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Contents

Diagnosis and Outcomes

A comprehensive understanding of the diagnosis and outcomes of pediatric pulmonary diseases is important for clinicians. Prompt diagnosis of diseases is crucial for clinicians to make decisions in choosing suitable interventions, providing appropriate therapeutic management options. This issue brings up three articles discussing the diagnosis of pneumonia and obstructive sleep apnea (OSA) in pediatric patients and outcomes of critically ill infants requiring transport.

Pneumonia is an infection that causes inflammation in the lungs and a potentially serious infection in children. Diagnosis of pneumonia includes a complete medical history, physical examination, and a chest radiograph (CXR). The main causes of pneumonia are bacteria, viruses, or fungi. CXRs are the most widely employed test; however, they cannot distinguish between viral and bacterial infections and have a misleading in patients with pulmonary edema, lung agenesis, or pseudopneumonia such as thymus.[1] In children, pneumonia caused by *Streptococcus pneumoniae* is the most common cause of community-acquired pneumonia.[2] However, following the introduction of the pneumococcal conjugate vaccine, a significant decline in pneumococcal pneumonia appears to have declined, accompanied by an increase in *Mycoplasma pneumoniae* pneumonia.[3] Understanding the epidemiology of health-care-associated infections and adequate awareness and recognition of pneumonia may provide affected children a prompt and appropriate treatment.

OSA is a potentially serious sleep disorder in children. Polysomnography (PSG) is currently the best approach to diagnose OSA.[4] The apnea–hypopnea index (AHI) is an index used to indicate the severity of sleep apnea. The AHI is the number of apneas or hypopneas recorded during the study per hour of sleep. In contrast, the McGill Oximetry Score (MOS) is a validated measure based on nocturnal pulse oximetry by measuring frequency of desaturations (<90%) and numbers of clusters of desaturations.[5] However, it must be emphasized that MOS is not accurate at detecting OSA in children who do not have such drops in oxygen saturation. Despite this, an abnormal MOS has a 97% positive predictive value at detecting moderate–severe OSA as in this issue. Although nocturnal pulse oximetry is an easy, low-cost screening tool for OSA in children when PSG is not available, the significant night-to-night variability between MOS scores suggests a combination with other techniques for a more reliable result.

In clinical practices, patient transportation is an important component of health-care delivery, especially in critically ill infants.[6] Serious problems may develop in relation to the patient's illness or injury during transport. In emergency situations, it is strongly recommended to assess patients by the transport team to anticipate and prepare for events that may occur during transport.[6] Infants are of those vulnerable populations; however, not all hospitals provide a dedicated specialized emergency medical service for transport. In this issue, patients require intubation or inotropic support during transport appears to be more likely to develop complications, including desaturation, severe hypoxia, and acidosis. This information not only offers insight into the importance of the role of a dedicated transport team in the outcomes of patient transport, but also provides information for improving health policies.

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Review Article

What Does It Mean When a Child is Diagnosed with Pneumonia?

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Abstract

Pneumonia is a frequent diagnosis without adequate consideration of the etiology. Pneumonia implies the presence of inflammation of the lung parenchyma with consolidation. That inflammation may be from infectious or noninfectious causes. Radiologic diagnosis of pneumonia is subject to interobserver interpretation and may misdiagnose noninflammatory radiological opacifications as pneumonia. The common diagnosis of community-acquired pneumonia in children most commonly has a viral rather than bacterial etiology. Antibiotics should be reserved for those where the clinical course, laboratory measure of biomarkers, and radiology are consistent with the diagnosis of pyogenic bacterial pneumonia.

Keywords: Antibiotics, bacterial infection, pneumonia, pseudopneumonia, viral infection

Introduction

The World Health Organization (WHO) describes pneumonia as the single largest infectious cause of death in children worldwide.[1] Diagnosis of pneumonia is described by the WHO as "the presence of either fast breathing or lower chest wall indrawing where the child's chest moves in or retracts during inhalation." Under the heading, "Treatment," the WHO states, "Pneumonia should be treated with antibiotics." However, the same WHO document acknowledges that "Pneumonia is caused by a number of infectious agents, including viruses, bacteria and fungi."

The WHO therefore provides the clinician with ambiguous recommendations. Is the observation of fast breathing or thoracic retractions sufficient for decision-making of the diagnosis and treatment of pneumonia? Diagnosing by observing chest movement and treating unreservedly with antibiotics is not consistent with the acknowledgment of the various etiologies of pneumonia. This review of pneumonia presents 6 cases illustrating various examples of children diagnosed with pneumonia. These contrasting cases set the stage for an evidence-based discussion of pneumonia diagnosis and treatment. The result is a more nuanced justification for treating pneumonia with antibiotics that that recommended by the WHO.

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Cases with a Diagnosis of Pneumonia

Case number 1

An 8-year-old boy presents with acute-onset fever and left-sided chest pain. He appears toxic and has rapid breathing. There are mild intercostal retractions but no supra- or sub-sternal retractions. There are diminished breath sounds on the left [Figure 1].

He is treated with antibiotics. One week later, his X-ray looks worse and he is still febrile [Figure 1].

Diagnosis

Pyogenic pneumonia (most commonly *Streptococcus pneumoniae*) complicated by a parapneumonic pleural effusion.

Comment

This is a typical clinical course of *S. pneumonia* exhibiting rapid onset of high fever, toxic appearance, and tachypnea, but respiration is not usually labored. There is a risk of fatality if not treated with an antibiotic to which the organism is sensitive. The fever may initially improve from the antibiotic, and the

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patient may become less toxic in appearance before return of fever and increased radiologic opacification. This indicates a parapneumonic effusion. Although a parapneumonic effusion can be associated with fever, it is generally not infected and can eventually resolve on its own. A diagnostic tap can sample the fluid and determine if there is infection. If substantial mediastinal shift with increasing respiratory distress from compression of the right lung occurs, removal of the fluid may become necessary.

Case number 2

An 8-year-old girl presents with cough, low-grade fever, malaise, and sore throat for a week. She is alert and in no major distress. Chest X-ray shows infiltrates [Figure 2].

Diagnosis

Mycoplasma pneumonia.

Comment

This is a classic example of pneumonia from *M. pneumoniae*. While this will resolve on its own, more rapid improvement may occur from use of a macrolide antibiotic.

Case number 3

A 6-year-old girl presents with worsening cough for the past 2 days. It was preceded by rhinorrhea with an initial low-grade fever 3 days ago. She is now afebrile and not toxic appearing, but she has labored breathing. She has had multiple prior similar episodes and many diagnosed as pneumonia. She has intercostal and supra- and sub-sternal retractions. She has decreased breath sounds throughout but no localizing signs [Figure 3].

Diagnosis

Viral respiratory infection-induced asthma exacerbation manifested by hyperinflation and right middle lobe atelectasis.

Comment

This is a common presentation of a young child with an asthma phenotype characterized by recurrent exacerbations of asthma initiated by a common cold viral infection, rhinovirus being the most common. Wheezing may be absent where there is severe airway obstruction. Treatment with a bronchodilator aerosol will provide some short-term relief of symptoms, but a short course of an oral corticosteroid is important to stop progression and shorten the course. Antibiotics are not indicated.

Case number 4

A 3-year-old boy presents with tachypnea and cyanosis for several weeks with gradual worsening. He is afebrile, has mild intercostal, but has no supra- or sub-sternal retractions. Pulse oximeter reads 80%, and arterial blood pCO_2 is 30 mmHg [Figure 4].

Additional history identifies pink doves (a type of pigeon) raised in the front room of his house [Figure 4].

Diagnosis

Pigeon breeder's lung disease, an allergic alveolitis.[2]

Comment

Hypoxemia without ventilatory insufficiency is characteristic of interstitial lung diseases. There are multiple antigens that can cause allergic alveolitis. Ouchterlony double gel diffusion identifies precipitins to pigeon serum antigen [Figure 4]. Treatment requires avoiding pigeon exposure. He improved slowly to normal physiology once no longer exposed to pigeons. The radial diffusing serum containing high levels of pigeon-specific antibody in the center well meets and interacts with the radial diffusing pigeon antigens. Precipitation of antigen-antibody complexes occurs that is visible in the gel. Treatment requires avoiding pigeon exposure. Continuous or repeated exposure may cause pulmonary fibrosis.

Case number 5

A healthy infant had this chest film taken during a febrile illness that subsequently self-resolved [Figure 5].

Diagnosis

A chest CT identified left upper lobe agenesis.

Comment

This is an example of pseudopneumonia. No treatment is indicated. Disability is unlikely in the absence of other abnormalities.

Case number 6

A healthy infant had this chest film taken during a period of prolonged cough that subsequently self-resolved [Figure 6].

Diagnosis

This is thymus exhibiting a classic "sail sign." Another potential pseudopneumonia.

Comment

The thymus may be a visible part of the mediastinum in infants. The radiologic shadow can vary and occasionally requires a chest CT scan to distinguish it from a pathologic mediastinal shadow. Older literature attributed the thymus as a cause of respiratory distress under the diagnostic name of "thymus status lymphaticus."[3] That diagnosis has long since been discarded.

