syndrome

This is an inherited neuromuscular disorder caused by defects of the neuromuscular junction (either presynaptic, synaptic, or postsynaptic) and occurs once in half a million live births. It should be distinguished from the syndrome which affects infants born to mothers with myasthenia gravis, which is transient and improves with supportive care.[19]

Prader–Willi syndrome

This syndrome, characterized by hypotonia (and hence respiratory insufficiency), hypogonadism, hypomentia, and obesity, is seen in 1/25,000–1/10,000 live births. It results from a deletion in the paternal chromosome 15 (q 11–13). Infants are often depressed or lethargic at birth and exhibit feeding difficulties as well as respiratory problems.[20]

Evaluation of Intractable Respiratory Failure in the Newborn

The evaluation of a newborn with intractable respiratory failure should begin with low-invasive, high-yield studies and only progress to the more invasive studies as the differential diagnosis is honed [Table 6]. Imaging, especially chest radiography, is usually the first step. If indicated, chest computed tomography or magnetic resonance imaging

Table 6: Diagnostic evaluation of neonatal intractable respiratory failure

Chest radiography
Chest CT/MRI
Bronchoscopy
Bronchoalveolar lavage
Genetic
Open lung biopsy
Muscle biopsy
Postmortem examination

CT: Computed tomography, MRI: Magnetic resonance imaging

may yield important information or rule out some entities. Flexible bronchoscopy is used to evaluate the upper airway and trachea, and is relatively safe when performed by skilled and experienced operators. Evaluation of lung fluid obtained by bronchoalveolar lavage is becoming a more widely utilized diagnostic test. Genetic studies should be obtained after consultation with a geneticist, who can help decide the appropriate analysis and adjuvant studies.

In cases where surgical biopsy is indicated, whether open lung or muscle, the diagnostic accuracy depends on the appropriate processing of the biopsy specimen. Care should be taken to orchestrate the entire procedure, among the various teams-surgery, laboratory, pathology, and ancillary services.

Finally, for patients who die without a definitive diagnosis, efforts should be taken to obtain a postmortem examination. While families are sometimes reluctant to give consent, a discussion which emphasizes the importance of finding an answer, as well as influencing subsequent family planning can do much to persuade parents to move forward.[21]

Redirection of Care

The decision to withdraw or withhold life support is a difficult one, subject to both individual beliefs and institutional practices and legal imperatives. It would seem reasonable that once the diagnosis of a lethal disorder has been made, efforts should focus on alleviation of pain and avoidance of suffering. In the case of a baby who is failing to respond, but does not have a specific diagnosis, it is less clear. A reasonable attempt to obtain a diagnosis and a reasonable attempt at therapeutic measures seems appropriate. It is up to the clinician and the family to determine what constitutes "reasonable."

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Conflicts of interest

There are no conflicts of interest.

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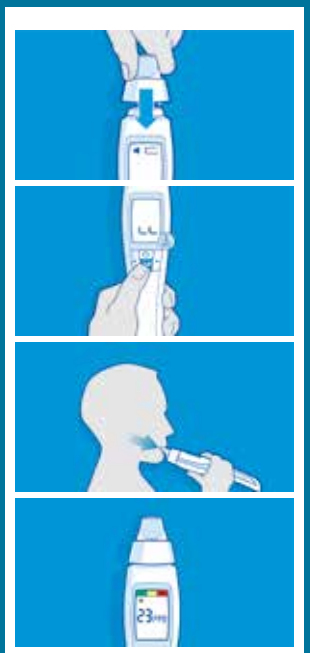
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Original Article

Comparison of Ventilator-associated Pneumonia in Children Using Disposable and Nondisposable Ventilator Circuits

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Abstract

Aims: The aim of the study was to compare the incidence of ventilator-associated pneumonia (VAP), mortality, and ventilator circuit-related cost associated with patients using disposable ventilator circuit to those associated with patients using nondisposable ventilator circuit. **Setting and Design:** A prospective randomized controlled study in a 10-bed Pediatric Intensive Care Unit at Queen Sirikit National Institute of Child Health between November 2011 and October 2012. **Subjects and Methods:** Children aged 1 month to 18 years who were ventilated >48 h were enrolled. Patients were randomized to be ventilated with a disposable or nondisposable heated wire ventilator circuit. **Statistical Analysis Used:** Statistical analysis was performed using SPSS version 17.0. The $P < 0.05$ was considered statistically significant. **Results:** Ninety-eight patients were enrolled. Of these, 48 were administered the disposable ventilator circuit, whereas 50 were administered the nondisposable ventilator circuit. The VAP rate was 20.53/1000 ventilator days for the former ($n = 7$) compared to 30.77/1000 ventilator days ($n = 12$) for the latter (odds ratio: 1.85; 95% confidence interval: 0.66–5.19, $P = 0.24$). The mortality rates were 2.1% in the disposable and 12% in the nondisposable circuit groups ($P = 0.06$). The unit cost of the disposable circuit (US dollar [USD] 51.60) was higher than that of the nondisposable circuit (USD 37.90). However, the total cost for the nondisposable group was higher due to the required use of more units (63 circuits for the disposable group vs. 95 circuits for the nondisposable group). **Conclusions:** The type of ventilator circuit is not likely to affect the VAP rate and mortality in children. The unit cost of a disposable circuit is higher than that of a nondisposable circuit. The total cost depends on the number of circuits used in each patient.

