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Contents

Updates in Pediatric Pulmonology: Transport, Home Ventilation, Spinal Muscular Atrophy, and Zinc

The June 2025 issue of Pediatric Respirology and Critical Care Medicine (PRCCM) presents an important selection of original and review articles that reflect the dynamic advances and ongoing challenges in pediatric respiratory and critical care. From interhospital transport of critically ill infants to the development of pediatric home ventilation, this issue signifies the collaborative efforts of multidisciplinary physicians and researchers to improve outcomes for vulnerable children that will benefit our readership.

Chee *et al*. reviewed the three-year clinical outcomes of a specialized Paediatric Critical Care Transport (CCT) service operating within Hong Kong's "hub-and-spoke" healthcare model.[1] With 283 transports analyzed, 180 (63.6%) were preterm infants. The two most common complications were metabolic acidosis (25.1%) and hypothermia (8.1%), and 36 (12.7%) required interventions during transfer, mostly fluid resuscitation. This article indicates the essential role of the specialized and well-trained transport team in achieving better outcomes for critically ill neonates and the opportunity to enhance subsequent quality improvement in the future.

Nusinersen is the first disease-modifying drug for patients with spinal muscular atrophy (SMA), which was approved by the US Food and Drug Administration (FDA) in 2016 but is still not available worldwide due to the extremely high cost. Hong Kong children were fortunate to receive this drug under the expanded access program. Hung *et al*. evaluated respiratory outcomes in children with SMA who received Nusinersen during 2018-2022; 10 of 23 patients (43.5%) were supported with noninvasive ventilation before commencing this drug.[2] Although Nusinersen did not significantly improve respiratory status, 2 patients with type 1 SMA needed noninvasive ventilation after one year of age, which was later than typically expected. The authors also proposed using the Queen Mary Hospital SMA Respiratory Score, which may have broader utility in research and clinical follow-up for patients with other neuromuscular weakness.

Wang *et al*. described another interesting aspect of respiratory care, which is home mechanical ventilation. This review provides the historical development, technological advancement, and the increasing trend of ventilator-dependent children globally. Various indications of children that differ from adults are discussed.[3] The authors call attention to the burden on caregivers who must be capable of managing the ventilators and related complications on their own. Future potential research on pediatric home mechanical ventilation is also suggested.

Finally, Wong and Ng presented a timely review of zinc deficiency in children and its impact on respiratory health.[4] Infants have shown to have the highest rate of zinc deficiency compared to other age groups. Serum zinc levels appear to be lower in children with COVID-19 infection than in controls, especially those with deteriorating conditions. In addition, zinc deficiency is shown to be associated with higher morbidity and mortality in childhood pneumonia, probably due to a compromised immune response against the pneumococcal pathogen. Surprisingly, zinc has also reported to be related to wheezing and the severity of asthma. Zinc supplementation may be another promising adjuvant strategy to reduce the duration, severity, and occurrence of respiratory diseases in children.

We hope this issue stimulates further inquiry, collaboration, and commitment to improving care across the continuum—from hospital transport bays to homes, from genetic therapies to nutritional strategies.

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There are no conflicts of interest.

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Review Article

Zinc Deficiency in the Pediatric Population and Its Impact on Respiratory Health: A Review

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Abstract

Zinc is an essential element for growth and immunity. Data from China suggested 27.0% of zinc deficiency in Chinese children. This review highlights the evidence of zinc deficiency on respiratory health, including COVID-19, pneumonia, and asthma. Evidence also suggests that supplementation for zinc deficiency significantly reduces the incidence and duration of various respiratory diseases.

Keywords: Asthma, COVID-19, pediatrics, pneumonia, zinc deficiency

Key messages: Given the negative respiratory implications of zinc deficiency, there is a need to screen for zinc deficiency in Hong Kong children, especially those with recurrent respiratory infections or allergic diseases like asthma.

Introduction

Zinc is an essential trace element with an important role in growth.[1] Zinc acts on growth at many levels, including appetite control, DNA and RNA synthesis, and hormonal mediation (growth hormone, insulin, thyroid hormones, and testosterone).[2] Growth failure and a reduced cellular turnover will affect the immune system and present with an increased prevalence of infectious disease in case of deficiency.[3] Zinc deficiency is also directly associated with decreased immunity as it is involved in the production and signaling of inflammatory cytokines.[4] A literature review was conducted to assess the impacts of zinc deficiency in the pediatric population from a respiratory viewpoint.

Zinc Requirement

Zinc is a divalent cation which cannot be synthesized within the human body and relies on dietary intake. During digestion, zinc is released as free ions from food and is absorbed through transcellular uptake primarily in the distal duodenum and proximal jejunum.[5] According to the World Health Organization (WHO), the recommended daily zinc intake ranges from 0.84 mg/day for children aged 6–12 months to 1.12 mg/day for children aged 6–10 years.[6]

Reference Range

Multiple studies have supported the use of plasma zinc concentrations or serum zinc concentrations (SZC) as biomarkers for evaluating zinc status, particularly in assessing zinc status in populations.[7-9] For simplicity, the following discussions on circulating zinc concentrations will refer to SZC for both types of specimens. The criteria of serum zinc deficiency recommended by the International Zinc Nutrition Consulting Group (IZiNCG) were adopted, with SZC <57 μg/dL (8.7 μmol/L) in the afternoon or <65 μg/dL (9.9 μmol/L) in the morning to be considered as zinc deficiency for children aged <10

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years. For children aged ≥10 years, morning fasting serum concentration <70 μg/dL (10.7 μmol/L) for girls and <74 μg/dL (11.3 μmol/L) for boys are considered as zinc deficiency.[10]

Prevalence of Zinc Deficiency

Worldwide, approximately 17.3% of the population was believed to have insufficient zinc intake, with the highest rates observed in Africa (23.9%) and Asia (19.4%).[11] It was estimated that zinc deficiency affects approximately 17–20% of the global human population.[12] Prevalence data for zinc deficiency in Hong Kong were not available, but regional data may provide a rough estimation.

A study from China found that for children aged 6–11 years, 10.44% had zinc deficiency. While for adolescents aged 12–18 years, 8.85% had zinc deficiency, adopting the standard of the IZiNCG.[13] A meta-analysis shows that the zinc deficiency rate of children aged 0–14 years in mainland China was 27.0% (95% CI: 22.8–31.3%).[14] The comparison of zinc nutrition status among different age groups indicated that the infant group (0–1 years) showed the highest zinc deficiency rate, and the difference from the toddler, preschool, and school-age group was significant. This is likely because breast milk may not provide enough zinc after 6 months of age, increasing the risk of zinc deficiency.[15]

Zinc Deficiency as a Risk Factors for Respiratory Illness

The critical role of zinc in immunity has been well established. Zinc has several documented effects on T cells, such as supporting the secretion of T-dependent interleukins (IL) and cytokines like IL-1, IL-2, IL-4, and IFN-γ,[16] promoting T lymphocyte proliferation,[17] and regulating the balance between Th1 and Th2.[18] From a respiratory viewpoint, zinc plays crucial roles in the lung by acting as an antioxidant and anti-apoptotic agent, stabilizing the cytoskeleton and cell membranes, regulating signal transduction pathways, modulating immune responses, promoting epithelial cell turnover, and reducing airway inflammation and repair processes.[19] Below is a summary of the evidence, suggesting that zinc deficiency is a risk factor for respiratory illnesses in severe COVID-19, pneumonia, and asthma in children:

Covid-19

A study was conducted by Doğan *et al.*[20] to measure the zinc level in children diagnosed with COVID-19 viral infection. 23.86% of the case group and 6.82% of the control group had zinc deficiency. Also, the mean serum zinc levels of COVID-19-positive patients were significantly lower than the control group ($P = 0.0001$). Another study[21] found that zinc deficiency at the time of COVID-19 diagnosis was associated with the deterioration of COVID-19 condition, with an adjusted OR of 7.29 (95% CI: 1.70–31.18). This finding aligned with a systematic analysis indicating that zinc deficiency was associated with poorer clinical outcomes of SARS-CoV-2 infection, particularly an increased risk of all-cause mortality ($P = 0.0048$). The mechanism of zinc in exhibiting its protective function is multifactorial. Zinc was found to inhibit the activity of the SARS-CoV RNA polymerase, thereby reducing its replication.[22] Research by Speth *et al.*[23] demonstrated that exposure to zinc (at 100 μM) reduced the activity of recombinant human ACE-2 in rat lungs. Moreover, disulfiram-induced release of Zn2+ from the papain-like protease in MERS-CoV and SARS-CoV led to viral protein destabilization.[24] Zinc is a critical regulator of toll-like receptor 4 (TLR-4)- and TLR-3-mediated signaling in innate immune cells. TLR-4 can potentially recognize external components of SARS-CoV-2, such as viral spike proteins. Consequently, zinc deficiency may disrupt the innate immune response to SARS-CoV-2. Also, in the context of T-cell function, zinc is essential for the signaling cascade of the T-cell receptor and IL-2 as a second messenger.[25]