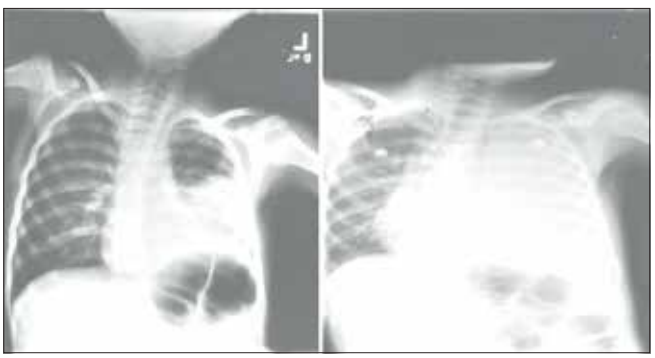

Figure 1: (left) First x-ray of Case number 1; (right) One week later.

What is "Pneumonia"?

Case number 1 is a classic bacterial pneumonia requiring urgent antibiotic treatment. A parapneumonic effusion can occur even when appropriate antibiotic treatment is provided. This child with bacterial pneumonia appeared toxic and was tachypneic. The clinical appearance of the patient justified the chest X-ray that demonstrated a consolidated left lower lobe. If measured, an elevated C-reactive protein (CRP), and procalcitonin would likely have been present.

Case number 2 is a typical clinical course of what used to be called atypical pneumonia that we know now is generally caused by Mycoplasma pneumoniae. Despite the segmental consolidation apparent on the chest X-ray, low-grade fever, and malaise, the relatively benign clinical appearance of this patient contrasts with the toxic appearance of the first case. Spontaneous improvement is typical but macrolide antibiotics may shorten the course.

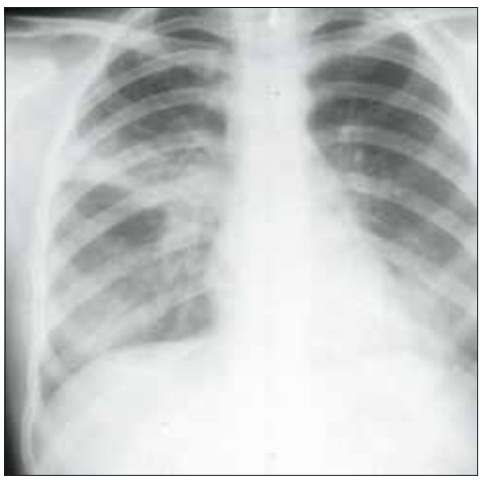

Figure 2: Chest X-ray of Case number 2.

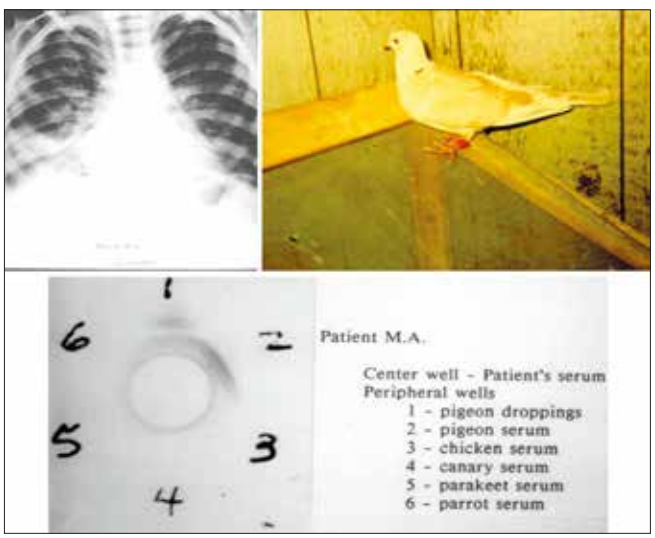

Figure 4: (upper left) Initial chest x-ray; (upper right) One of the pink doves, a type of pigeon, that were raised in the front room of their house; (lower) Ouchterlony double-gel diffusion plate with precipitin lines for pigeon droppings and pigeon serum.

Case 3 illustrates a child with recurrent episodes of increased work of breathing as manifested by suprasternal, substernal, and intercostal retractions. Those observations are consistent with airway rather than the parenchymal disease of pneumonia. Common cold viruses are the etiologic agents. In susceptible patients with this common asthma phenotype, rhinovirus and other common cold viruses cause inflammation of the airways resulting in airway narrowing from mucosal edema, excess mucous secretions, and bronchial smooth muscle constriction. The resulting airway obstruction causes increased work of breathing and expiratory wheezing. The inflammation typically does not involve the lung parenchyma, so a diagnosis of pneumonia is not appropriate. Opacities seen on chest X-ray are most likely from atelectasis resulting from mucous plugging of an airway. The lingula and right middle lobe are most commonly affected. The opacities from atelectasis are frequently misdiagnosed as pneumonia, but the clinical history and symptoms are consistent with airway, not parenchymal, disease from a respiratory viral illness.

Case 4 is an example of an interstitial lung disease. There are many causes of interstitial lung disease. The evidence

Figure 3: Chest X-ray of Case number 3.

Figure 5: Ches X-ray of Case number 5.

Figure 6: Chest X-ray of Case number 6.

Table 1: Pseudopneumonia areas of opacification on a chest film from consolidation not from inflammation of the lung parenchyma may result in misdiagnosis as pneumonia

Thymus	Atelectasis
Pulmonary sequestration	Pulmonary hemosiderosis
Bronchogenic cysts	Neoplastic disease
Lung agenesis	Congenital cystic adenomatoid malformation
Asthma	Congenital pulmonary airway malformation

Table 2: Descriptive terminology for pneumonia

By location	Epidemiological
Bronchopneumonia	Congenital
Lobar	Nosocomial
Segmental	Community acquired
Interstitial	Hospital acquired

While these diagnoses may have implications regarding the etiology, they lack the specific etiology that provides the best option for treatment

Table 3: Specific etiologic causes of pneumonia

Infections	Aspiration
viral	foreign body
bacterial	chronic aspiration
mycoplasma	acute hydrocarbon aspiration
chlamydia	
rickettsia	Hypersensitivity
fungal	allergic bronchopulmonary aspergillosis
protozoan	allergic alveolitis
spirochetal	

of precipitating antibody to an allergen that corresponds to environmental exposure identified an allergic mechansim as the cause of the parenchymal lung inflammation. The pneumonia in this case is known as allergic alveolitis from exposure to pigeon antigen.

Cases 5 and 6 illustrate opacities unrelated to any disease process that may initially be misdiagnosed as pneumonia based on a chest X-ray taken during an incidental illness. There are several of these radiologic observations that may initially be read as pneumonia [Table 1].

These cases illustrate that an opacity on a chest-ray cannot, by itself, make a diagnosis of pneumonia, nor can it identify the etiology of pneumonia if present. The inflammatory process that results in pneumonia may be from infectious agents or immunological reactions. The infectious agents may be viral, fungal, or bacterial infection. A treatment decision therefore ideally requires an etiologic diagnosis. The reality facing the clinician who encounters a suspected pneumonia is that there are many pneumonias. In addition to acute pneumonias there are chronic pneumonias, and pneumonias not caused by an infectious agent. Pneumonias are sometimes described in terms of anatomical location or epidemiological characteristics [Table 2]. While that descriptive term may have some utility in suspecting etiology, a specific etiology is more useful for providing the most specific treatment [Table 3].

What Causes Pneumonia?

A common diagnosis is "community-acquired pneumonia." That is defined as an acute infection of the pulmonary parenchyma in a patient who has acquired the infection in the community. For children, this essentially includes any previously healthy child where a diagnosis of pneumonia is made. A comprehensive assessment of the etiology of children with community-acquired pneumonia requiring hospitalization was performed at three hospitals in different major U.S. cities.[4] A viral or bacterial pathogen was identified in 81% of 2222 children with radiographic evidence of pneumonia. The radiographic evidence varied. Descriptions included the presence of consolidation (58%), linear and patchy alveolar or interstitial densities (51%), or pleural effusion (13%). Forty-five percent of the children were <2 years of age and 25% were of ages 2–4 years. Interestingly, 33% had asthma or asthma-like symptoms (Case number 3). At all ages, viral pathogens were identified as the major etiology associated with pneumonia in those children [Figure 7].

Respiratory syncytial virus (RSV) was the most common isolate in children <4 years of age and continued to be identified in older children. Human rhinovirus was the second most common isolate, only somewhat less frequent than RSV in children under 4 years of age. Rhinovirus was the most common isolate in the 5–9-year-old group and second in frequency only to *M. pneumoniae* in those 10–17 years old. *M. pneumoniae* became an increasing etiology of pneumonia with age. *S. pneumonia*, the most serious etiology, made up a small fraction of pneumonia at all ages.