Keywords: Disposable ventilator circuit, nondisposable ventilator circuit, ventilator day, ventilator-associated pneumonia

Introduction

Ventilator-associated pneumonia (VAP), the most important hospital-associated infection (HAI) in the Intensive Care Unit (ICU), is defined as pneumonia that occurs in a patient who is mechanically ventilated for at least 48 h.[1-5] It is associated with increased mortality, morbidity, length of stay, and health-related costs. The presence of an endotracheal tube (ETT) is the most important risk factor of VAP. Additional risk factors in children are underlying respiratory disease, longer duration of mechanical ventilation, genetic syndromes, immunodeficiency, continuous enteral feeding, the use of H_2 antagonist, the use of narcotics or neuromuscular blocking agents, previous antibiotic exposure, gastroesophageal reflux, younger age, reintubation, and supine positions.[2-4]

The prevention of VAP is essential in all ventilated patients.[1-13] Several strategies with the aim of preventing microaspiration, the colonization of the respiratory or the gastrointestinal tract by pathogenic organisms, or the contamination of ventilator equipment have been proven to be effective in adults and children. The possibility of cross infections from improperly cleaned nondisposable ventilator circuits and humidifiers was previously documented.[10,12,14,15] The use of disposable ventilator-related equipment is a standard practice in many developed countries because it involves a lower chance of infection and is more convenient to use. In contrast, the use of nondisposable ventilator circuits is more common in developing countries, including Thailand, due to their lower

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costs.[14] There have been no previous studies comparing the incidence of VAP across different types of ventilator circuits. Therefore, this study was conducted to compare the incidence of VAP in children administered a disposable ventilator circuit to that in children administered a nondisposable ventilator circuit. The ventilator circuit-related costs and mortality of both groups were also compared.

Subjects and Methods

This research was a prospective randomized controlled study in the 10-bed-multidisciplinary pediatric ICU (PICU) of the Queen Sirikit National Institute of Child Health. The study was approved by the Institutional Review Board.

All the pediatric patients aged 1 month to 18 years who were intubated and mechanically ventilated for at least 48 h between November 2011 and October 2012 were enrolled. The exclusion criteria were ventilation for >48 h before admission to the PICU, postelective surgery, prior palliative care, and refusal of consent of a parent or a guardian.

The patients were randomly allocated to be ventilation with a disposable or a nondisposable ventilator circuit. The disposable circuit in this study was a dual heated wire breathing circuit (Evaqua™ 1, Fisher and Paykel Healthcare Ltd., Auckland, New Zealand). The nondisposable heated wire circuit came equipped with the ventilator having been sold to the hospital. The frequency of a ventilator circuit change was every 7 days for the former (Evaqua™ 1 user instruction) and every 5 days for the latter (our hospital policy). The disinfection process for the nondisposable circuit included wash with soap and clean water, chemical disinfection with sodium dichloroisocyanurate (Mediklean™), hot-air drying, and ethylene oxide gas sterilization, which was approximately 7 h.

The data collected included age, sex, weight, underlying disease, the pediatric risk of mortality (PRISM) III score, the risk factors of VAP, the duration of mechanical ventilation (number of ventilator days), the length of PICU stay, and mortality. VAP was diagnosed using the Centers for Disease Control and Prevention definition of nosocomial pneumonia.[16] That is, the incidence of VAP refers to the number of VAP cases per 1000 ventilator days. Ventilator utilization was expressed as a ratio of ventilator days to a PICU stay. The semi-quantitative culture of blood, sputum, or tracheal aspirate was used in this study.

The total ventilator circuit-related cost is the sum of material, labor, and maintenance costs. The labor cost is the total wage incurred on preparing, providing, and disinfection a ventilator circuit. The maintenance cost is calculated from the equipment and the depreciation cost of the disinfection process. All the costs were calculated in Thai Baht together with its equivalent in US dollars (USDs).

The sample size was calculated based on the VAP rate of 26.0/1000 ventilator days in nondisposable circuits (our previous VAP incidence) at the estimated VAP rate reduction of 30%. The result was 49 cases in each group.