Pneumonia

Zinc deficiency is a risk factor for pneumonia in the pediatric population, with zinc deficiency associated with morbidity (RR = 1.23; 95% CI: 1.2–1.4) and mortality (RR =1.18; 95% CI 0.9–1.5) of childhood pneumonia shown from a meta-analysis of observed risk reductions from randomized controlled trials (RCTs).[26] Lower serum zinc levels were significantly associated with the treatment burden[27] and severity[28] of pneumonia. A pooled analysis of trials in India, Jamaica, Peru, and Vietnam revealed a 41% decrease in the occurrence of pneumonia among children who were supplemented with zinc.[29] In a systematic review[30] of six RCTs involving children aged 2 to 59 months, the addition of zinc supplements decreased the occurrence of pneumonia by 13% and lowered the prevalence of pneumonia by 41%. These results were corroborated by research supporting the immunomodulatory role of zinc. Zinc is essential for the expression of genes encoding IL-2 and IFN-gamma, and IL-2 production enhances natural killer cell and T cytotoxic cell activities.[31] Zinc deficiency was shown to cause a compromised immune response against pneumococcal surface protein A[32] and decreased killing activity of phagocytes during pneumococcal infections.[33]

Asthma

A meta-analysis[34] found that circulating zinc was associated with a significant risk for childhood asthma and its related symptom, wheezing ($P < 0.001$). For pediatric asthmatic patients, 42% had zinc deficiency, while this rate was 12% in healthy children ($P < 0.001$).

Additionally, there was a significant association between the zinc level and the severity of asthma ($P < 0.001$).[35] In a cross-sectional analysis,[36] an inverse relationship between dietary zinc intake and asthma in the overweight pediatric population was observed. The mechanism behind this can be attributed to the antioxidant properties of zinc, which help to reduce oxidative stress.[37] Additionally, zinc exhibits immunomodulatory and anti-inflammatory effects by regulating the balance of Th1/Th2 cells and inhibiting the nuclear factor-kappa B pathway.[38] Research demonstrates that zinc supplementation boosts the activity of the zinc finger protein A20, which suppresses the NF-κB pathway by degrading receptor-interacting protein 1. This inhibits the inflammatory cascade triggered by NF-κB activation, reducing inflammatory cell infiltration and TNF-α release in airways, while significantly decreasing airway hyperresponsiveness and serum IgE levels.[39] A zinc deficiency can render the airway epithelium susceptible to damage and cell apoptosis, thereby exacerbating airway inflammation.

Zinc Supplementation for Zinc Deficiency

For zinc supplements to prevent zinc deficiency, 0.5 to 1 mg/kg/d of elemental zinc is currently advised.[40,41]

A comprehensive meta-analysis[42] revealed that zinc supplementation significantly reduced the occurrence of acute lower respiratory infections (ALRIs) in children under the age of five. While for the treatment of pneumonia, a meta-analysis[43] revealed that when used as an adjunct in treating severe pneumonia, zinc showed a significant decrease in mortality. The findings were supported by a randomized controlled trial,[44] showing that zinc supplementation enhanced pneumonia treatment outcomes by reducing the resolution period of pneumonia and restoring normal oxygen levels and body temperature in hospitalized children with pneumonia ($P = 0.014$).

For treatment in children with asthma, zinc supplementation (at a dose of 50 mg daily for 8 weeks) in children with asthma and baseline zinc deficiency resulted in enhanced clinical symptoms and improved pulmonary function test results when compared to subjects in the control group.[45] This is corroborated by a study reaffirming zinc supplementation functions as an anti-inflammatory agent by modulating NF-κB activity, reducing airway reactivity, and impacting serum IgE levels.[46]

Conclusion

Zinc deficiency is common in children with clinical consequences, and studies have confirmed that both therapeutic and preventive zinc supplementation can decrease the duration, severity, and occurrence of acute respiratory infections (adopting the WHO definition of ALRI, based on age-specific elevated respiratory rates).[39,47] Zinc is abundant in various foods, with the highest concentrations in animal-derived sources, such as the organs and flesh of beef, pork, poultry, fish, and shellfish, and lower levels in eggs and dairy products. The IZiNCG establishes upper limits for zinc intake, ranging from 6 mg/day for infants aged 7–12 months to 44 mg/day for males and 39 mg/day for females aged 14–18 years. Chronic zinc overdosage in adults, typically 100–300 mg/day, can induce copper deficiency and alter immune responses, leading to reduced lymphocyte stimulation, impaired chemotaxis, and diminished bacterial phagocytosis by polymorphonuclear leukocytes.[48] Thus, careful regulation of zinc intake is essential to prevent adverse effects. Further studies are needed to assess the effect of prophylactic zinc supplementation in reducing the incidence of respiratory diseases and the effect of zinc supplementation on each respiratory disease as adjuvant therapy.

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Author contributions

YMAW and KKN designed the study. YMAW performed the literature search and drafted the manuscript. KKN edited and reviewed the manuscript.

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There are no conflicts of interest.

Ethical Approval

No ethical approval was required for this review article.

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Review Article

Development and Use of Home Ventilators for Pediatric Care

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Abstract

Home mechanical ventilation (HMV) has revolutionized pediatric care by enabling children with chronic respiratory insufficiency to transition from hospital to home settings, significantly enhancing their quality of life. This review examines the historical development, technological advancements, and current practices in pediatric HMV, emphasizing its impact on patients, caregivers, and healthcare systems. Initially developed in the 1970s to address respiratory failure in neuromuscular disorders, HMV has since evolved with innovations such as portable ventilators, enhanced safety features, and improved patient–ventilator synchronization. These advancements have facilitated its application across diverse conditions, including bronchopulmonary dysplasia, congenital central hypoventilation syndrome, and scoliosis, allowing many children to benefit from home-based care. While HMV offers numerous advantages, including reduced incidence of hospitalizations and the ability for children to engage in family and community life, it also presents challenges. Caregivers must navigate complex technical, financial, and emotional demands, often experiencing significant stress and anxiety. The lack of comprehensive home respiratory care infrastructure and inconsistent access to multidisciplinary support further complicates caregiving. Ethical considerations and financial feasibility also influence decisions to initiate HMV, highlighting the need for systemic support and policy enhancements. Despite these challenges, HMV has improved the survival and quality of life in ventilator-dependent children. Future efforts should focus on advancing device technology, fostering family-centered care models, and strengthening the collaboration among healthcare teams. Comprehensive training for caregivers and the integration of holistic support systems are critical to optimizing outcomes for pediatric patients and their families. This review underscores the transformative potential of HMV in pediatric care while advocating for continued innovation and systemic improvements to address unmet needs and ensure sustainable home-based respiratory care.

Keywords: Chronic respiratory failure, home mechanical ventilation, pediatrics

Introduction

Home mechanical ventilation (HMV) has transformed the care of children with chronic respiratory insufficiency, enabling many to leave hospital environments and thrive in home settings.[1] It represents a significant leap forward in pediatric care, allowing children with severe respiratory conditions to experience improved quality of life and participate in daily family activities. Over the past several decades, advancements in ventilator technology and respiratory care strategies have made it possible to medically support many pediatric patients at home.[2] Innovations such as portable ventilators, enhanced alarm systems, and better battery backup have improved the safety and practicality of home-based care. The introduction of HMV not only benefits the patients but also alleviates the burden on hospital resources by reducing the need for prolonged inpatient stays. This transition from institutional care settings to home environments aligns with the broader movement toward patient-centered and community-based healthcare models. By providing children with an opportunity to grow up in a familiar and nurturing environment, HMV contributes significantly to their overall development and wellbeing. However, this complex medical intervention comes with significant technical,

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financial, and emotional challenges for families and healthcare providers.[3-5] Families must become adept at operating ventilators, managing associated medical equipment, and responding to potential emergencies. Additionally, the emotional toll on caregivers, who must remain vigilant and often sacrifice personal and professional aspirations, is considerable. Studies have documented elevated levels of stress and anxiety among parents of ventilator-dependent children, highlighting the need for comprehensive psychosocial support. This review explores the historical development of ventilator technology, the evolution of home ventilator use, indications for its application, and the current state of pediatric home ventilator care, with a focus on improving the quality of life and addressing future needs.