Diagnosing Pneumonia

The diagnosis of pneumonia is commonly made or confirmed radiologically. While consolidation can certainly be seen

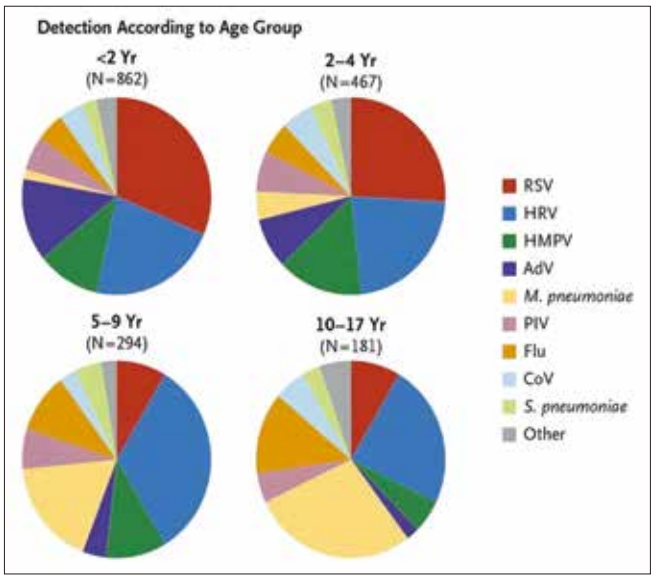

Figure 7: The proportion of pathogens for each age group. RSV: Respiratory syncytial virus; HRV: Human rhinovirus; HMPV: Human metapneumovirus; ADV: Adenovirus; *M. pneumonia*: *Mycoplasma pneumoniae*; PIV: Parainfluenza virus; Flu: Influenza A or B virus; CoV: Corona virus; *S. pneumonia*: *Streptococcus pneumoniae*.[3] Reproduced with permission from Jain S *et al*. N Engl J Med 2015;372:835-845.

radiologically, the best radiograms with the best radiologists can not identify inflammatory cells in the lung parenchyma, nor can the various etiologic agents be distinguished. A chest X-ray is essentially a shadowgram. Areas of localized atelectasis and anatomical anomalies may all result in opacities that could be misinterpreted as a pneumonic infiltrate [Table 1].

Moreover, there is a degree of subjectivity involved in the interpretation of chest X-rays. In an evaluation of the World Health Organization criteria for diagnosing pneumonia from a radiograph, this subjectivity was apparent in the lack of uniformity in interpretation, particularly for patchy and perihilar changes.[5,6] It is among children under age 6, the age with the highest frequency of pneumonia diagnoses, that the radiologic interpretation is most likely to suffer from such variability in interpretation. A critical commentary on chest radiographs for childhood pneumonia agreed that a negative chest film, i.e., the absence of consolidation, excludes pneumonia, but the presence of areas of consolidation alone should not dictate treatment.[7]

Over-diagnosing of pneumonia is common, especially among children under age 6. At a university hospital outpatient clinic in Turkey, 126 children diagnosed as pneumonia and prescribed antibiotics were subsequently reevaluated in a Pediatric Chest Disease Department of the same hospital.[8] That reevaluation determined that the diagnosis of pneumonia was not supported in 40% of the patients, and antibiotics were judged to be unnecessary in 85%. An observational study at four hospitals in India of 516 children under 5 years of age found that 43% had what was called "wheezy disease" consistent with asthma or bronchiolitis, neither of which requires antibiotics.[9]

Because of the history of a high fatality rate from pneumonia in less developed countries, especially before *S. pneumonia* and *Haemophilus influnenzae* immunizations, the World Health Organization guidelines had recommended empirical treatment with antibiotics, based on the clinical presentation.[10] A placebo-controlled clinical trial of amoxicillin in children who met the criteria for that guideline was performed in 1126 Malawian children <6 years old.[11] Treatment failures were 4% and 7% in the amoxicillin and placebo group, respectively. No treatment failures by day 4 occurred in over 90% of the children, and there were no differences in the frequency of treatment failures or relapses by day 14 in those without treatment failures by day 4. Thus, most of the patients improved without antibiotics.[12] This was consistent with the relative infrequency of bacteria as a cause of pneumonia seen in the U.S., Turkey, and India.[4,8,9]

How to Determine Who to Treat

The question is not whether the child has pneumonia, as defined by radiologic imaging, but does the child have pneumonia due to bacterial infection. To identify those with bacterial pneumonia from the majority with viral etiology, efforts have been made to examine the value of biomarkers, white blood cell count and differential, C-reactive protein (CRP), and procalcitonin. Of those inflammatory markers, CRP values are significantly higher in the presence of bacterial infection, but some degree of overlap has been seen.[13] There is general agreement that procalcitonin is the most useful biomarker for identifying those with bacterial infection.[14]

Antibiotics therefore should be considered primarily after careful clinical assessment of how sick the child appears, the presence of fever, an elevated CRP, an elevated procalcitonin, and a radiologic image of a distinct lobar or lobular infiltrate. Fever and a toxic appearance may be the exception where antibiotics are appropriate without further initial assessment. While there also may be cases where the clinical and laboratory data are equivocal, the great majority of what has been called pneumonia does not justify more than supportive treatment without the use of antibiotics.

Summary

Pneumonia is a generic term for inflammation of the lung parenchyma with consolidation. Pneumonia may be acute or chronic, from various types of infectious or noninfectious causes or inflammation. Various respiratory diseases or abnormalities can be misdiagnosed as pneumonia. Few common acute pneumonias of children have bacterial infection. Overuse of antibiotics for "pneumonia" results from inadequate diagnostic consideration before a treatment decision. Identifying those patients with bacterial etiology of pneumonia is important because of the morbidity and occasional fatality that can occur from pyogenic bacterial pneumonia. A combination of clinical assessment, laboratory obtained biomarkers, and radiology can generally distinguish

pneumonia with bacterial infection requiring antibiotic treatment from the majority that are viral and not likely to benefit from antibiotics.

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Conflicts of interest

There are no conflicts of interest.

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Clinical Outcomes of Critically Ill Infants Requiring Interhospital Transport to a Paediatric Tertiary Centre in Hong Kong

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Abstract

Background: Specialised transport teams are associated with fewer complications during interhospital transport. Such teams are currently unavailable in Hong Kong. The aim of this study was to review the clinical outcomes of critically ill infants requiring interhospital transport in Hong Kong. **Methods:** We retrospectively reviewed the characteristics and clinical outcomes of all infants transported from the neonatal units of regional or private hospitals into the neonatal or cardiac intensive care unit (ICU) of Queen Mary Hospital, a tertiary-wide academic centre in Hong Kong from 1st August 2013 to 31st July 2016. **Results:** A total of 256 infants with a mean gestational age of 31.7 ± 5.5 weeks and birth weight of 1732 ± 1007 g were included in the study. While 143 (55.9%) patients were intubated during transport, there was no documentation of close monitoring of physiological parameters for 91.4% of the patients. Close to half of the patients (44.1%) had complications on admission and 23.4% required significant interventions immediately after the transfer. The median length of stay in the ICU was 3.3 (range: 0.5–342.6) days. Five patients died of non-transport-related causes within 7 days of admission. Multiple logistic regression analysis showed that intubated patient ($P = 0.001$) or patient requiring inotropic support during transport ($P = 0.027$) were more likely to develop complications. Higher birth weight ($P = 0.022$) and younger chronological age at transfer ($P = 0.030$) were also significant risk factors for complications. **Conclusions:** Complications and interventions are considerable during interhospital neonatal transport in Hong Kong. The complication rate was higher than medical infrastructures that provided a specialised team for this process. Documentation during transport was inadequate.

Keywords: Complications, interhospital transport, morbidity, neonatal intensive care, paediatrics, patient outcome assessment

Introduction

Care of critically ill children during transport is important yet often overlooked. Based on international experiences and data, the involvement of a specialised paediatric transport team is strongly correlated with fewer adverse events,[1-3] and patients were less likely to deteriorate in clinical conditions during the transport.[2,4] Conversely, mortality rates are higher among patients transported by non-specialised teams.[5] In most developed countries, the health-care infrastructure includes a dedicated specialised service to transport patients between points of care.

Hong Kong is one of the most densely populated places in the world, with a population of 7.24 million.[6] The public health-care system provides 90% of total hospital bed-days.[7] There are 13 paediatric departments in the public health-care system and interhospital transport of paediatric patients takes place on a daily basis. At present, patient care during transport usually rests with the referring hospital. Although there are local guidelines for interhospital transport of adult patients, there is currently no legislation, Paediatric College recommendations or Hospital Authority guidelines or recommendations on the training or qualifications of doctors responsible for the escort of critically ill children. In 1984, a local study showed that hypothermia, acidaemia, hypercapnia, hypoxaemia, central cyanosis and circulatory failure were common complications after transport of preterm infants.[8] In 1998, an audit of the transport of paediatric cardiac patients in Hong Kong showed that retrieval of such

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patients by a dedicated team can prevent significant acidosis and hypothermia for ventilated patients.[9]

To date, a dedicated paediatric transport team in Hong Kong is still under development. A specialised transport team equipped with proper training, equipment and accreditation may improve the standard of care and patient outcomes. The availability of the team might also expand treatment opportunities for critically ill patients requiring high-frequency ventilation, nitric oxide or extracorporeal membrane oxygenation support, who are currently deemed unsafe for transport under our current health-care system setting.