All descriptive data were expressed as mean ± standard deviation or number (percentage). Categorical variables were analyzed using the Chi-square or the Fisher's exact test. The unpaired *t*-test or the Mann–Whitney U-test was used to compare continuous variables. The $P < 0.05$ was considered statistically significant. Statistical analyses were performed using the SPSS Statistical software version 17.0 (SPSS: International Business Machines Corp., New York, USA) (http://th.softonic.com/s/spss-17).

Results

Ninety-eight patients were enrolled. Of these, 50 (51%) were in the nondisposable circuit group, while 48 (49%) were in the disposable circuit group. The patient demographic data, the PRISM III scores, and the underlying diseases were not significantly different between the two groups. The most common underlying diseases in the disposable and the nondisposable circuit groups were cardiovascular diseases and genetic syndromes, respectively. The risk factors of VAP, including previous antibiotic exposure, retained nasogastric or orogastric tube, the use of H_2 antagonist, sedation, open suction system, and reintubation, were not significantly different between the two groups [Table 1]. The most common cause of intubation was pneumonia with acute respiratory failure.

From the results, VAP occurred in 19 patients, 7 in the disposable circuit group and 12 in the nondisposable circuit group. The total VAP rate was 26.0/1000 ventilator days. The VAP rate was 14.6% and 20.53/1000 ventilator days in the disposable circuit group compared to 24% and 30.77/1000 ventilator

Table 1: Patient characteristics (*n*=98)

Patient data	Ventilator circuits		*P*
	Disposable (*n*=48)	Nondisposable (*n*=50)	
Age (years) (mean±SD)	2.23±3.80	3.16±3.87	0.24
Male, *n* (%)	29 (60.4)	26 (52.0)	0.71
Body weight (kg) (mean±SD)	9.95±9.73	13.22±10.25	0.11
PRISM III score (mean±SD)	2.79±2.8	3.38±3.62	0.37
Underlying diseases, *n* (%)	29 (60.4)	24 (48.0)	0.22
Cardiovascular	14 (29.2)	5 (10.0)	
Genetic syndrome	5 (10.4)	6 (12.0)	
Pulmonary	3 (6.3)	1 (2.0)	
Neurological	2 (4.2)	3 (6.0)	
Others	5 (10.4)	9 (18.0)	
H_2 antagonist, *n* (%)	22 (45.8)	24 (48.0)	0.83
Previous antibiotic exposure, *n* (%)	47 (97.9)	49 (98.0)	1.00
NG or OG tube, *n* (%)	42 (87.5)	41 (82.0)	0.45
Sedation, *n* (%)	40 (83.3)	44 (88.0)	0.51
Open suction system, *n* (%)	27 (56.3)	31 (62.0)	0.56
Reintubation, *n* (%)	2 (4.2)	1 (2.0)	0.61

NG: Nasogastric, OG: Orogastric, SD: Standard deviation, PRISM: Pediatric risk of mortality

days in the nondisposable circuit group (odds ratio [OR]: 1.85; 95% confidence interval [CI]: 0.66–5.19, $P = 0.24$). There were no significant differences in ventilator days, PICU stays, and ventilator utilization between the two groups [Table 2]. The organisms isolated from the tracheal aspirates were *Acinetobacter baumannii* (50%), *Pseudomonas aeruginosa* (40%), and *Klebsiella pneumoniae* (10%).

Of all the cases, there were 7 deaths, 1 in the disposable circuit group (only in the non-VAP group) and 6 in the nondisposable circuit group (3 in the non-VAP group and 3 in the VAP group). The mortality rate in the disposable circuit group (2.1%) was not significantly different from that in the nondisposable circuit group (12%) (OR: 0.16; 95% CI: 0.02–1.35, $P = 0.06$). Such deaths were caused mainly by severe sepsis (5/7), followed by pulmonary hemorrhage (1/7) and chronic lung disease (1/7). The OR for VAP death in the nondisposable circuit group was 3.9 [Table 2].

In terms of costs, the unit cost of a ventilator circuit was USD 51.60 for the disposable circuit compared to USD 37.90 for the nondisposable circuit. Nevertheless, due to its use of more circuits, the nondisposable circuit incurred a higher total cost of USD 3600 (95 circuits) compared to USD 3250 for the disposable circuit (63 circuits) [Table 3].