Evolution of Mechanical Ventilation

The description of artificial airways can be traced back to ancient Egypt, where early methods of airway management were documented. Ancient Greek and Roman texts also discussed the role of the heart and lungs in air and blood circulation, highlighting the foundational understanding of respiratory physiology in early medicine. However, a more detailed and accurate conceptualization of double-loop circulation only emerged during the Renaissance period, when significant advancements in anatomy and physiology were made. During this era, positive pressure ventilation (PPV) through tracheostomy was first recorded, marking a significant milestone in respiratory care. The development of mechanical ventilation with the "iron lung" has played a crucial role in managing respiratory failure during the polio pandemic era. Initial advances began in the mid-20th century, with significant improvements in patient outcomes following the introduction of PPV in concordance with the "iron lung" in 1949. The first application of PPV during inspiration improved survival rates from 21% to 84%. By 1952, the use of PPV through tracheostomy became standard practice. This method not only improved the efficiency of ventilation but also provided a more stable and controlled airway for long-term use. These innovations reduced mortality, especially among patients with conditions affecting the respiratory muscles or bulbar function.[6]

Over subsequent decades, technology advancements with better understanding and management of ventilation mechanics were observed. Innovations included improved ventilator designs, enhanced monitoring systems, and specialized settings for different types of respiratory insufficiency. By the 1970s, mechanical ventilation became more accessible. These advancements laid the groundwork for home-based mechanical ventilation (HMV), addressing the needs of patients with chronic respiratory failure. Innovations such as pressure and volume control modes, sophisticated alarm systems, and backup battery support further improved the reliability and safety.

Mechanical ventilation plays a life-saving role for a wide range of conditions. Historically, respiratory failure from neuromuscular diseases, severe infections like poliomyelitis, or acute respiratory distress syndrome necessitated intensive care ventilators.[7-9] The advent of noninvasive ventilation advanced the therapeutic options by reducing the need for tracheostomy and its associated complications.[1,10]

Development of Home Ventilators

The concept of HMV emerged in the 1970s, coinciding with the growing recognition and understanding of chronic respiratory conditions.[11,12] This innovation was initially focused on managing respiratory insufficiency in patients with neuromuscular disorders, such as Duchenne muscular dystrophy, spinal muscular atrophy, and post-polio syndrome. These conditions often lead to progressive respiratory muscle weakness, making assisted ventilation essential for sustaining life and improving quality of care. Observational studies have since shown that HMV not only enhances patients' quality of life but also significantly reduces hospitalizations and overall healthcare costs, underscoring its value in long-term disease management. The earliest indications for its use included nocturnal hypoventilation and chronic gas exchange deficiencies, which are common complications in patients with neuromuscular and restrictive thoracic disorders.[13]

The prevalence of HMV has steadily increased worldwide, driven by advancements in medical technology, improved survival rates for patients with chronic and complex conditions, and a growing recognition of its benefits in managing long-term respiratory failure. In 2021, the prevalence was approximately 6.6 per 100,000 individuals, although this number reflects considerable heterogeneity among conditions and populations.[14-16] The indications for HMV also differ between adult and pediatric populations, with pediatric patients often requiring ventilator support for distinct underlying causes compared to adults. Among children, the most common indications include severe bronchopulmonary dysplasia (BPD), a chronic lung disease seen in premature infants; congenital central hypoventilation syndrome (CCHS), a rare genetic condition affecting respiratory control; and complex airway or chest wall abnormalities, such as tracheomalacia or scoliosis. Additionally, advances in neonatal care have led to the survival of more preterm infants with chronic respiratory conditions, further contributing to the increasing use of HMV in pediatric populations.[14]

Modern home ventilators have undergone significant advancements, making them more adaptable, efficient, and patient-centric. Designed with portability, energy efficiency, and ease of use in mind, these devices are

revolutionizing the way chronic respiratory conditions are managed outside the hospital setting. These features make HMV a practical and effective solution for both patients and caregivers. Devices are equipped to deliver both invasive and noninvasive ventilation to meet the diverse needs of patients with varying levels of respiratory insufficiency, and enhancements in humidification systems, patient–ventilator synchrony, and noise reduction have increased patient comfort. Alarm features provide essential safety alerts, improving monitoring reliability for caregivers.[17]

The development of more sophisticated ventilators has revolutionized care for pediatric patients with chronic respiratory insufficiency, enabling prolonged survival and significantly improved outcomes. Studies have shown that home-based care can significantly enhance the quality of life. By minimizing the need for frequent hospitalizations and invasive interventions, these devices enable children to participate more fully in schooling, extracurricular activities, and family life.[9,18-20]

Indications for Home Ventilator Use

The decision to initiate HMV in pediatric patients is a complex process influenced by various clinical conditions and the unique needs of each child. Chronic respiratory failure, the primary indication for HMV, is characterized by alveolar hypoventilation due to advanced lung disease, neuromuscular dysfunction, chest wall deformities, or central respiratory control disorders. Alveolar hypoventilation results in impaired gas exchange, leading to hypercapnia, hypoxemia, and, ultimately, increased morbidity and mortality if left untreated [Table 1]. Airway and lung diseases are among the most common causes of chronic respiratory failure in children. Conditions such as BPD, subglottic stenosis, and tracheomalacia often lead to significant airflow obstruction and reduced lung compliance, making mechanical ventilation necessary for maintaining adequate oxygenation and ventilation. Similarly, children with severe chest wall deformities, such as scoliosis or ribcage malformations, may experience compromised lung function as these abnormalities restrict thoracic cavity expansion, limiting respiratory capacity in severe cases. Central respiratory control disorders, such as CCHS, Prader–Willi syndrome, or central nervous system trauma, are associated with hypoventilation.[21-24] Despite the absence of universally accepted criteria for initiating HMV in the pediatric population, the primary objective is to alleviate the burden of respiratory insufficiency while correcting oxygen and ventilation deficiencies. The primary goal is to improve alveolar ventilation, enhance overall health, and reduce morbidity and mortality among technology-dependent children. This requires a careful assessment of clinical indicators, including arterial blood gases, polysomnography results, and clinical symptoms such as frequent desaturation episodes, poor growth, or recurrent hospitalizations due to respiratory failure.[1]

Table 1: Potential indication for home mechanical ventilator

Chronic respiratory failure
Alveolar hypoventilation
Advanced lung disease
Bronchopulmonary dysplasia
Airflow obstruction
Reduced lung compliance
Neuromuscular dysfunction
Chest wall deformity
Scoliosis
Ribcage malformations
Central respiratory control disorder
Congenital central hypoventilation syndrome
Prader–Willi syndrome
Central nervous system trauma

In addition to clinical considerations, several practical factors play a critical role in the decision to initiate HMV for pediatric patients. The availability of trained caregivers is a key determinant as home ventilation requires continuous monitoring and a thorough understanding of ventilator operation, emergency procedures, and patient-specific care plans. Caregivers must be capable of recognizing alarm signals, responding to equipment malfunctions, and managing complications such as airway obstruction or accidental disconnections.[25] Financial resources also significantly impact the feasibility of HMV. The cost of ventilators, consumable supplies (such as masks, tubing, and filters), and ongoing maintenance can be substantial. Additional expenses may include those involved in home modifications, such as installing backup power systems, purchasing medical-grade beds, or creating dedicated care spaces. Ethical considerations further complicate the decision to initiate HMV, particularly in cases where the benefits of long-term ventilation may be uncertain.[26] The decision to initiate home ventilation extends beyond clinical factors to encompass practical and ethical considerations. The availability of caregivers, financial and logistical feasibility, and ethical complexities all influence whether HMV is a viable and appropriate option.

Current Use of Home Ventilators in Children

The number of ventilator-dependent children has increased significantly globally. In a study conducted in Taiwan from 1987 to 1990, 83 children below 17 years of age required long-term ventilator support. Among them, 50.6% were managed at home, while others received institutional care.[27] Central nervous system conditions were the most common indications for ventilation, accounting for 73.5% of cases. Severe enterovirus infections contributed to 24.1% of the cases. In a study

conducted in Serbia, the number of patients has increased steeply, particularly during the last 5 years. The increase in the number of invasive and noninvasive ventilator-dependent children is equally distributed. This study also emphasized a critical role of pediatric pulmonologists in decision-making for these children.[28] A similar growing trend of home ventilator–dependent children was also observed in Hong Kong. A significant growing prevalence was observed (from 3 to 53 per 1,000,000 children per year) with a 7-year interval from 1997 to 2017, especially a steep rise during 2013 to 2017, although the exact annual data not provided in this study.[29] These data suggest that the use of HMV has become more acceptable to caregivers, and this kind of device is widely applied in pediatric chronic care.