The primary objective of this study was to review the clinical outcomes of critically ill infants requiring interhospital transport without any specialised paediatric transport team in Hong Kong. The outcome variables and measures were complications, length of stay and early mortality. The secondary objective was to analyse the associated patient characteristics and potential factors that may affect these outcomes.

Methods

Study design

This is a retrospective observational study of infants transported from regional or private hospital's neonatal unit to intensive care units (ICUs) at Queen Mary Hospital (QMH) over a 3-year period. This study was approved by the Institutional Review Board of the University of Hong Kong/Hospital Authority West Cluster (Reference number: UW 16-499).

Data collection and outcome measures

Records of infants transported into QMH from regional or private hospital's neonatal unit between 1st August 2013 and 31st July 2016 were captured by our hospital database (Clinical Data Analysis and Reporting System) and verified by handwritten admission records. Those transported into the ICU were included as study participants while those admitted into other paediatric wards were excluded. Relevant data were extracted and inputted into a standardised template for data analysis.

Patient characteristics included gender, birth weight, mode of delivery, Apgar scores at 5 min, gestational age at birth, chronological age and weight on the day of transport. Patients were marked as small for gestational age (SGA) if their birth weights were <10th percentile according to the reference ranges for Chinese newborns.[10] Patients were categorised as extreme preterm if they were born before 28 weeks of gestation, very preterm if they were born at 28 to <32 weeks of gestation, mild preterm if they were born at 32 to <37 weeks of gestation and term if they were born ≥37 weeks of gestation.[11,12]

The names of the referring hospital, indications for transport, type of transport (emergency or elective) and mode of transport were collected. The duration of interhospital transport was calculated as the time between the discharge time from the referring hospital and the admission time at QMH as recorded in the Hospital Authority's computerised record system (clinical management system). Since similar data were not available from private hospitals, only transports between Hospital Authority hospitals were included in the analysis involving transport duration. The interhospital transport distance was the ground travel distances estimated from the Google Map application. The intensive care support that the patients received during transport (mode of respiratory support, inotropic support, prostaglandin infusion and sedation if any), the type of access (arterial access, central access) and details of patient monitoring and conditions during transport were also retrieved. The patient was considered to have documentation of close monitoring if the 'Hospital Authority Neonatal Emergency Transport Observation Chart' during transport or equivalent documentation was used with documentation of at least one set of vital signs. The standardisation of 'Hospital Authority Neonatal Emergency Transport Observation Chart' was implemented from 2015, but there are no guidelines on when to use the form and it is not mandatory to fill in all parameters or utilise the form. In general, it is used by the Hospital Authority Neonatal ICUs during the interhospital transfer of critically ill patients. There is no standardisation of transport documentation form among the private hospitals. The transport record was considered as equivalent if it was intended to document the patient demographics, details of interhospital transport and vital signs during transport. All the medical record was reviewed by the principal investigator based on the criteria defined. The types of surgical operation received by the patients after admission were also included.

Pre-transport and post-transport physiological parameters and significant interventions required during and within 1 h after transport were analysed. Pre-transport physiological parameters taken in the referring hospital closest to the time of transport was captured. Post-transport physiological parameters were extracted from the first set of recorded information within 1 h of admission to the ICU.

For the ease of reference, adverse events and interventions associated with interhospital transport are categorised and defined in Table 1.

The length of stay in the ICU and total hospital stay (including the referring hospital) were also analysed. Early mortality was defined as death within 7 days of admission. The causes of death were reviewed.

Statistical analysis

Results are presented as frequencies, means or medians as appropriate. Fisher's exact test was used to compare categorical variables. All continuous variables were tested for normal distribution. Unpaired *t*-test and one-way analysis of variance were used to compare continuous variables with a normal distribution. Skewed data were transformed by $\log_{10}$ base before comparison and non-parametric methods. The Mann–Whitney U-test or Kruskal–Wallis test was used for analysis. Univariate

Table 1: Definitions of adverse events and interventions associated with transport

Variables	Definitions
Significant changes in physiological parameters	
Significant decrease in oxygen saturation	Post-transport SpO_2 ≤85% and decrease ≥10% from pre-transport SpO_2
Significant decrease in blood pressure	Post-transport SBP <10th centile from literature reference and decrease >10% from pre-transport SBP [13,14]
Significant decrease in heart rate	Post-transport heart rate <60 bpm and decrease ≥30% from pre-transport heart rate [14]
Significant increase in heart rate	Post-transport heart rate >180 bpm and increase ≥30% from pre-transport heart rate
Significant decrease in temperature	Post-transport temperature ≤35.6oC and decrease of >2oC from pre-transport temperature [14, 15]
Complications upon arrival	
Critical complications	
Severe hypoxia	SpO_2 ≤65% [16]
Endotracheal tube obstruction	Endotracheal tube obstruction [2,14]
Hypotension	Systolic blood pressure ≤40mmHg [17]
Bradycardia	Heart rate <60 bpm [18]
Critical hypoglycaemia	Capillary blood glucose <2 mmol/L
Severe acidosis	Arterial pH <7.00 and more acidotic compared to baseline post transport [19]
Severe alkalosis	Arterial pH >7.55 and more alkalotic compared to baseline post transport [19]
Serious complications	
Desaturation	Preterm infants - SpO_2 66-84%[20]
	Term infants - SpO_2 66-95%[20]
	Cyanotic heart disease infants - SpO_2 66-74% [20]
Hyperventilation	Arterial pCO_2 <3.4kPa [21]
Hypothermia	Rectal temperature <36.5°C[15]
	Axillary temperature <35.6°C[15]
	Tympanic temperature <35.7°C [15]
Mild hypoglycaemia	Capillary blood glucose 2.0-3.3 mmol/L [22, 23]
Mild acidosis	Arterial pH 7.00-7.28 and more acidotic compared to baseline post transport [19]
Mild alkalosis	Arterial pH 7.48-7.55 and more alkalotic compared to baseline post transport [19]
Loss of venous access	Loss of venous access
Equipment failure	Equipment failure
Significant interventions during transport or within one hour of admission	
Respiratory interventions during transport	Manual bagging
Respiratory interventions after arrival	Step up of respiratory support
	Breathing in room air/oxygen to requirement of mechanical ventilation
	From non-invasive ventilation to invasive ventilation
	Requirement of the change of endotracheal tube
Cardiovascular interventions after arrival	Requirement of fluid resuscitation
	Commencement of inotropic support
Correction of hypoglycaemia	Correction of hypoglycaemia
Re-establishment of intravenous access	Re-establishment of intravenous access

SpO_2=pulse oximetry, SBP=systolic blood pressure, bpm=beats per minute

statistical analysis was carried out to test for associations between the transport condition and complications. A probability value (*P* value) of <0.05 with two sides was considered statistically significant. Significant variables in the univariate analysis were included in a multiple logistic regression analysis to verify an independent association. These results were reported as odds ratio with 95% confidence intervals. Analyses were performed using the SPSS® version 24 (IBM Corp, IBM SPSS Statistics for Macintosh, Armonk, NY: USA).

Results

During the study, 256 infants were transported from neonatal units of regional or private hospitals to QMH ICUs. Their characteristics are summarised in Table 2. There were slightly more male infants (*n* = 141) than female infants (*n* = 115). The mean birth weight was 1732 ± 1007 g. Forty-five infants were born small for the gestation of age. Patients were divided into four groups according to their gestational age. The two main groups of patients being transported were extreme preterm (*n* = 92, 35.9%) and term infants (*n* = 69, 27.0%). The

Table 2: Patient characteristics and relevant details of transport

Variables	Number of transfers (*n*=256)
Gender	
Female	115 (44.9%)
Male	141 (55.1%)
Birth weight (gram), mean±SD	1732±1007
Small for gestational age	45 (17.6%)
Caesarean section	128 (50.0%)
Apgar <7 at 5 min	39 (15.2%)
Gestational age at birth (week), mean±SD*	31.7±5.5
Extreme preterm<28, *n*=92	25.8±1.1
Very preterm 28 - <32, *n*=45	29.8±1.3
Mild preterm 32 - <37, *n*=50	34.4±1.4
Term ≥37, *n*=69	38.8±1.1
Age at transport (day), median (range)*	13.1 (0.4-150.6)
Extreme preterm<28, *n*=92	29.1 (0.8-150.6)
Very preterm 28 - <32, *n*=45	17.5 (0.4-81.5)
Mild preterm 32 - <37, *n*=50	4.8 (0.4-97.5)
Term ≥37, *n*=69	2.5 (0.4-71.5)
Weight at transport (gram), mean±SD	1898±945
Indication for transport	
Cardiac assessment/management	117 (45.7%)
Surgical assessment/management	72 (28.1%)
Respiratory support and management	41 (16.0%)
Other secondary level neonatal care	18 (7.0%)
Ophthalmology assessment	5 (2.0%)
Bed status issue from other HA hospitals	3 (1.2%)
Emergency transport	145 (56.6%)
Hospital Authority Hospital	182 (71.1%)
Transport duration (minute)†, mean±SD	47.2±15.2
Transport distance (kilometre), median (range)	10.7 (5.1-731.4)
Support during transport	§179 (69.9%)
Invasive ventilation	143 (55.9%)
Non-invasive ventilation	32 (12.5%)
Inotropic support	37 (14.5%)
Sedation	26 (10.2%)
Prostaglandin infusion	9 (3.5%)
Central line	119 (46.5%)
Arterial line	131 (51.2%)
Monitoring during transport	22 (8.6%)
Escorted by doctors‡	126 (88.7%)

*Statistically significant differences between sub-groups, $P<0.001$. †Data were only available for the 182 transfers from Hospital Authority Hospitals. ‡ Data were only available for 142 transfers. §Number of support each patient required - 117 required 1, 56 required 2, 6 required 3. Data are number (%), unless otherwise indicated.. SD=standard deviation, HA=Hospital Authority

group of extremely preterm infants were transported at an older chronological age with a median of 29.1 (range 0.8–150.6) days, whereas term infants were transported at a younger chronological age with a median of 2.5 (range 0.4–71.5) days ($P < 0.001$).