Discussion

VAP has been reported to occur in approximately 20% of all HAIs in PICU, with the range of 1–63/1000 ventilator days.[2,3] The incidence of VAP in this study (26.0/1000 ventilator days) was similar to that in our previous study in 2008 (26.0/1000 ventilator days) (unpublished data). In contrast, VAP rates in children have varied greatly depending on surveillance definitions, PICU settings, and national income levels.[1-3,10,16-18] Several studies from Asia, including Thailand, reported VAP rates between 8 and 70/1000 ventilator days with the mortality between 5% and 23%.[3,18,19] The pathogenesis of VAP involves the complex interactions between the presence of ETT, VAP risk factors, the virulence of bacteria, and host immunity. Pathogenic organisms can originate from either endogenous or exogenous sources. The aspiration of contaminated oropharyngeal secretion into the lower airway is a prerequisite for VAP development. The colonization of ETT, ventilator circuit, humidifier, nebulizer, or other respiratory equipment can also lead to lower airway contamination. VAP is rarely caused by hematogenous spread.[1,5,6,10-15] The most common causative organisms are Gram-negative pathogens such as *P. aeruginosa*, *A. baumannii,* and *Enterobacteriaceae* with increasing reports of multidrug-resistant strains in Asia.[3,5,15,18,19]

Recommendations for VAP prevention in children and adults include hand hygiene, head of bed elevation, oropharyngeal cleansing, sterilization or disinfection of respiratory equipment, no routine change of ventilator circuit, daily sedation interruption and assessment of readiness for weaning, active surveillance of VAP, and education of health-care staff.[1-14] Multiple VAP preventive strategies are already implemented in our PICU, which may explain the comparable VAP rates between disposable and nondisposable circuits in this study.

From the findings, the main cost of a disposable circuit is material cost, whereas the costs of a nondisposable circuit predominantly involve both material and labor ones. In our hospital, the nondisposable circuit is usually used until it is broken (2–3 years). Despite its high cost, disposable circuits are increasing popular due to their elimination of cross infections and ease of use. However, a number of other factors need to be taken into consideration, especially labor availability, wage rates, and circuit change intervals. Labor shortage is currently an important issue worldwide, including in developing countries. A rise in wage rates will increase the labor and the unit costs of nondisposable circuits. Besides, if the circuit change interval can be extended, the number and costs of ventilator circuits will be decreased. Clinical practice guidelines recommend that ventilator circuits should not be changed routinely for infection control purposes. Although the maximum duration that circuits can be used safely is unknown, previous studies demonstrated that the extension of a ventilator circuit change interval for children from 3 to 7 days did not increase VAP rates and was cost-effective.[1,6,11,12,18] The reason for the difference in the number of circuits was the use of a high-frequency oscillator required for some patients in the nondisposable circuit group.

Table 2: Ventilator-related and clinical outcomes

Outcomes	Ventilator circuits		*P*
	Disposable (*n*=48)	Nondisposable (*n*=50)	
VAP case, *n* (%)	7 (14.6)	12 (24.0)	0.24
Ventilator day (days) (mean±SD)	7.10±4.19	7.80±5.24	0.47
PICU stay (days) (mean±SD)	8.38±4.63	9.22±5.18	0.40
Ventilator utilization[a] (%)	84.73	84.60	0.71
Death, *n* (%)	1 (2.1)	6 (12.0)	0.06
VAP death	0	3	
Non-VAP death	1	3	

[a]Ventilator utilization=(ventilator day/PICU stay) × 100. PICU: Pediatric Intensive Care Unit, VAP: Ventilator-associated pneumonia, SD: Standard deviation

Table 3: Ventilator circuit-related costs per circuit

Costs/set (USD)	Ventilator circuit	
	Disposable	Nondisposable
Total cost/set	51.60	37.90
Material cost	51.43	28.20
Labor cost	0.16	9.42
Maintenance cost	-	0.27
Number of circuits used (*n*)	63	95
Total cost	3250	3600[a]

[a]*P*=0.58. USD: US dollar

There was a trend toward mortality in the nondisposable group (12%), compared to the disposable group (2.1%) ($P = 0.06$). In the nondisposable circuit group, VAP death was 25% (3/12) and non-VAP death was 7.9% (3/38), with the OR of 3.9. If the number of patients was increased, the significant difference in mortality between disposable and nondisposable circuit groups might be demonstrated, included the difference between VAP and non-VAP death in the disposable circuit group.

VAP-related cost was not considered in this study as there was no difference in VAP rates between both groups. Nevertheless, VAP caused by multidrug-resistant bacteria is an emerging global problem, resulting in higher mortality and healthcare-related costs.[3,20]

Conclusions

Our study suggests that the VAP rates between children using disposable and nondisposable ventilator circuits are not different. In addition, the ventilator circuit-related costs of disposable circuits are likely to be high.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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Original Article

Airway Disease and Environmental Aeroallergens in Eczematics Approaching Adulthood