More recent data reveal evolving practices and persistent challenges. Comprehensive home respiratory care infrastructure remains underdeveloped. Families often struggle to access consistent home nursing, respiratory therapists, and specialized pediatric services.[30,31] Family members serving as primary caregivers bear significant physical, emotional, and financial burdens.[5,32,33] Qualitative research indicates that while parents appreciate the opportunity to care for their children at home, they frequently report high levels of stress, anxiety, and social isolation. Financial strain is a recurrent theme, particularly in systems lacking robust healthcare subsidies.[18,33]

Studies emphasize the importance of family-centered care models. Unlike hospital settings, home environments offer opportunities for better developmental stimulation, social interaction, and schooling. However, gaps in communication between hospitals and home care teams hinder the continuity of care. Integration of coordinated support systems remains a critical area for policy improvement.[9,34]

Recent studies have emphasized the need for personalization in home ventilator management. For example, Khirani *et al*.[35] underscored the importance of individualized face mask selection in pediatric noninvasive ventilation to improve comfort, compliance, and skin integrity in children, especially those with craniofacial anomalies or neuromuscular weakness. The development of soft, adaptive, and pediatric-specific interfaces is a growing area of research, and future innovation may focus on sensor-integrated masks that adjust fit in real-time.

Moreover, emerging data on long-term HMV use point to new concerns about complications and adverse outcomes. Akangire *et al*.[36] analyzed children with BPD-associated pulmonary hypertension on home ventilators and reported increased risks for rehospitalization and progressive right heart dysfunction. Their findings highlight the need for longitudinal monitoring of cardiopulmonary outcomes and more robust risk stratification models in chronic HMV populations.

Additionally, wearable technology and remote monitoring platforms are being piloted to enhance follow-up and early identification of complications. These technologies offer promise for reducing the frequency of emergency visits and improving health-related quality of life by enabling real-time ventilator data transmission to clinicians.

Quality of Life and Future Directions

Home-based ventilation provides several advantages, including improved quality of life, fewer hospitalizations, and a more personalized care setting. Nonetheless, it comes with significant responsibilities for caregivers and families.[37] Maintaining the balance between technological advances and holistic care is required. A comprehensive training for caregivers, including education on ventilator use, troubleshooting, and emergency protocols, is essential. Multidisciplinary teams involving respiratory therapists, social workers, and pediatric specialists should be readily available to involve in the decision-making to initiate HMV use and act as a backup support for these home care children. Future devices should prioritize patient comfort, ease of use, and advanced monitoring capabilities.

Looking forward, research priorities include optimizing long-term outcomes for children on HMV by addressing both clinical and psychosocial domains. Future studies should examine the neurodevelopmental trajectory of ventilator-dependent children, particularly those with early-life exposure to chronic hypoventilation or multiple hospitalizations. Understanding how chronic ventilation impacts learning, behavior, and mental health will be vital in constructing comprehensive care models.

Another important research frontier is the integration of artificial intelligence-driven algorithms in ventilator settings. These systems can adjust ventilator parameters based on real-time physiological signals, potentially reducing clinician workload and improving patient comfort and adherence.

Policy-level changes are also warranted. National pediatric HMV registries, which systematically track patient characteristics, complications, and outcomes, are essential to establish standardized benchmarks and guide quality improvement initiatives.

In conclusion, pediatric home ventilation is a transformative but complex intervention. It underscores the need for systemic support, multidisciplinary collaboration, and ongoing technological innovation to optimize outcomes for children and their families.

Author contributions

Dr. Y-JW: acquisition of data and drafting of the manuscript; Ms. S-JD and Y-JC: provide clinical aspect and drafting data; Dr. Y-JL: conception and drafting

review; Dr. J-NW: conception and design the whole manuscript, and final approval of the published version.

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Original Article

Respiratory Outcomes of Spinal Muscular Atrophy Patients Receiving Nusinersen in Hong Kong

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Abstract

Background: Patients with spinal muscular atrophy (SMA) have significant respiratory morbidity, and their healthcare burden is high. Nusinersen, the first disease-modifying drug available for treating SMA, was administered to our patients in Hong Kong since 2018. We performed a retrospective review of the respiratory outcomes of patients who received Nusinersen at Queen Mary Hospital (QMH) between May 2018 and December 2022 using a new scoring system. **Methods:** All SMA patients enrolled in the expanded access program (EAP) were recruited. For the primary outcome, the QMH SMA Respiratory Score (QMR score) was used to assess the patient's respiratory status. This was calculated at the 1st loading dose, 4th loading dose, and every maintenance dose thereafter. For the secondary outcome, forced vital capacity (FVC) was used to reflect the patient's lung function and was determined annually. **Results:** Twenty-three patients with types 1–3 SMA were included, of whom all but one were symptomatic at the time of starting the treatment. By using the QMR score, Nusinersen was found not to have a statistically significant effect on respiratory outcomes in types 1–3 SMA. Two patients with type 1 SMA were started on noninvasive ventilation at 18 and 40 months of age, which was considerably later than usual. **Conclusions:** Our study found that there was no significant positive effect of Nusinersen on respiratory outcomes in SMA patients who were mostly symptomatic, which was consistent with previous studies. The overall "stabilization" may still be considered an improvement compared to the natural disease course.

Keywords: Nusinersen, respiratory outcome, QMR score, spinal muscular atrophy

Introduction

Spinal muscular atrophy (SMA) is a neuromuscular disease characterized by progressive muscle atrophy and weakness, with an estimated incidence of 1 in 53,000 births in the southern Chinese population.[1] It is classified into types 1–4 based on age at presentation and motor function milestones achieved. Affected individuals have weaker intercostal and bulbar muscles, leading to weak cough, increased risk of oromotor dysfunction, and aspiration. They may also develop restrictive lung disease due to muscular weakness and neuromuscular scoliosis and are prone to developing sleep-disordered breathing due to reduced upper airway tone.[2] For type 1 SMA, the natural disease course is that by 20 months, 90% of patients either do not survive or require more than 16 h of ventilation.[3] The local healthcare burden for SMA patients without disease-modifying treatment, especially type 1 and type 2 SMA, is extremely high.[4]

In December 2016, the US Food and Drug Administration (FDA) approved the use of Nusinersen (Spinraza) as the first disease-modifying drug for patients with SMA. Nusinersen is an antisense oligonucleotide that modifies the pre-messenger RNA splicing of the SMN2 gene and increases the levels of full-length functional SMN proteins, which is lacking in affected patients. The "ENDEAR" trial revealed a significant improvement in

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motor milestone response after 13 months of Nusinersen treatment compared to the control group.[5] Since April 2018, patients with type 1 SMA in Hong Kong started receiving Nusinersen treatment under the expanded access program (EAP). This expanded to include type 2 and type 3 SMA patients in April 2019.

The increasing availability of Nusinersen worldwide has changed the disease trajectory of SMA.[3] Sansone *et al.*[6] reported stable respiratory conditions in 77% of the type 1 SMA patients receiving Nusinersen. In 2017, Edel *et al.*[7] devised The Great Ormond Street SMA1 Respiratory score (GSR score) as a tool to assess the respiratory status of type 1 SMA patients over the course of Nusinersen treatment. The score consisted of seven items, was focused on the airway clearance technique and the use of noninvasive ventilation (NIV), and was only available for type 1 SMA patients. By the 8th dose of Nusinersen, the GSR scores of all patients stabilized. Small changes in the respiratory status, such as changes in ventilator support and frequency of pneumonia, were not reflected in the GSR score and may be important. Therefore, we adopted a modified scoring system called the Queen Mary Hospital (QMH) SMA Respiratory Score (QMR score) to fill this gap and capture these changes in the respiratory status. We hoped that it would be more useful in Hong Kong, especially as most of the patients were already symptomatic when they started receiving Nusinersen. As the GSR score was limited to use in type 1 SMA patients, we also hoped to use the QMR score on all patients with types 1–3 SMA. For this reason, in the QMR score, we assessed the SMN2 copy number instead of the type of SMA 1. Studies have demonstrated that the higher the SMN2 copy number, the more SMN proteins produced, and thus the milder the SMA phenotype.[8]

Given the significant number of respiratory comorbidities in SMA, it is important to understand how Nusinersen alters the disease course. We performed a retrospective review of the respiratory outcomes of all SMA patients who received Nusinersen between May 2018 and December 2022. We hypothesized that they would have improved respiratory status throughout treatment. Our primary outcome was to assess the patients' overall respiratory status using the QMR score, as well as the GSR score for comparison. Our secondary outcome was to evaluate the effect of Nusinersen on FVC.