The indications for transport were for higher levels of cardiac (*n* = 117, 45.7%), surgical (*n* = 72, 28.1%) and respiratory (*n* = 41, 16.0%) care. The remaining reasons for transport were for ophthalmological assessment, severe sepsis, seizure, hypoglycaemia requiring central venous access, perinatal depression or those requiring therapeutic hypothermia and bed status issues. The majority of the cardiac surgery required was patent ductus arteriosus ligation (*n* = 97), followed by the management of cyanotic heart disease (*n* = 6) and extracorporeal membrane oxygenation (*n* = 3). The most common indications for non-cardiac surgery were necrotising enterocolitis (*n* = 21) and malrotation (*n* = 5).

Over half of cases (*n* = 145, 56.6%) were emergency transports. Most of the transports (*n* = 182, 71.1%) were from Hospital Authority Hospitals. The majority of transports (*n* = 248, 96.9%) were ground transport by ambulance, whereas the rest involved a combination of ambulance and ferry. The mean transport time was 47.2 ± 15.2 min, and the median transport distance was 10.7 (range 5.1–731.4) km.

Evidence of close monitoring of physiological parameters during transport were found in 22 (8.6%) transports. For the 142 transports that recorded details of the transport personnel involved, 126 (88.7%) were escorted by doctors. Nearly 70% (*n* = 179) of patients were critically ill during transport; 143 (55.9%) required invasive mechanical ventilation, 32 (12.5%) required non-invasive ventilation support, 37 (14.5%) required inotropic support, 26 (10.2%) were under sedation and 9 (3.5%) required continuous prostaglandin infusion. Other transport details are summarised in Table 2.

A total of 154 complications were documented in 113 (44.1%) patients with 33 patients affected by >1 complication. The types and numbers of complications immediately after transport are shown in Table 3. The majority (*n* = 49) of complications involved the respiratory system, including desaturation (*n* = 27), hyperventilation (*n* = 12), severe hypoxia (*n* = 9) and endotracheal tube obstruction (*n* = 1). Other complications were hypothermia (*n* = 30), hypoglycaemia (*n* = 29) and acidosis (*n* = 17).

Fifty-nine patients (23%) required significant interventions during transport or within 1 h of admission. There was a total of 68 interventions, and 9/59 patients (15%) required two interventions. The majority (*n* = 41) were respiratory interventions, including manual bagging (*n* = 7), step up of respiratory support (*n* = 33) and change of endotracheal tube (*n* = 1). Other types and number of interventions are summarised in Table 4.

Complete sets of all four physiological parameters (pulse oximetry [SpO_2], (systolic blood pressure (SBP), heart rate and temperature) before and after transport were available for 47 patients. Individual physiological parameters before and after transport were available for another 85 patients for SpO_2, 23 patients for temperature, 22 patients for SBP and 44 patients for heart rate. Using these available data sets, there were 24 significant changes in physiological parameters affecting

Table 3: Type and number of critical and serious complications upon admission

Types of complications	Severity of complication	Number of complications/Total number of cases with the available monitoring or intervention (%)
Desaturation	Serious	27/256 (10.5%)
Severe hypoxia (SpO_2 ≤65%)	Critical	9/256 (3.5%)
Endotracheal tube obstruction	Critical	1/143 (0.7%)
Bradycardia (Heart rate <60)	Critical	1/256 (0.4%)
Hypotension (Systolic BP ≤40mmHg)	Critical	14/256 (5.5%)
Hypothermia	Serious	30/256 (11.7%)
Mild hypoglycaemia (D'stix 2-3.3 mmol/L)	Serious	25/243 (10.3%)
Critical hypoglycaemia (D'stix <2 mmol/L)	Critical	4/243 (1.6%)
Mild acidosis (Arterial pH 7.00-7.28)*	Serious	16/77 (20.2%)
Severe acidosis (Arterial pH<7.00)*	Critical	1/77 (1.3%)
Mild alkalosis (Arterial pH 7.48-7.55)†	Serious	4/77 (5.2%)
Severe alkalosis (Arterial pH>7.55)†	Critical	2/77 (2.6%)
Hyperventilation (Arterial pCO_2<3.4 kPa)	Serious	12/164 (7.3%)
Loss of venous access	Serious	7/250 (2.8%)
Other equipment failure	Serious	1/256 (0.4%)

*77 patients had pre and post transport arterial blood gas. More acidotic compared to baseline. †77 patients had pre and post transport arterial blood gas. More alkalotic compared to baseline. ‡113 patients out of 256 patients (44.1%) had complications - 14 patient had critical complications only, 84 patient had serious complications only, 15 patient had both critical and serious complications

Table 4: Significant interventions during transport or within one hour of admission

Variables	Number of interventions/Total number of potential cases requiring interventions (%)
Respiratory interventions during transport	
Perform manual bagging	7/256 (2.7%)
Respiratory interventions after transport	
Step up of respiratory support	33/256 (12.9%)
Requirement of change of endotracheal tube	1/143 (0.7%)
Cardiovascular interventions after transport	
Requirement of fluid resuscitation	3/256 (1.2%)
Commencement of inotropic support	3/256 (1.2%)
Correction of hypoglycaemia	14/256 (5.5%)
Re-establishment of intravenous access	7/250 (2.8%)

* 59 of 256 patients (23%) had significant interventions - 59 patients had 1, 9 patients had 2

20 patients. The majority of changes involved the respiratory system (n = 15). Other significant changes were significant decrease in temperature (n = 4), significant decrease in blood pressure (n = 2), significant increase (n = 2) and significant decrease (n = 1) in heart rate.

Patients were more likely to develop complications if they have high birth weight (P = 0.020), transported at younger chronological age (P < 0.001), intubated during transport (P = 0.015) or required inotropic support during transport (P = 0.007). After adjustment using multiple logistic regression, all of these risk factors remained as signification risk factors for complications. There were no statistically significant associations between complications and gender, gestational age at birth, SGA, weight at transport, transport distance, type of referring hospital, type of transport, type of referral and if there were monitoring during transport. These details are summarised in Table 5.

The median length of ICU stay was 3.3 (range: 0.5–342.6) days and total hospital stay was 87.0 (range 2.0–885.0) days. There were five non-transport-related deaths within 7 days of admission. The causes of death were post-operative arrest (n = 2) and withdrawal of care (n = 3).

Discussion

In Hong Kong, interhospital transport of critically ill paediatric patients is common. A previous retrospective 7-year review of neonatal transport across Paediatric Departments under the Hospital Authority in Hong Kong showed that there was an average of 255 transports per year.[24] Our centre is a major tertiary academic referral centre for neurosurgery, paediatric surgery, burn, liver transplant, oncology and bone marrow transplant. It is also the only cardiology centre which can provide extracorporeal membrane oxygenation support and cardiothoracic surgery. We receive referrals from all public and private hospitals in Hong Kong, as well as from Macau and the Chinese Mainland near our locality. The result from this study may provide important information for future health-care

Table 5: Univariate analysis and multiple logistic regression analysis of risk factors for patients with complications