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Abstract

Background: Atopic eczema (AE) is one of the most common skin diseases affecting children and adults worldwide. The "Atopic March" paradigm suggests AE is part of a complex condition with related airway disease. **Objective:** This study aimed to evaluate the prevalence of airway disease, environmental aeroallergens, and review factors associated with eczema severity and quality of life (QoL) when AE patients approached adulthood. **Methods:** Patients who were diagnosed with AE at a young age were included in the study and followed up till their adolescence at pediatric dermatology clinics from 2000 to 2017. Demographic characteristics, clinical laboratory parameters, treatment history, personal atopic history, as well as disease outcomes assessed by Nottingham Eczema Severity Score (NESS) and Children Dermatology Quality Life Index (CDLQI) were reviewed. **Results:** Three hundred and eighty-three patients (55.4% males) with latest NESS at mean (standard deviation) age 16.23 (2.50) years were reviewed. Personal history of asthma (45%), allergic rhinitis (74%), and family history of atopy were prevalent. Seventy-two percent of the patients were skin prick testing positive for house dust mite, 27% for cockroach, 33% for cat fur, and 13% for dog fur. Fourteen percent reported "smokers in family". Multiple logistic regression showed "food avoidance ever" (adjusted odds ratio [OR] =3.00, 95% confidence interval [CI] =1.08–8.32; $P = 0.035$) and log-transformed immunoglobulin E (IgE) (adjusted OR = 1.45, 95% CI = 1.09–1.92; $P = 0.011$) were significantly associated with more severe AE. Linear regression showed "food avoidance ever" ($\beta = 1.79$, 95% CI = 0.34–3.24; $P = 0.016$), higher log-transformed IgE ($\beta = 0.62$; 95% CI = 0.22–1.03; $P = 0.003$), dog dander sensitization ($\beta = 2.07$, 95% CI = 0.24–3.89; $P = 0.027$), and severe disease ($\beta = 2.97$, 95% CI = 2.26–3.68; $P < 0.001$) were significantly associated with QoL impairment. **Conclusions:** A number of patients do not grow out of their eczema, and many of them have allergic rhinitis and asthma co-morbidities. Toward adulthood, AE severity and QoL are associated with food avoidance and high IgE, but generally independent of family or personal history of airway disease and allergen sensitization. Blood IgE measurement may help assess the risk for more severe eczema when patients are becoming adults.

Keywords: Adult, asthma, allergic rhinitis, aeroallergen, atopic eczema, Children Dermatology Life Quality Index, Nottingham Eczema Severity Score, prognosis

Introduction

Atopic eczema (AE) or atopic dermatitis is a chronically relapsing skin disorder affecting children and adults worldwide, with clinical symptoms of rash, inflammation, dry skin, and itch.[1-3] It is one of the most common skin diseases with global prevalence of 7.9% according to a cross-sectional questionnaire survey (International Study of Asthma and Allergies in Childhood Phase Three [1999–2004]), which showed an increasing trend comparing to the global prevalence of 6.1% reported in Phase One (1992–1997).[4] In Hong Kong, AE prevalence among children aged 6–7 years old increased from 3.9% to 4.6%, and among children aged 13–14 years old from 2.7% to 3.3%.

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With the increasing prevalence of AE, there are grave individual and social sequelae in terms of quality of life (QoL), financial, academic, and occupational burdens.[5-7] For children with AE, not only physical symptoms such as itching, scratching, and sleep disorder impact their daily life but also psychological pressure such as social isolation, low self-esteem, and low self-confidence.[8,9] The impacts of eczema including economic

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burdens and QoL impairment are not only confined to the patients but also to their families. In most cases, families, especially parents with young AE patients would spend substantial financial costs, time, and effort in caring for them.

The etiology of eczema is complex, involving both genetic and environmental factors. Genetic mutation and environmental stimuli impair skin barrier, which ultimately manifests as eczema. Researches focusing on eczema etiology attract great attention because the elucidation of eczema pathophysiology would potentially lead to novel therapeutic strategies. The *filaggrin* gene (*FLG*) encoding a structural epidermal protein, along with a set of other proteins comprising epidermal differentiation complex, plays an important role in the intactness of skin barrier.[10] Recent studies gave evidence that loss-of-function mutation in *FLG* gene is associated with eczema.[11,12]

Epidemiologic researches on eczema identified a number of environmental risk factors including climate, diet, lifestyle, microbial agents, aeroallergens, and stress.[13] Aeroallergens such as house dust mite (HDM), pet fur, pollen, and smoke have been studied.[1] Broad spectrum antibiotic abuse might alter gut microbiota and lead to eczema exacerbation. High fat, low fruit and fish intake might be associated with increasing risk of eczema, there is no consistent evidence on the protective effect of exclusive breastfeeding.