Materials and Methods

Participants

All SMA patients enrolled in the EAP were recruited, including those receiving follow-up at QMH and those referred from other hospitals in Hong Kong. Inclusion criteria for the EAP included genetic confirmation of SMA with a compatible clinical presentation and adequate nutrition for sex and age. Patients continued to receive medical care according to the Consensus Statement of Standard of Care for SMA.[9] Patients requiring invasive ventilation, with other life-limiting conditions or comorbidities precluding the possibility of lumbar puncture, were excluded from the EAP. Patients were taken out of the EAP if they fulfilled any of the following exclusion criteria: deterioration in both motor scores and respiratory function, as defined by an increase in NIV requirement or invasive ventilation, or significant adverse effects of Nusinersen, or if they failed to comply to the necessary evaluation for treatment efficacy and SMA standard of care management.

Patients were followed-up from the start of their treatment, which was as early as May 2018, and up to their last dose of Nusinersen or until they were switched to oral risdiplam, which was as late as December 2022. Nusinersen was administered intrathecally with four loading doses on days 1, 15, 30, and 60, followed by 4-monthly maintenance doses.

Outcome measure

For the primary outcome, the QMR score [Table 1] was used to assess the respiratory status of patients with types 1–3 SMA. This consisted of nine items, including SMN2 copy number, age of starting ventilator support, the type

Table 1: Queen Mary Hospital SMA Respiratory (QMR) score

		Categories	Score
1	SMN 2 copy number	≥ 3 / 2	1 2
2	Age of ventilator support initiation	None / > 24 m / 18–24 m / 12–17 m / 6–11 m / 3–5 m / 0–3 m	0 1 2 3 4 5 6
3	Mode of ventilator support	None / NIV / tracheostomy	0 1 2
4	Duration of ventilator support	None / PRN or illness / Nocturnal / > 16 h	0 1 2 3
5	Change of ventilator settings	Step down / same / step up	-1 0 1
6	Age of MIE initiation (cough assist)	None / > 24 m / 18–24 m / 12–17 m / 6–11 m / 3–5 m / 0–3 m	0 1 2 3 4 5 6
7	Physiotherapy	None / other PT / cough assist PRN / cough assist-dependent	0 1 2 3
8	Nebulized hypertonic saline	None / sodium chloride	0 1
9	No. of pneumonia incidences (per 4 months)	None / 1 /2 / > 2	0 1 2 3

Table 2: Great Ormond street SMA1 respiratory (GSR) score

		Categories	Score
1	Type of SMA 1	A / B / C	3 2 1
2	Physiotherapy	None / other PT / cough assist PRN / cough assist-dependent	0 1 3 6
3	Nebulized therapy	None / sodium chloride	0 1
4	Age of MIE initiation (cough assist)	None / > 24 m / 13–24 m / 7–12 m / 3–6 m / 0–3 m	0 1 2 3 4 5
5	Age of NIV initiation	None / > 24m / 13–24 m / 7–12 m / 3–6 m / 0–3 m	0 1 2 3 4 5
6	Reason for NIV initiation	Not on / elective / acute	0 1 2
7	Use of NIV	None / PRN or illness / nocturnal / > 16 h	0 1 3 6

and duration of ventilator support, change in ventilator settings, the type of chest physiotherapy, age of starting cough assist, the use of nebulized hypertonic saline, and the number of episodes of pneumonia. Each item was classified into several categories, and each was assigned a numerical value. The QMR score was calculated as the total of all the categories and ranged from 0 to 27. For patients with type 1 SMA, the GSR score [Table 2] was also calculated. Compared to the GSR score, the QMR score could be used for all types of SMA, and additional factors such as change in ventilator settings and number of episodes of pneumonia are considered. A higher QMR and GSR score reflected a more unstable respiratory status. QMR and GSR scores were calculated at the 1st loading dose (baseline), at 4th loading dose, and at every maintenance dose thereafter.

For the secondary outcome, FVC was used to reflect the patient's lung function. Patients who were able to cooperate with lung function performed either spirometry or full lung function test annually.

Study design

This was a single-center retrospective cross-sectional study performed at QMH. The study was approved by the Institutional Review Board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster on 29 August 2023 (reference UW 23-447). Written informed consent was waived due to the retrospective nature of the study and as no patient identifiers were required in the analysis.

Statistical analysis

Descriptive statistics were calculated for subject demographics. Continuous data were reported as mean (SD) or median (IQR) as appropriate. Categorical data were reported as frequency (%). Statistical analyses were performed with IBM SPSS Statistics for Windows, Version 27.0 (IBM Corp., Armonk, NY, USA). Independent-sample *t* test was used to compare the patients' final QMR and GSR score from their baseline QMR and GSR score. One-way ANOVA was used for comparison of the QMR score between different types of SMA. Statistical significance was achieved when P value ≤ 0.05.

Results

Subject demographics

Twenty-three SMA patients receiving Nusinersen were followed-up from as early as May 2018 to as late as December 2022 [Table 3]. Of these, eight (34.8%) had type 1 SMA, 11 (47.8%) had type 2 SMA, and four (17.4%) had type 3 SMA. The median age at starting Nusinersen was 6.7 years (IQR 3.8–11.1). Twenty-two (95.7%) patients were already symptomatic at the time of starting treatment. The mean follow-up duration was 2.5 ± 1 year. One patient with type 1 SMA defaulted follow-up after 8th dose of Nusinersen, and another type 1 SMA patient left EAP due to deterioration in respiratory function, warranting a tracheostomy.

At the time of starting Nusinersen, 10 (43.5%) patients required NIV, six (60%) of whom had type 1 SMA. Thirteen (56.5%) patients required regular chest physiotherapy.

Effect of Nusinersen on the respiratory status as reflected in the QMR and GSR score

Two (25%) patients (patients 2 and 8) with type 1 SMA had higher final GSR [Figure 1A] and QMR score [Figure 1B] compared to baseline, reflecting more unstable respiratory status. This was due to the initiation of nocturnal NIV and MI-E. Three (38%) patients (patients 3, 4, and 6) had lower final GSR and QMR scores. Patient 1, who had a lower final QMR score, was able to reduce ventilator settings and had less frequent pneumonia compared to baseline. However, this was not reflected in the final GSR score, which remained the same. Patient 4, who had apparent improved final GSR and QMR scores, required tracheostomy after the 7th maintenance dose and was no longer eligible for Nusinersen treatment. Her final GSR and QMR scores were calculated prior to her clinical deterioration. Two (25%) patients (patients 5 and 7) maintained the same final GSR and QMR score.

Five (45.5%) patients (patients 1, 3, 4, 5, and 10) with type 2 SMA had a higher final QMR score compared to baseline due to initiation of nocturnal NIV and increase in ventilator settings [Figure 2A]. One (9%) patient (patient 2)

Table 3: Patient demographics at baseline

	Total	Type 1 SMA	Type 2 SMA	Type 3 SMA
	n = 23	*n* = 8	*n* = 11	*n* = 4
SMN2 copy number, *n* (%)				
2	4 (17.4%)	4 (50%)	0 (0%)	0 (0%)
3	17 (73.9%)	4 (50%)	11 (100%)	2 (50%)
4	2 (8.7%)	0 (0%)	0 (0%)	2 (50%)
Age on starting Nusinersen in years, median (IQR)	6.7 (3.8–11.1)	3.5 (1.7–8.2)	6.5 (5.3–9.3)	10.2 (7.5–13.4)
Symptomatic on starting Nusinersen	22 (95.7%)	8 (100%)	10 (90.9%)	4 (100%)
Duration of follow-up in years, mean ± SD	2.5 ± 1.0	3 ± 0.9	2.2 ± 1.1	2.1 ± 0.5
Require NIV at baseline, *n* (%)	10 (43.5%)	6 (75%)	3 (27.3%)	1 (25%)
Age of initiation of ventilator support in years, median (IQR)	2.1 (0.9–5.4)	1.1 (0.6–1.7)	6.1 (4.2–6.7)	11.5
Duration of ventilator support at baseline, *n* (%)				
None	11 (47.8%)	2 (25%)	6 (54.5%)	3 (75%)
PRN or illness	2 (8.7%)	0 (0%)	2 (18.2%)	0 (0%)
Nocturnal	7 (30.4%)	3 (37.5%)	3 (27.3%)	1 (25%)
> 16 h	3 (13.1%)	3 (37.5%)	0 (0%)	0 (0%)
Physiotherapy, *n* (%)				
None	10 (43.5%)	1 (12.5%)	6 (54.5%)	3 (75%)
Other PT	4 (17.4%)	2 (25%)	1 (9.1%)	1 (25%)
Cough assist PRN	2 (8.7%)	1 (12.5%)	1 (9.1%)	0 (0%)
Cough assist dependent	7 (30.4%)	4 (50%)	3 (27.3%)	0 (0%)
Age of initiation of cough assist in years, median (IQR)	2.3 (1.8–3.3)	1.8 (0.9–2.2)	3.9 (3.1–5.9)	–
Nebulized hypertonic saline, *n* (%)	1 (4.3%)	1 (12.5%)	0 (0%)	0 (0%)
Number of pneumonia incidences in the past 4 months, mean ± SD	0.6 ± 1.2	0.9 ± 1.5	0.5 ± 1.2	0

had a lower final QMR score as a result of less frequent pneumonia. Five (45.5%) patients (patients 6, 7, 8, 9, and 11) maintained the same final QMR score.