Variable	Univariate analysis		OR (95% CI)	*p*	Multiple logistic regression	
	Patient with complications				Adjusted OR (95% CI)	*p*
	Yes	No				
Gender						
Male, *n* (%)	69 (49.3)	71 (50.7)	1.59 (0.96 - 2.62)	0.077	NT	-
Female, *n* (%)	44 (37.9)	72 (62.1)				
Gestational age at birth (week), mean±SD	32.31±5.93	31.16±5.00	1.04 (1.00 - 1.09)	0.098	NT	-
Birth weight (gram), mean±SD	1899±1073	1599±935	1 (1.00 - 1.00)	0.020*	1.00 (1.00 - 1.00)	0.022*
Small for gestational age						
Yes, *n* (%)	14 (31.1)	31 (68.9)	0.51 (0.26 - 1.02)	0.068	NT	-
No, *n* (%)	99 (46.9)	112 (53.1)				
Age at transport (Log day), mean±SD	0.81±0.62	1.08±0.62	0.50 (0.34 - 0.75)	<0.001*	0.03 (0.96 - 1.00)	0.030*
Weight at transport (gram), mean±SD	2016±981	1806±908	1.00 (1.00 - 1.00)	0.080	NT	-
Transport distance (Log kilometre), mean±SD	1.45±0.23	1.19±0.25	0.49 (0.17 - 1.43)	0.238	NT	-
Transport from Hospital Authority Hospitals						
Yes, *n* (%)	80 (43.2)	105 (56.8)	0.88 (0.51 - 1.52)	0.675	NT	-
No, *n* (%)	33 (46.5)	38 (53.5)				
Intubated during transport						
Yes, *n* (%)	73 (51.0)	70 (49.0)	1.92 (1.15 - 3.21)	0.015*	3.02 (1.55 - 5.86)	0.001*
No, *n* (%)	38 (35.2)	70 (64.8)				
Inotropic support during transport						
Yes, *n* (%)	24 (64.9)	13 (35.1)	2.70 (1.30 - 5.58)	0.007*	2.51 (1.11 - 5.67)	0.027*
No, *n* (%)	89 (40.6)	130 (59.4)				
Emergency transport						
Yes, *n* (%)	70 (48.3)	75 (51.7)	1.55 (0.93 - 2.57)	0.098	NT	-
No, *n* (%)	41 (37.6)	68 (62.4)				
Referral for surgical management						
Yes, *n* (%)	80 (41.5)	113 (58.5)	0.64 (0.36 - 1.14)	0.145	NT	-
No, *n* (%)	33 (52.4)	30 (47.6)				
Monitoring during transport						
Yes, *n* (%)	10 (45.5)	12 (54.5)	1.06 (0.44 - 2.55)	1.000	NT	-
No, *n* (%)	103 (44.0)	131 (56.0)				

*p<0.05 - statistically significant values; SD=Standard deviation, OR=Odds ratio, CI=Confidence interval, NT=Not tested

Table 6: Comparison of complication rates of our study with previous study in our centre in 1984 and complication rates reported by specialised transport team in the literatures

Complications	Fok and Lau, 1984 [10]	Our study	Specialised transport team
Hypothermia	26.3%	11.7%	0 - 0.3% [4,14]
Acidaemia	24%	16.8%	-
Hypercapnia	23.4%	-	-
Hypoxaemia/Desaturation	23.4%	10.5%	0.5 - 1.8% [4,14]
Central cyanosis/ Significant desaturation	18.7%	3.5%	0% [12]
Circulatory failure/ Hypotension	11.7%	5.4%	0.2% - 6.3% [4,14]

planning and reference data for other countries where specialised paediatric transport services are lacking.

During the defined 3-year study, we received an average of 85 critically ill infants per year. The paediatric service model in Hong Kong is currently being reorganised and the tertiary paediatric services has commenced relocation to the Hong Kong Children's Hospital (HKCH). After the centralisation of tertiary paediatric services to the HKCH, interhospital transports are expected to be more frequent.

The median transport distance of 10.7 (range: 5.1–731.4) km from this study was relatively short compared to other health-care systems (22.2–47.8 km),[2,4,25] the mean transport duration was similar (47.2 ± 15.2 vs. 30–113 min).[2,4,5,14,26] The heavy traffic in urban Hong Kong is the most likely reason for the longer transport period. A majority (~70%) of the transported patients were critically ill, but there was no evidence of close monitoring of physiological parameters for 91.4% of the patients in this study. This could reflect that the importance of documentation was still underestimated or the escort team was not specialised in transport. Standardised record should be maintained so that events are available for review by the receiving hospital.

Complications occurred for close to half (44.1%) of the transports. Although this local complication rate seems much higher than transport carried out by specialised transport

teams elsewhere in the world (1%–4%),[2,3,5] it was lower than the figure in transport conducted without a specialised team (61%–75%).[1,2,5,8] It is difficult to draw comparison across studies to explain this lower rate of complication. Some explanations may include the possibilities that our cohort consisted of more stable patients or more experienced staff, even though they were not specialised in transport *per se*.

The majority (26.5%) of complications were related to the respiratory system. This rate appears to be comparable to the figures reported by non-specialised transport teams (18.4–53%),[5,14,27] but was much higher than the rate of 0.5%–1.8% observed by specialised transport teams.[5,14] Most of the interventions required during or shortly after admission were also due to airway compromise. Multiple logistic regression analysis in our study revealed that intubation was a significant risk factor for complications. There were these possible contributing factors to respiratory complications. First, there was a lack of sophisticated monitoring of end-tidal volumes and serial blood gas during transport to provide feedback that may have indicated the need for ventilator adjustments. Second, humidification of the ventilator circuit may have been suboptimal. Finally, regular suctioning could have been difficult due to environmental factors during transport, for example, motion and noise, and limited space, workforce and equipment.

Acidosis was another common complication (22.1%). Although this was lower than the rate reported in the literature by non-specialised teams (24%–50%),[8,27] our study might have underestimated the number of acidosis case as paired pre- and post-transport arterial blood gas results were only completed in 30% (77 patients) of the patient transported for analysis. Acidosis could be a result of haemodynamic or respiratory instability. Hypothermia was found in 11.7% of the patients, which appears to be comparable to the rates in the literature reported by non-specialised teams (3.8%–30%).[5,8,14,27,28] Again, it seems higher than that achieved by specialised transport teams (0%–1%).[5,14] Hypothermia could be due to changes in ambient temperature during interhospital transport, insufficient insulation of the transport incubator and suboptimal humidification inside the transport incubator. Hypoglycaemia occurred in 11.3% of the patients, higher than that (7%) reported by non-specialised transport teams.[27] This could be caused by the lack of glucose monitoring before and during transport.

When comparing our results to historical data of the same hospital in 1984, improvements were noted in complication rates after transport. These improvements could be contributed by advancement in medical equipment (e.g., transport incubators and ventilators). However, the rates of hypothermia and respiratory complications were still considerably higher than that reported by studies with specialised transport teams [Table 6]. Our study suggests that, in our locality, the lack of specialised transport teams may be associated with higher rates of complication during interhospital transports. More studies will be needed to determine whether a specialised transport team will result in better outcomes and a significant reduction in adverse events for these patients.[29]

Limitations

There are four major limitations. First, this is a single-centre study limited to inbound transport of critically ill infants for tertiary/quaternary care. Therefore, the study might have included more critically ill infants than other series. Second, this was a retrospective study. Despite efforts made to locate the missing information from referring hospitals through our Hospital Authority's computerised record, some information, especially the pre-transport physiological parameters, were not found. There were also discrepancies in the methods of measuring physiological parameters across different referring hospitals, for example temperature (rectal, axillary, tympanic and skin), blood pressure (arterial blood pressure vs. non-invasive blood pressure monitoring), glucose reading (different brands of glucometer vs. blood gas machine) and arterial blood gas (i-STAT® vs. blood gas analyser). As a result, only 18.3% of the patients had complete sets of pre-transport and post-transport physiological parameters, and most patients' condition during transport could only be deduced by analysing the post-transport physiological parameters. Third, although indications for transport and patients' diagnoses might affect the complication and mortality rate, stratified analysis was not performed as there were not enough data to retrospectively categorise the patient's disease severity with a validated scoring system, for example, 'Paediatric Risk of Mortality' score. Finally, the retrospective nature of this study did not allow the inclusion of all confounding factors in the analyses. For example, referrals were received from 19 different hospitals, and experiences of the escort personnel, monitoring skills during transport and transport equipment varied across these hospitals.

Conclusions

The study showed that complications and interventions are considerable during interhospital transport, particularly in intubated and patients requiring inotropic support. Higher birth weight and younger chronological age at transfer were also significant risk factors for complications. The complication rate was higher than medical infrastructures that provided a specialised team for this process. Documentation during transport was inadequate.

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Conflicts of interest

There are no conflicts of interest.

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Original Article

McGill Oximetry Score to Predict Risk of Obstructive Sleep Apnea in Pediatric Patients

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Abstract

Objective: The aim of this study is to investigate the use of overnight oximetry to predict high Apnea–Hypopnea Index (AHI) in Hong Kong children with habitual snoring. **Methodology:** We have retrospectively analyzed the polysomnography (PSG) of 573 patients with habitual snoring with age ranged from 6 months to 18 years old. Patients with syndromal diagnosis or neuromuscular disorders were excluded from the study. The sensitivity, specificity, positive predictive value , and negative predictive value (NPV) of oximetry to predict AHI were calculated. **Results:** McGill score >1 had high specificity 99.07% and low sensitivity 16.81% to detect AHI >1. SpO_2 nadir <95% has high sensitivity 98.56% and NPV 97.56% to predict AHI >5. **Conclusion:** The use of the McGill score together with nadir SpO_2 in overnight oximetry can help in stratifying the severity of obstructive sleep Apnea and thus prioritizing PSG testing.