It is a popular notion adopted by some parents and clinicians that children will outgrow eczema when they reach adolescence, but some long-term follow-up studies do not concur with this point of view. In a cross-sectional and cohort study targeting long-term registry of childhood eczema in the United States, it is concluded that eczema is probably a lifelong disease which persists into the second decade of children's life.[14] A Hong Kong study similarly shows that eczema may persist when children grow older.[15] However, the follow-ups for both studies are too limited to draw conclusion on the progression of eczema when patients are reaching adulthood. According to the "Atopic March" paradigm, AE is part of a complex condition with related allergic hypersensitization involving the airways.[16-18] This study aimed to evaluate the prevalence of airway disease, environmental aeroallergens, and factors associated with eczema severity and QoL when AE patients approach adulthood.

Methods

Demographic characteristics of AE patients who were followed at the pediatric dermatology clinics of a teaching hospital between 2000 and 2017 to at least 16 years of age were reviewed. Patients diagnosed with AE were included in the study. Clinical information was recorded by the physicians on their first visit by means of clinician history taking, questionnaires, and laboratory tests which included disease severity, QoL, family and personal history of atopy, household pets, smoking, and therapeutic data. Clinical laboratory parameters included blood immunoglobulin E (IgE) (highest if multiple measurements), eosinophil counts, and skin prick testing if available.

Eczema onset age, prematurity, family atopy history, pets keeping, food avoidance, history of treatment (traditional Chinese medicine [TCM], immunomodulant, and wet wrap), feeding (breastfeeding or formula feeding) were recorded in clinicians' consultations over the years.

Eczema severity is assessed by Nottingham Eczema Severity Score (NESS), which is a self-administered questionnaire with score ranging from 3 to 15, that divides patients into mild, moderate, and severe categories.[19,20] The validated Cantonese version of NESS questionnaire shows good agreement with SCORing Atopic Dermatitis (SCORAD).[21] The secondary outcome is assessed by Children Dermatology Life Quality Index (CDLQI), which is a questionnaire measuring the QoL of patients with skin disease.[22] Validation of the Cantonese version CDLQI shows that CDLQI scores correlated with physician-rated disease severity with good test-retest correlation ($P < 0.01$).[20,23]

Patients younger than 10 years of age or older than 22 years (if no prior NESS measurement) were excluded, and the characteristics of included and excluded patients were compared to assure that there is no substantial difference between them.

One-way ANOVA (Kruskal–Wallis one-way ANOVA for nonparametric data) was conducted to assess the association between categorical (more than three levels) and continuous variables. For binary and continuous variables, two sample *t*-test (Mann–Whitney test for nonparametric data) was performed. Chi-square test (Fisher's Exact test for nonparametric data) was applied to investigate the association of categorical variables. Simple logistic regression was carried out to assess factors influencing odds for mild eczema versus moderate or severe disease. Multiple logistic regression was performed taking into account of sex, AE onset age, mother atopy status, breastfeeding ever, smoker in family ever, food avoidance ever, skin prick test (SPT), and highest IgE. Linear regression was performed to assess the effect of each factor with CDLQI. $P < 0.05$ was considered statistically significant. The University ethics committee approved this review.

Results

Totally 403 eczema patients were reviewed, 383 of whom with mean (standard deviation [SD]) age 16.23 (2.50) years were analyzed [Table 1].

When these patients approached adulthood, 123 patients had mild eczema, 137 patients with moderate eczema, and 123 patients with severe eczema. The percentage of male increased with more severe disease, which was 48.4% in mild group, 57.4% in moderate group, and 61.7% in severe group ($P = 0.037$). AE onset age was significantly associated with eczema severity, and patients with early disease

onset (usually <1-year-old) generally had more severe AE in adolescence. The proportion of patients with treatment history including wet wrap, TCM, immunomodulant, and food avoidance increased with more severe eczema level ($P \leq 0.001$).

About 48.3% of eczema patients had asthma comorbidity, while the proportion did not differ between groups ($P = 0.637$); 78% of patients had allergic rhinitis, the difference of proportion between groups was not significant ($P = 0.175$).

64.6% of patients with mild eczema had reported they had food allergy, with 73.2% in moderate group, and 81.6% in severe group ($P = 0.013$).

Eosinophil percentage and highest IgE were both significantly associated with more severe eczema (Kruskal–Wallis test, $P < 0.001$).

SPT assessed sensitization to cat dander, dog dander, cockroach, house dust mite (HDM), and foods: 40.2% for cat, 16.0% for dog, and 33.7% for cockroach. Most patients were sensitized to HDM (88.4%). There was a significant association between HDM sensitization and eczema severity ($P < 0.001$). Sensitization to common foods occurred in 72.8% of patients, and the trend was not significantly associated with more severe disease ($P = 0.085$).

Multiple logistic regression was conducted to assess the adjusted odds ratio (OR) of mild eczema versus moderate or severe disease [Table 2]. Controlling for gender, AE onset age and mother atopy status, the adjusted OR for food avoidance ever was 3 (95% confidence interval [CI]: 1.08–8.32), and the adjusted OR for log-transformed IgE was 1.45 (95% CI: 1.09–1.92). None of the other clinical factors reached significance.