One (25%) patient (patient 1) with type 3 SMA had a higher final QMR score, and one (25%) patient (patient 3) had a lower final QMR score compared to baseline [Figure 2B]. Two (50%) patients (patients 2 and 4) maintained the same final QMR score.

There was no statistically significant difference when comparing the baseline and final GSR score among patients with type 1 SMA ($P = 0.437$). For the QMR score, there was no statistically significant difference for patients with types 1–3 SMA throughout the course of Nusinersen ($P = 0.778$, 0.237, and 0.664 respectively), as reflected in the difference in the QMR score at each time point. Similarly, there was no statistically significant difference when comparing the baseline and final QMR score for patients with type 1–3 SMA ($P = 0.672$, 0.172 and 0.5, respectively). When comparing the effect of Nusinersen on the baseline and final QMR score between types 1–3 SMA, there was no statistically significant difference ($P = 0.907$).

Effect of Nusinersen on FVC

All patients with type 1 SMA were too young or weak to cooperate with spirometry or lung function testing. There was limited evaluation of lung function due to different protocols for lung function assessment among regional hospitals where patients continued to receive follow-up. Six patients had FVC measurements at baseline and after 1 year of treatment [Table 4], four of whom had type 2 SMA and two with type 3 SMA.

Patients with type 2 SMA had a 21% mean increase in absolute FVC value from baseline after 1 year of treatment, although this was not statistically significant ($P = 0.201$). For type 3 SMA, there was a 4.8% mean decrease in absolute FVC value from baseline after 1 year of treatment. This was not statistically significant ($P = 0.052$). None of the patients underwent scoliosis surgery during the first year of treatment.

Discussion

Twenty-three SMA patients were included in our study. All but one were already symptomatic on starting Nusinersen, with a median age of 6.7 years old (IQR 3.8–11.1) at the start of treatment. Studies reported greater peripheral muscle function response with early treatment,[10,11] yet the effect on respiratory muscles and thus respiratory status was conflicting.[12-15] This may be due to the development of fibrotic respiratory muscles and contractures of the rib cage following muscle weakness.[16,17] Despite improvement in muscle strength with Nusinersen, the contractures may persist. By using a newly derived scoring system that captured even small changes in the respiratory status of patients with types 1–3 SMA, of whom the majority were already symptomatic, our study also failed

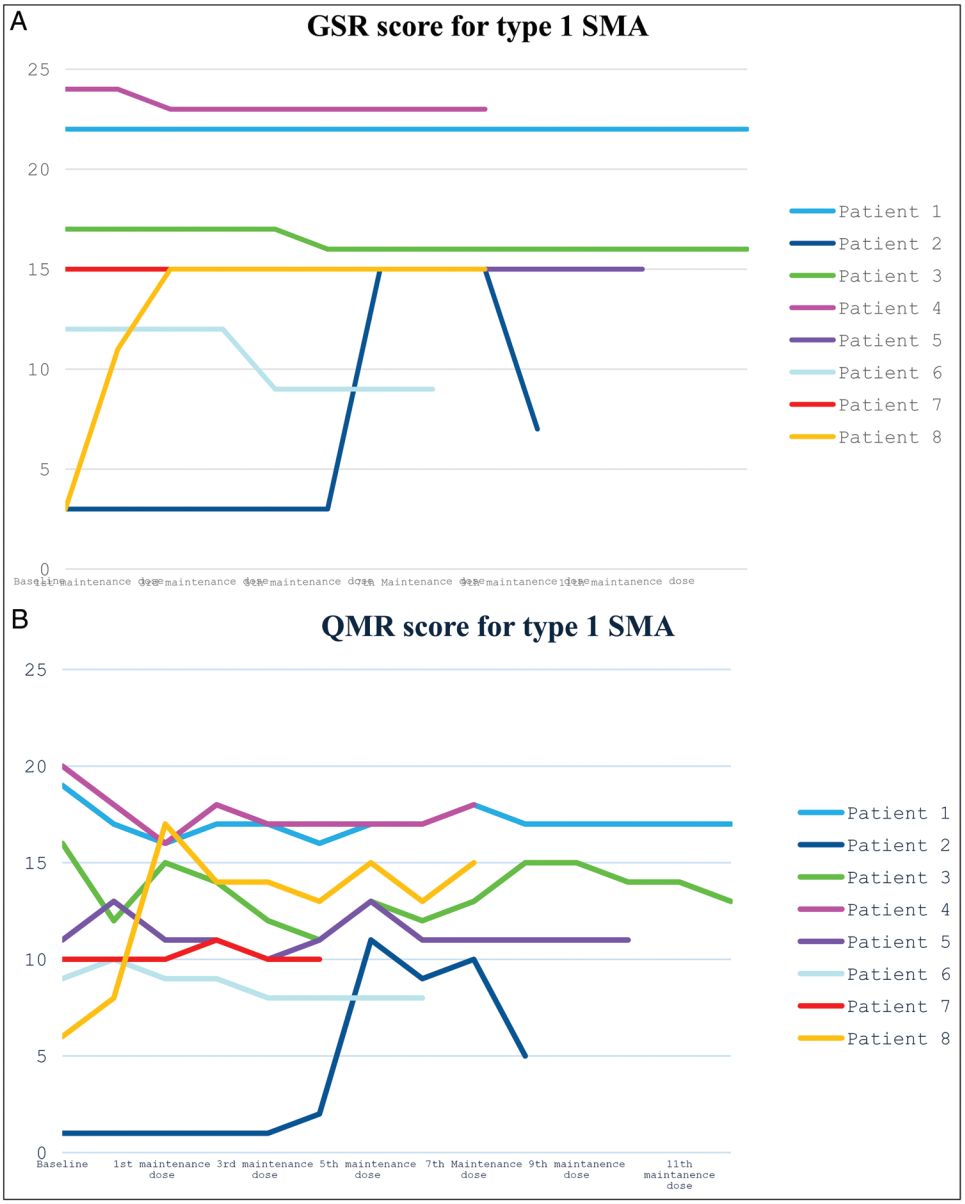

Figure 1: Individual scores for each patient with type 1 SMA throughout the course of treatment using (A) GSR score and (B) QMR score

to show significant positive effects of Nusinersen. This was concurrent with the findings of previous studies. We applied the GSR score to our type 1 SMA patients and did not observe any statistical significance either. We believed our result was genuine as our study had a mean follow-up duration of 2.5 ± 1 years, which was already longer than that in other studies.[9]

Compared to type 2 and type 3 SMA, patients with type 1 SMA were younger when initiated on Nusinersen. This was likely due to earlier clinical presentation, resulting in earlier diagnosis, as well as earlier availability of EAP to these patients. Furthermore, a larger proportion of type 1 SMA patients required NIV at baseline, and the median age at which NIV was started was less. This was compatible with the earlier onset of respiratory problems in type 1 SMA.

Although there was no statistically significant change in the respiratory status for all patients throughout treatment, 15 (65.2%) patients maintained a stable respiratory status, as reflected in improved or same final QMR score. In our cohort, improvements were observed due to less frequent pneumonia, reduction in ventilator settings, and less dependence on cough assist. In spite of few improvements, this could be significant in improving the quality of life. Additionally, there were no deaths among those receiving Nusinersen. Two patients with type 1 SMA were started on NIV at 18 and 40 months of age, which was considerably later than usual.[4] This suggested a potential role of Nusinersen in "stabilizing" respiratory status and delaying the need for NIV, based on the real-life clinical situation that Nusinersen was started when they were already symptomatic.