Keywords: Apnea–Hypopnea Index, McGill score, obstructive sleep Apnea

Introduction

Obstructive sleep Apnea (OSA) is common in children. OSA syndrome is associated with snoring, excessive daytime sleepiness, morning headache, hyperactivity, and nocturnal enuresis. This might be complicated by learning difficulty, growth failure, and increased risk of cardiovascular events (e.g., dysregulation of blood pressure).[1,2] Polysomnography (PSG) is the gold standard to diagnose OSA. PSG is a resource-dependent investigation.[3] A screening tool to triage patients with potentially severe OSA for early PSG is, therefore, reasonable and valuable.

OSA is frequently accompanied by nocturnal desaturations.[4-6] Compared to PSG, oximetry is simple, inexpensive, and readily available in most hospitals. Brouillette *et al*. stated that in the setting of a child suspected of having OSA, positive nocturnal oximetry has at least 97% positive predictive value (PPV) to OSA, while negative oximetry cannot exclude OSA.[7] By retrospectively analyzing 349 patients, Nixon *et al*. commented that higher oximetry scores were associated with a higher Apnea–Hypopnea Index (AHI; $P < 0.001$), higher desaturation index ($P < 0.001$), lower SaO_2 nadir ($P < 0.001$), and higher respiratory arousal index ($P < 0.001$).[8] Based on these findings, he has devised the McGill oximetry score. The score has 4-level severity (McGill 1–4), based on the numbers and depth of desaturations in an overnight pulse oximetry recording. A score above one was suggested to be indicative of OSA.[8]

Objective

In this study, we aim to investigate the use of overnight oximetry to predict high AHI in Hong Kong children with habitual snoring.

Methodology

We retrospectively analyzed the PSG of Chinese patients with habitual snoring, who were being followed up in the Sleep Clinic of the Department of Paediatrics, Kwong Wah Hospital from January 2010 to December 2014. All patients aged 6 months to 18 years old who underwent PSG were included in the study. Patients with syndromal diagnosis (e.g., Down syndrome, Crouzon syndrome) or neuromuscular disorders (e.g., Duchene Muscular Dystrophy) were excluded from the study.

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The PSGs were scored by pediatricians according to 2007 and 2012 American Academy of Sleep Medicine (AASM) scoring criteria. AHI is the total number of apneas and hypopneas divided by the total sleep time in h. An apnea is defined as a drop in the peak thermal sensor excursion of ≥90% from baseline for the whole event. An obstructive apnea is scored if it meets apnea criteria for at least the duration of 2 breaths during baseline breathing and is associated with the presence of respiratory effort throughout the entire period of absent airflow. A hypopnea is identified as a drop-in nasal pressure signal by ≥30% of pre-events baseline for at least 2 breaths, in association with either ≥3% oxygen desaturation or an arousal.

In this study, we define normals as having an AHI ≤1. OSA was diagnosed when AHI >1. The severity of OSA was graded as mild (AHI 1.1–5 per h) and moderate-to-severe (AHI >5 per h). The tracing for the oximetry scoring was extracted from that used for the full PSG (model: Siesta, Compumedics). A trained nurse who was blinded to the diagnoses and PSG results was responsible for grading all of the McGill scores.

All statistical analyses were conducted using IBM SPSS Statistics for Windows, Version 22.0. (IBM Corp., Inc., Armonk, NY, USA). A value of $P < 0.05$ was taken as statistically significant. Continuous variables were presented as the mean ± standard deviation (SD). Differences in the variables between groups were analyzed using Student's *t*-test. Categorical variables were analyzed using the Chi-square test. Kruskal–Wallis statistic was used to compare ordinal variables among the four McGill score groups. *Post hoc* analysis was performed using the Mann–Whitney test with Bonferroni correction. The sensitivity, specificity, PPV, negative predictive value (NPV), and Youden's index (sensitivity + specificity − 1)[9] of oximetry to predict AHI were calculated.

This study was approved by the Research Ethics Committee of the Kowloon West Cluster of the Hospital Authority in Hong Kong (KW/EX-15-073[86-09]).

Results

Polysomnograms of 573 patients (males 419, females 154) with a mean age of 10.86 ± 4.22 years (mean ± SD, range: 0.5–17.9 years old) were analyzed. Three hundred and fifty-seven (63%) patients had AHI more than 1, in which 139 (39% of the OSA group) had AHI >5 [Table 1].

Figure 1 shows the AHIs of different McGill scores, with the number of patients in each group. There were significant differences between all groups ($P < 0.05$) except McGill score 3 and 4. Five hundred and eleven patients were scored McGill Grade 1. Among them, 214 (42%) had AHI <1. The remaining 58% comprised OSA with different degrees of severity (AHI 1.1–5 = 208, AHI >5 = 89). Figure 2 shows that SpO_2 nadir was significantly lower in patients with AHI >1 ($P < 0.0001$*).

Table 2 shows the specificity, sensitivity, PPV, and NPV of McGill scores and nadir SpO_2 to predict AHI >1. McGill score >1 had specificity 99.07%, sensitivity 16.81%, PPV 96.77%, and NPV 41.88% to detect AHI >1. McGill score ≥3 had 100% specificity and PPV to detect OSA. Table 3 shows the specificity, sensitivity, PPV, and NPV of McGill scores and nadir SpO_2 to predict AHI >5. SpO_2 nadir <95% has high sensitivity 98.56% and NPV 97.56% to predict moderate OSA.

Discussion

We are one of the pediatric sleep centers in Hong Kong receiving referrals for suspected sleep-disordered breathing.

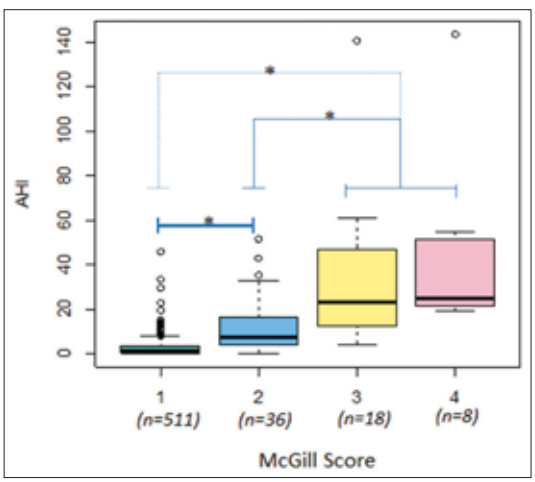

Figure 1: Apnea–Hypopnea Index of McGill scores 1–4. *Denotes significant differences among the groups ($P < 0.05$). *n*: Number of patients.

Table 1: Demographic characteristics between those Apnea-Hypopnea Index ≤1 versus Apnea-Hypopnea Index >1

Characteristic	All patients (*n*=573)	AHI ≤1 (*n*=216)	AHI >1 (*n*=357)	*P*
Age (year)	10.86±4.22	10.86±4.17	10.87±4.25	0.972
Gender, *n* (%)				
Male	419 (73.12)	148 (68.52)	271 (75.91)	0.066
Female	154 (26.88)	68 (31.48)	86 (24.09)	
Weight (kg)	44.78±24.00	42.47±21.32	46.21±25.42	0.060
Height (cm)	141.10±25.55	142.52±25.39	141.53±25.68	0.654
BMI	20.46±6.00	19.45±5.22	21.07±6.36	0.001
Nadir SpO_2	89.40±6.96	92.14±5.13	87.74±7.38	<0.001

Data are expressed as mean±SD unless otherwise indicated. SD: Standard deviation, AHI: Apnea-Hypopnea Index, BMI: Body mass index

After clinical evaluation in the sleep clinic, patients who were considered high risk for OSA would proceed to PSG. This preselection accounted for the high prevalence (62%) of OSA in our study.

Our data showed a low sensitivity 16.81% of McGill score ≥2 to predict OSA. This was lower than the sensitivity 43% from the originally validated study by Nixon *et al*.[8] Unlike us, the Nixon *et al*. group only evaluated children who were scheduled for adenotonsillectomy instead of all referrals with suspicious OSA, and they might, therefore, at higher risk.

McGill score of 1 did not imply normal PSG study and in fact, missed 58% of patients with OSA. This is not surprising as desaturation is not ubiquitous, especially in mild OSA. In the AASM definition of apnea, desaturation is not a prerequisite. Therefore, patients with McGill score 1 should still be put in the normal queue for formal PSG.