There were 247 patients with CDLQI data when they reached adolescence. Regression analysis showed that CDLQI increased by 1.79 point on average with food avoidance ever ($P = 0.016$) and by 0.62 per unit increase in log (IgE) ($P = 0.003$); CDLQI would increase or worsen by 2.07 points on average for patients with dog fur allergy ($P = 0.027$) [Table 3].

Discussion

We followed up patients toward adulthood with the mean (SD) age 16.23 (2.50) years and recorded NESS scores as primary outcome. Our study was compatible with previous study that AE severity when patients were reaching adulthood may be associated with gender, young-onset age, treatment history, IgE and blood eosinophil counts, HDM, foods, cat fur, and dog fur sensitization.[24] Importantly, the majority of AE patients in this cohort were troubled with moderate-to-severe disease. The secondary outcome, CDLQI, is associated with food avoidance, highest IgE, and skin sensitization for dog fur.[24] Common to both outcomes, however, regression analysis showed that many of the clinical parameters were not predictive of AE severity or QoL when patients are approaching adulthood. The only relevant parameters were history of food avoidance and the IgE levels. A high blood IgE level may be predictive of a more severe disease course and quality of life impairment when the child grows up.

Another important observation is that many patients do report airway co-morbidities of asthma and allergic rhinitis, and food and aeroallergen sensitization. However, airway disease is

Table 1: Demographics and clinical factors associated with atopic eczema severity toward adulthood

	AE severity by NESS			*P*
	Mild (*n*=123)	Moderate (*n*=137)	Severe (*n*=123)	
Mean age±SD (years)	16.10±2.35	16.50±2.41	16.18±2.65	0.380
Male (%)	59 (48.4)	78 (57.4)	74 (61.7)	0.037**
AE onset age				
Mean±SD (years)	3.01±3.37	3.26±4.08	1.94±2.97	0.010†
Onset age <1 year (%)	40 (41.2)	56 (45.2)	66 (58.4)	0.012**
Treatment history (%)				
Wet wrap ever	21 (18.8)	48 (37.8)	71 (62.8)	<0.001**
TCM ever	44 (40.4)	78 (62.9)	76 (68.5)	<0.001**
Immunomodulant ever	5 (4.3)	18 (13.7)	22 (19.1)	0.001**
Food avoidance ever	49 (48.0)	84 (68.3)	87 (76.3)	<0.001**
Personal atopy				
Reported food allergy ever (%)	51 (64.6)	71 (73.2)	71 (81.6)	0.013*
Eosinophils (Mean ± SD) %	7.69±5.03	9.32±6.63	12.14±8.10	<0.001†
IgE (Mean ± SD) IU/L	2126.23±3897.68	5741.39±9200.92	9871.42±13932.47	<0.001†
Skin prick test				
HDM sensitization (%)	73 (77.7)	106 (94.6)	98 (93.3)	<0.001
Foods sensitization (%)	62 (66.7)	84 (73.7)	80 (77.7)	0.085**
CDLQI (mean ± SD)	4.45±3.96	6.89±4.11	10.35±5.03	<0.001

*Fisher's exact test, †Kruskal-Wallis test, **Trend test. SD: Standard deviation, CDLQI: Children Dermatology Life Quality Index, HDM: House dust mite, AE: Atopic eczema, NESS: Nottingham Eczema Severity Score, TCM: Traditional Chinese medicine

generally independent of AE severity and QoL. Nevertheless, another study reported significant relationship between AE severity, bronchial asthma, allergic rhinitis, and the duration of the skin lesions.[25] Regardless, these associated atopic diseases are prevalent among AE patients.

Table 2: Multiple logistic regression analysis of patient characteristics on atopic eczema severity

	Unadjusted OR (95% CI)	*P*	Adjusted OR (95% CI)	*P*
Male	1.56 (1.01-2.41)	0.044	0.94 (0.37-2.39)	0.896
AE onset age <1	1.51 (0.94-2.44)	0.090	0.88 (0.34-2.28)	0.791
Mother atopy	0.74 (0.47-1.17)	0.200	0.54 (0.21-1.39)	0.202
Breastfed ever	0.79 (0.44-1.41)	0.422	0.51 (0.20-1.29)	0.155
Smoker ever	1.24 (0.67-2.29)	0.489	3.03 (0.7911.60)	0.106
Food avoidance ever	2.80 (1.73-4.53)	<0.001	3.00 (1.08-8.32)	0.035
Skin prick test				
HDM positive	4.51 (2.15-9.48)	<0.001	3.01 (0.74-12.22)	0.123
Cat fur positive	1.48 (0.89-2.44)	0.129	0.38 (0.14-1.04)	0.059
Dog fur positive	1.91 (0.91-4.00)	0.087	3.66 (0.84-16.04)	0.085
Log transformed IgE	1.50 (1.27-1.77)	<0.001	1.45 (1.09-1.92)	0.011