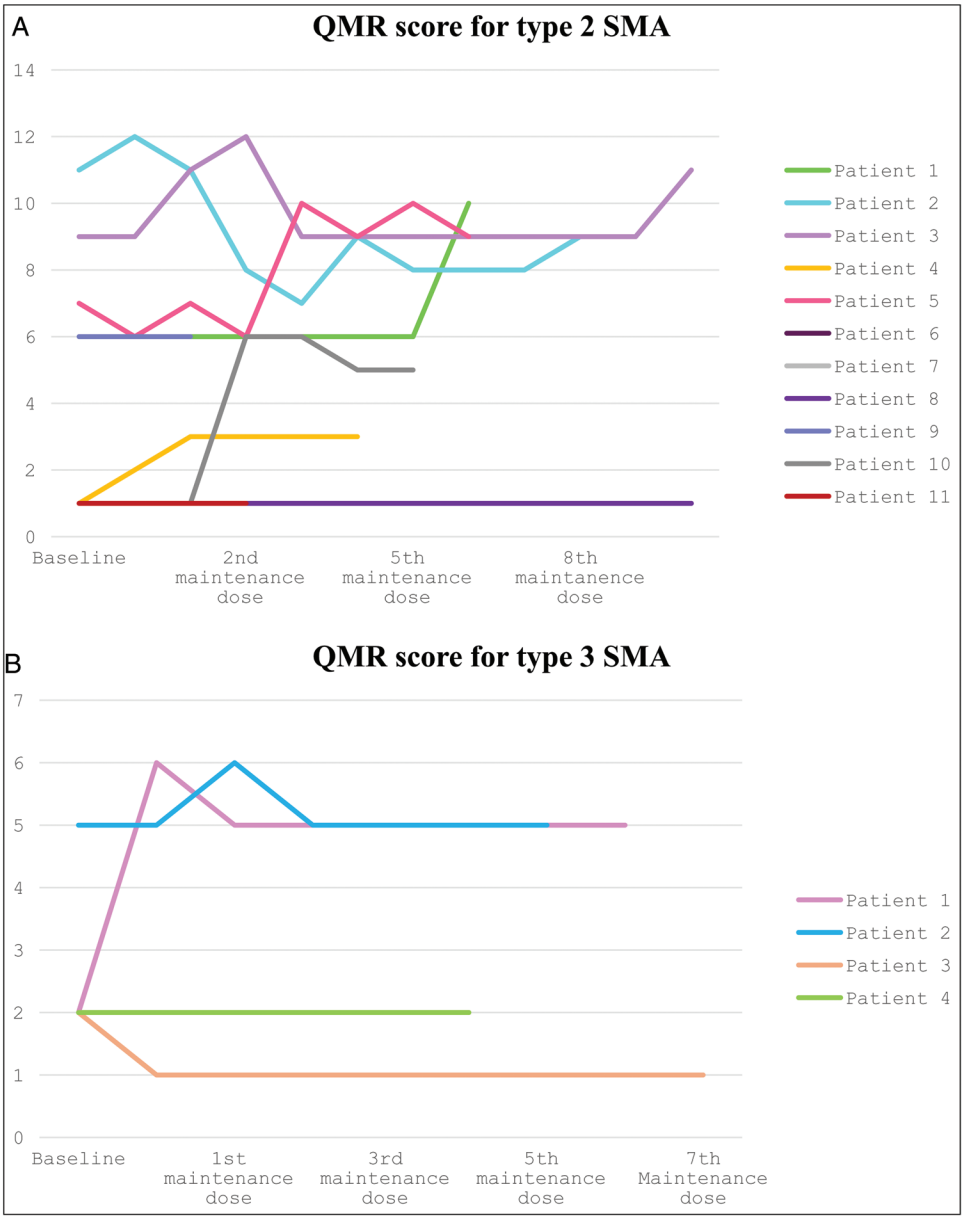

Figure 2: Individual QMR scores for each patient with types 2 and 3 SMA throughout the course of treatment (A) type 2 SMA and (B) type 3 SMA

Table 4: Effect of Nusinersen on FVC after 1 year of treatment in patients with types 2 and type 3 SMA

Patient	FVC in mL (% predicted)		% change in FVC	Mean % change in FVC ± SD	*P* value
	Baseline	After 1 year			
Type 2					
1	500 (19%)	730 (24%)	+46%	+ 21 ± 26%	0.201
5	400 (48%)	340 (35%)	-15%		
9	610 (40%)	800 (43%)	+31.1%		
10	2020 (54%)	2480 (74%)	+22.8%		
Type 3					
2	3100 (106%)	2940 (106%)	-5.2%	− 4.8 ± 0.6%	0.052
3	2490 (69%)	2380 (64%)	-4.4%		

There was one pre-symptomatic patient with SMN2 copy number 3, who was started on Nusinersen at 4 weeks of age. On latest assessment at 12 months of age, there was no evidence of clinical disease with normal respiratory and neurological examination.

Among the four patients with type 2 SMA, we observed an improvement in FVC after 1 year of treatment in three patients. Patient 5, who demonstrated FVC decline, also had concomitant deterioration in scoliosis up to 82°. This echoed findings reported by Chacko *et al.* who observed lack of decline in FVC after 1 year of treatment.[16] While this could also be due to natural variability in lung function with age,[18] the lack of decline in FVC that would be expected in progressive SMA disease, suggests the role of Nusinersen in stabilizing lung function.

Due to varying practices among parent teams from different hospitals, other lung function parameters such as maximum inspiratory pressure (MIP), maximum expiratory pressure (MEP), and peak cough flow (PCF) were not consistently measured. Sleep polysomnography (PSG) was not universally performed due to limitation of resources within the hospital authority. Therefore, these were not included in our study.

A strength of our study is that it is one of the few studies in Asia to report on the effect of Nusinersen on respiratory outcomes. Recruited patients underwent a vigorous screening process to enter the EAP and received regular review by designated physicians throughout treatment. Moreover, we evaluated patients with types 1–3 SMA, whereas most studies focused on type 1 SMA only.[3,6,9] We also had a longer follow-up duration, meaning that we were able to observe the Nusinersen effect for a longer period. As we were the only pediatric unit providing Nusinersen treatment in Hong Kong until January 2024, our data represents the local territory-wide situation. Our study provides real-world data on patients who received Nusinersen at symptomatic age, which may be applicable in countries without newborn screening and early detection of SMA. It provides realistic expectations for patients, as well as a valuable outlook for physicians in their respiratory management.

We must address our limitations as well. Our sample size was small; thus, there was limited power to detect statistical differences. However, we were the only pediatric unit providing Nusinersen treatment in our locality at the time of subject recruitment, and our sample size was similar to that in Western studies.[6-9,15] Most patients were symptomatic with a wide age range on starting treatment, meaning that we could have underestimated the effect of Nusinersen, which has been reported to be more prominent in pre-symptomatic patients.[12] On the other hand, this provides real-world data on the effect of Nusinersen in symptomatic patients. The QMR score was not validated as there is no gold standard or validated scoring system for respiratory assessment of patients with SMA published in literature. Our score was similar to the GSR score but included additional items,[7] including SMN2 copy number, change of ventilator support, and the number of pneumonia incidences. The QMR score was also limited to patients, while they were enrolled in the EAP and was unable to reflect those who left the EAP due to clinical deterioration. For lung function assessment, resources varied among hospitals. Moreover, the COVID-19 pandemic and thus suspension of lung function services spanned throughout most of the duration of the study. The lung function test was also limited to older and cooperative children, most of whom were type 2 and type 3 SMA patients. Other important outcome measures such as MIP, MEP, PCF, and PSG were not included due to resource limitation in our locality. Lastly, we were unable to compare our cohort with untreated subjects as the majority of SMA patients in Hong Kong were already receiving treatment.

With the introduction of newborn screening of SMA in Hong Kong since October 2023, early pre-symptomatic diagnosis is expected. Studies focusing on the effect of Nusinersen in this population are needed. Furthermore, with US FDA approval of oral Risdiplam and gene therapy for SMA, longitudinal studies are needed to evaluate their impact on respiratory outcomes.

Conclusions

In this study, we found that Nusinersen did not have a statistically significant difference on respiratory outcomes in patients with types 1–3 SMA. Additionally, there was no statistically significant change in FVC after 1 year of treatment for types 2 and 3 SMA patients. The overall "stabilization" of respiratory condition may be considered an improvement and is encouraging compared to the natural disease course of SMA. Further studies examining the effect of Nusinersen and other disease-modifying treatments in pre-symptomatic individuals are needed.

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Author contributions

Dr. Jacqueline Hung and Dr. Ka Siu conceptualized and designed the study. Dr. Jacqueline Hung performed literature search, data acquisition and statistical analysis, as well as manuscript preparation and editing. Drs. Ka Ka Siu, Shuk Kuen Chau, and So Lun Lee performed manuscript review. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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There is no funding in the form of grants and equipment of drugs for this study.

Conflicts of interest

The are no conflicts of interest.

Data availability

Patient demographics were obtained from the Hospital Authority clinical management system, a computerized database that captures all clinical information.