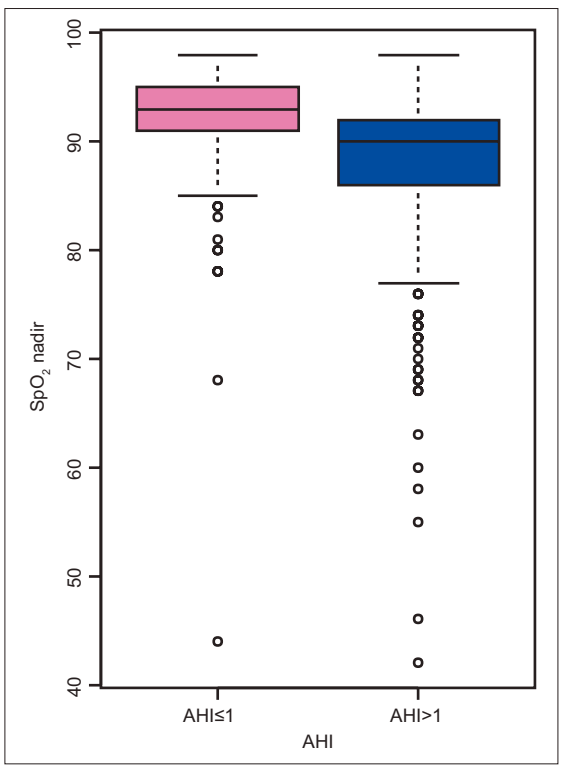

Figure 2: SpO_2 nadir between Apnea-Hypopnea Index ≤1 and Apnea-Hypopnea Index >1 ($P < 0.0001$).

In comparison, McGill score ≥2 had a high PPV of 96.77% to rule in patients with OSA. Hence, these patients are recommended to have an earlier referral for PSG. In a Cohort by Horwood *et al*.,[10] children with clinical adenotonsillar hypertrophy and preoperative McGill score ≥2 had expedited surgery without the need for further testing, and the major complication rate was found to be low. While this could be considered in resource-limited countries, we still advocate PSG in a relative resourceful place like Hong Kong before definitive surgery. It is more affirmative to perform surgery, in parents' and patient's perspective, when OSA is diagnosed based on PSG, which is the current gold-standard.

Independent of McGill score, we found that a SpO_2 nadir ≥95% excluded nearly all moderate OSA (AHI >5) with sensitivity of 98.56% and NPV 97.56%. This is one additional factor to consider when prioritizing patients in PSG queue who have the same McGill score of 1.

With PPV of 96.15%, we are confident that most of the patients with a McGill score of 3 or 4 have moderate-to-severe OSA. They should be arranged with urgent PSG to facilitate management. While awaiting PSG, immediate intervention, including positive airway pressure, should be administered.

Compared to PSG, oximetry is readily accessible in the hospital. The McGill score, together with the lowest SpO_2 is a simple way to provide a more reliable and objective triage method. In addition, reading an oximetry examination takes much shorter duration then scoring a full PSG.

There are two major limitations of this study. First, owing to a high pretest probability, our results and recommendations are only applicable to specialized centers with high-risk OSA cases. Second, this study is not applicable to patients with syndromes and neuromuscular disorders because their nocturnal desaturations might be secondary to central instead of obstructive apnea, which is indistinguishable in oximetry. Figure 3 shows the proposition of the use of oximetry in prioritizing a long PSG queue.

Table 2: Different cutoffs of McGill scores and nadir SpO_2 to predict Apnea-Hypopnea Index >1

	AHI >1				
	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Youden index (%)
McGill 4	2.24	100.00	100.00	38.23	0.02
McGill 3+4	7.28	100.00	100.00	38.92	0.07
McGill 2+3+4	16.81	99.07	96.77	41.88	0.16
Nadir SpO_2 <90%	47.62	87.96	86.73	50.40	0.36
Nadir SpO_2 <91%	54.06	81.94	83.19	51.91	0.36
Nadir SpO_2 <92%	66.95	65.74	76.36	54.62	0.33
Nadir SpO_2 <93%	77.87	55.56	74.33	60.30	0.33
Nadir SpO_2 <94%	84.87	43.52	71.29	63.51	0.28
Nadir SpO_2 <95%	94.40	28.70	68.64	75.61	0.23

PPV: Positive predictive value, NPV: Negative predictive value, AHI: Apnea-Hypopnea Index

Table 3: Different cutoffs of McGill scores and nadir SpO_2 to predict Apnea-Hypopnea Index >5

	AHI >5				
	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Youden index (%)
McGill 4	5.76	100.00	100.00	76.81	0.06
McGill 3+4	17.99	99.77	96.15	79.16	0.18
McGill 2+3+4	35.97	97.24	80.65	82.58	0.33
Nadir SpO_2 <90%	69.78	77.19	49.49	88.86	0.47
Nadir SpO_2 <91%	74.82	70.51	81.25	89.74	0.45
Nadir SpO_2 <92%	84.89	55.07	60.51	91.92	0.40
Nadir SpO_2 <93%	89.93	42.63	50.20	92.96	0.33
Nadir SpO_2 <94%	93.53	32.03	44.07	93.92	0.26
Nadir SpO_2 <95%	98.56	18.4	38.70	97.56	0.17

PPV: Positive predictive value, NPV: Negative predictive value, AHI: Apnea-Hypopnea Index

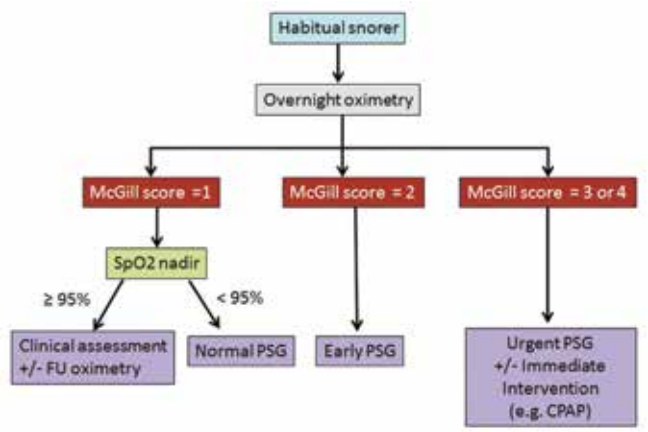

Figure 3: Flow chart for the proposition of oximetry in prioritizing polysomnography.

Conclusion

In a referral population of children suspected to have OSA, the use of the McGill score together with nadir SpO_2 in overnight oximetry can help in stratifying the severity of OSA and thus prioritizing PSG testing.

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Conflicts for interest

There are no conflicts for interest.

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- MCTs can be easily absorbed and quickly used as energy[2,3]

References:
1. Alexander DD, et al. Nutritional and health benefits of semi-elemental diets: A comprehensive summary of the literature. World J Gastrointest Pharmacol Ther 2016;7(2):306-319. **2.** Sucher KP. Medium chain triglycerides: A review of their enteral use in clinical nutrition. Nutr Clin Pract 1986;1(3):146-150. **3.** Ruppin DC, Middleton WR. Clinical use of medium chain triglycerides. Drugs 1980;20:216-224

IMPORTANT NOTICE: The World Health Organization recommends exclusive breastfeeding for 6 months. Nestlé fully supports this and continued breast-feeding, along with the introduction of complementary foods as advised by your doctor or health authority.

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ALLERGY PREVENTION

WNSC HK Expert Interview
The Forefront of Allergy Prevention in the Hong Kong Paediatric Population

Dr Marco H.K. Ho
Specialist in Paediatric Immunology and Infectious Diseases
President, Hong Kong Institute of Allergy

Topics addressed include:

- What are the trends in childhood allergy and adverse food reactions in Hong Kong over the past decade?
- Have there been changes in the prevalence and severity of allergies in relation to the Hong Kong Institute of Allergy's recommendations for allergy prevention?
- What is the latest science in the treatment/prevention of allergies?
- Is there potential for the use of oral immunotherapies?
- Sharing of some noteworthy cases of allergies in children encountered during practice
- Tips for healthcare professionals for the prevention of allergies

What are some noteworthy cases of allergies in children you have encountered during your practice?

Dr Ho: While the most common triggers of food allergies among children in Hong Kong are shellfish, eggs, dairy products, peanuts and fruit;[1] after many years of practice I've come to realise that any food item can potentially cause a reaction. Notable examples specific to this part of the world include lotus seed allergies, rendering children unable to enjoy mooncakes and other traditional Hong Kong desserts. I've also encountered allergies to bird nests, pandan leaves, and buckwheat – which is a seed rather than a grain and is the main ingredient of the soba noodle. Shellfish allergies in Hong Kong are interesting because many cases appear to be secondary to dust mite allergies. The causative allergen in shellfish appears to be tropomyosin, a protein involved in muscle contraction for invertebrates.[2,3] Dust mites, which thrive in warm and humid environments like Hong Kong,[2] share a similar tropomyosin structure with shellfish, which can result in cross-reactivity where individuals who become allergic to dust mites can then develop an adverse reaction to shellfish.[2-4]

Read more at:
https://hongkong.wyethnutritionsc.org/en/learning-corner/expert-interviews

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1. Ho MHK, et al. Asian Pacific J Allergy Immunol 2012;30:275–284. 2.Wong L, et al. Allergy Asthma Immunol Res 2016;8:101–106. 3. Ayuso R, et al. Int Arch Allergy Immunol 2002;129:38–48. 4. Santos ABR, et al. J Allergy Clin Immunol 1999;104:329–337.

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