HDM: House dust mite, AE: Atopic eczema, OR: Odds ratio, CI: Confidence interval

Table 3: Simple linear regression analysis of patient characteristics on Children Dermatology Life Quality Index

	β (95% CI)	*P*
Sex (male)	−0.41 (−1.68-0.85)	0.521
Premature	−1.51 (−5.96-2.94)	0.502
First born	−0.48 (−1.83-0.88)	0.490
AE onset age		
AE onset age (year)	0.08 (−0.11-0.27)	0.391
AE onset age <1	0.06 (−1.25-1.36)	0.934
Feeding patterns		
Formula fed ever	6.06 (−3.51-15.63)	0.212
Breastfed	0.31 (−1.23-1.85)	0.698
Breastfed period (month)	−0.08 (−0.26-0.11)	0.423
Family atopy		
Father atopy	−0.83 (−2.10-0.44)	0.200
Mother atopy	−0.69 (−1.98-0.59)	0.290
Siblings atopy	−1.15 (−2.96-0.67)	0.215
Personal atopy		
Personal AR	−1.33 (−2.85-0.20)	0.088
Personal AS	−0.17 (−1.42-1.08)	0.795
Pet ever	−0.37 (−2.41-1.66)	0.718
Smoker ever	−0.24 (−1.91-1.42)	0.773
Food avoidance ever	1.79 (0.34-3.24)	0.016
Log-transformed IgE	0.62 (0.22-1.03)	0.003
Eosinophils (%)	0.07 (−0.02-0.17)	0.127
Food allergy ever	−0.44 (−2.21-1.33)	0.624
Skin prick test		
Cat sensitization	0.98 (−0.37-2.33)	0.155
Dog sensitization	2.07 (0.24-3.89)	0.027
Cockroach sensitization	0.15 (−1.25-1.55)	0.833
HDM sensitization	0.17 (−2.06-2.39)	0.883
Food sensitization	−0.42 (−1.94-1.10)	0.586
NESS	2.97 (2.26-3.68)	<0.001

AR: Allergic rhinitis, AS: Asthma, NESS: Nottingham Eczema Severity Score, HDM: House dust mite, AE: Atopic eczema, CI: Confidence interval

For strength of the study, it is a long-term follow-up study, with focus on eczema severity toward adulthood. We recorded the clinical factors from early years and updated the clinical information from time to time. NESS was used as instrument to assess AE severity which is more appropriate in comparing long-term change of disease status than SCORAD which assesses AE severity within 1 week. CDLQI toward adulthood as the secondary outcome is another innovative point for our study.

For the weakness of the study, there are missing data for some factors, notably the laboratory tests. Also, many young children are not reaching adulthood after years of follow-ups and have to be excluded from this review. Some children may refuse laboratory tests, and hence only clinical parameters are available. Consequently, multiple regression is hard to perform due to considerable loss of power. Furthermore, genetic confounders or lifestyle and socioeconomic status confounders were not included. Inevitably, in the tertiary hospital setting, the population of subjects are likely to be biased toward more severe disease.[26]

In terms of foods sensitization (as evidenced by SPT), the increasing trend with more severe eczema is consistent with other studies. Two-thirds of mild eczema patients are sensitive to foods by SPT.[27-31] Considering that most children are not exposed to many foods before 3 years of age, interpreting the frequency of those who are sensitive to foods by SPT and reported foods allergen exposure after age 3 would be more meaningful. However, food sensitization does not equate with genuine food allergy. Food allergen sensitization as evidence by positive skin prick testing is not associated with more severe disease or worse quality of life in children with AE. Conversely, food avoidance, often indiscriminatively practiced, is associated with more severe disease and worse quality of life.

Many parents may report adverse food reactions in their children with AE. Although sensitization to food and aeroallergens are prevalent, it has been demonstrated that the prevalence of genuine food allergy is low and indiscriminate food avoidance does not alleviate symptoms of AE and airway allergies.[29,32-34]

Conclusions

A number of patients do not grow out of their eczema, and many of them have allergic rhinitis and/or asthma. AE may remain severe toward adulthood. AE severity and QoL are associated with food avoidance and high IgE, but generally independent of family or personal history of airway disease and allergen sensitization. As the age when the IgE was assessed was not standardized in this retrospective study, it is not sure if blood IgE measurement may truly help assess

the risk for more severe eczema when patients are becoming adults. Nevertheless, higher IgE can serve as a marker of more severe atopy.

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Conflicts of interest

There are no conflicts of interest.

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