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Original Article

Development of a Critical Care Transport Service: A Three-year Review of Interhospital Transport of Critically Ill Infants

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Abstract

Background: Since the commencement in 2019, the first specialised designated paediatric critical care transport (CCT) team with a standardised workflow was created to safely transport patients to and from our hospital and their respective neonatal intensive care unit (NICU) and paediatric intensive care unit. The aim was to review the first 3 years' clinical outcomes of critically ill infants requiring interhospital transfer to and from our hospital's NICU. **Methods:** This is a retrospective observational study of infants transported between NICUs of regional hospitals under the hospital authority retrieved and repatriated to our hospital's NICU by the CCT team between July 1, 2019, and July 31, 2022. **Results:** A total of 283 infants with a mean gestational age at birth was 33.3 ± 5.1 weeks and a birth weight of 2060 ± 984 g were included. About 70% were classified as emergency transport (167/240), with a mean transport time of 34 ± 16 min and a dispatch time of 57 ± 43 minutes. A total of 84 (critical/serious) complications were documented in 71 patients (25.1%) and a total of 39 interventions were required from 36 patients (12.7%). The most common complications were mild acidosis (30.6%; 26/85) and hypothermia (8.1%; 23/283). **Conclusions:** This study provides a good benchmark for the introduction of a designated and standardised workflow for a CCT team at a centralised tertiary-level children's hospital. This study also identifies areas of enhancement for subsequent quality improvement projects in the future.

Keywords: Complications, infants, interhospital transport, neonatal intensive care, paediatric critical care

Key Messages: First review of data from a designated and specialized Paediatric Critical Care Transport team in our city. A good benchmark of complications encountered (25.1%) and interventions required (12.7%). This is comparable and improved upon similar international and local data. Identifies area of enhancement as service workforce expands within our city.

Introduction

Our hospital in Hong Kong SAR offers tertiary and quaternary services in highly specialised paediatrics subspecialties like cardiac, cardiothoracic surgery, oncology, metabolic, nephrology, neonatal surgery as well as neonatal intensive care unit (NICU), and paediatric intensive care unit to patients from birth to 18 years of age. The hospital adopted a "hub- and spoke" model for its specialised services. This model structure resulted in the need for a designated and standardised paediatric critical care transport (CCT) team to be commissioned and developed to safely retrieve patients from referring regional hospitals for subspecialty management and repatriate patients back for further care.

The NICU services commenced in July 2019. Our hospital NICU predominantly received neonates transferred from other hospitals with neonatal surgical problems and congenital cardiac abnormalities. As further subspecialties were centralised to our hospital, referrals for suspected oncology, metabolic, and nephrology patients were also sought by regional hospitals.

The designated CCT team comprises trained medical and nursing manpower equipped with knowledge, skills,

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and experience in transport and paediatric/neonatal intensive care. The nursing team has completed their Post registration Certificate Course in Paediatric or Neonatal Intensive Care Nursing, whereas the medical team has training in both paediatric and neonatal intensive care. The team also received on-site training and attended and taught the local Paediatric and Neonatal Emergency Transport Simulation course, which is held annually.

A standardised protocol to assess workflow for case referrals and a safe and systematic referral system involving teleconferencing between multiple specialties involved (our hospital NICU team, CCT, subspecialty team, and regional referring hospital NICU team) was created. During the teleconference, clinical details using an ISBAR (Introduction, Situation, Background, Assessment, Recommendation) format; specific management plans including advice on stabilisation and pre-transport preparation are written on a specific systems-based handover sheet.

A pre-transport preparation checklist including weight-based resuscitation charts, pre-prepared and checked transport equipment bags, and transport medication boxes ready for an efficient mobilisation time as well as to minimise any potential equipment or medication error was created.

The primary objective of this study was to review the first specialised designated paediatric CCT team and their first 3 years' clinical outcomes of critically ill infants requiring retrieval to our hospital NICU and repatriated from our hospital.

The outcome measures were the total number of complications including serious or critical (or both) during transport and the intervention during or within 1-h post transport.

Materials and Methods

Study design

This was a retrospective observational study of infants transported between NICUs of regional hospitals under the hospital authority (HA) retrieved and repatriated to our hospital NICU over 3 years between July 1, 2019, and July 31, 2022. Ethical approval was obtained by the Central Institutional Review Board for the Hospital Authority, on the 21st March 2023 and the IRB/REC number is PAED-2023-013.

Data collection

Digital records of infants retrieved and repatriated from our hospital were collected from the hospital database (HA clinical management system & Clinical Information System Citrix). All admissions were verified by handwritten transfer documents. The inclusion criteria for this study were any NICU patients who were retrieved from the regional hospitals under the HA by our hospital CCT team and any repatriated NICU patients back to their referring hospital NICU between the collection dates. Two cases were cross-border retrievals with collaborations with their respective referring hospitals, one was retrieved from the Shenzhen–Hong Kong border and the other from the Macao–Hong Kong border; both were included in the study. All other patients transferred by the referring hospital medical or nursing team to the NICU or special care baby unit or any Paediatric intensive care transfer by the CCT team were excluded. Relevant data was extracted and charted on an Excel template for data analysis.

Demographics collected

The data collected included the patients' demographics, date of birth, gestational age at birth, gender, birth weight, mode of delivery, Apgar Score at 5 min, gestational age at transfer, and weight at transfer. Patients were analysed for being small for gestational age (SGA) if their weight were below the 10th percentile according to the reference ranges for Chinese newborns.[1]

The names of referring hospitals were recorded, the subspecialty admitting the patient, the potential diagnosis, and the transfer urgency time (time critical ≤1-hr dispatch from our hospital, urgent ≤2-hr, priority ≤8-hr, or elective transfers). This subdivision of transfer urgency time was only available from July 2020; after a new version of the referral form was created, and data was collected on all subsequent patients. Emergency transport were any transfers with a ≤ 8-hr dispatch time from our hospital (time critical, urgent, and priority transfers), the nonemergency transports included the elective transports and the repatriations.

Timings

The timings of transfers were collected. "Transport time" for retrieval cases was calculated as the time of arrival back to our hospital minus the time of dispatch from the retrieving hospital and for repatriated cases, the time was calculated as the time of arrival at the repatriated hospital minus the time left from our hospital.

"Dispatch times" were only calculated for the retrieval cases and could only be calculated if the referral time was known. They were calculated as the time of departure from our hospital minus the time of referring the case; this was subsequently later compared with the transfer urgency classifications.

If the dispatch time from our hospital was during the working hours of 08:30–17:30, 7 days a week; it was considered a daytime transfer. If outside those hours 17:31–08:29; it was considered an out-of-hours transfer. The transport distance was calculated as the ground distance from our hospital to the respective hospitals or meeting places as calculated on the Google Maps application.

Clinical data

The clinical data obtained from the records included the intensive care support the patient required for transfer (mode of respiratory support, sedation support, ionotropic support, or prostaglandin infusion if any). Details of central and arterial access and monitoring were also noted.

All documentation regarding the transport was reviewed on the criteria defined. 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 were captured. Post-transport physiological parameters were extracted from the first set of recorded information within 1 h of admission to the intensive care unit. The definitions of the significant changes in physiological parameters are defined in Table 1. The definitions of critical and serious complications are described in Table 2, whereas the definitions of interventions are described in Table 3.

Early mortality was defined as death within 7 days of admission following transfer from the referring hospital. The causes of death were reviewed.

We used the Strengthening the Reporting of Observational Studies in Epidemiology checklist for observation studies.

Statistical analysis

The results are presented using descriptive statistics, reporting categorical variables as numbers with percentages and ordinal variables as medians with interquartile ranges. The Chi-square test of independence and Fisher's exact test were applied to the categorical variables. All continuous variables were tested for normal distribution. The unpaired t test and one-way analysis of variance were used for the continuous variables with a normal distribution. These statistical tests were used to calculate the probability value (P value). If the P value was <0.05 between the two variables, it was considered statistically significant. All statistical analyses were performed by using IBM SPSS Statistics for Windows, version 25.0 (IBM Corp. Armonk, NY, USA).

Table 1: Definitions of the significant changes in physiological parameters, critical complications, serious complications and interventions associated with transport

Variables	Definitions
Significant changes in physiological parameters	
Significant decrease in oxygen saturation	Post-transport SpO2 ≤85% and decrease ≥10% from pre-transport SpO2
Significant decrease in blood pressure	Post-transport SBP <10th centile from literature reference and decrease >10% from pre-transport SBP[2,3]
Significant decrease in heart rate	Post-transport heart rate <60 bpm and decrease ≥30% from pre-transport heart rate[3]
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[4]

SpO2 = Pulse oximetry, SBP = Systolic blood pressure, bpm = Beats per minute

Table 2: Number of both critical and serious complications. No. of complications/total number of cases with the available monitoring. Count, (%)

Types of complications	Severity of complication	CCT cohort (2019–2022)
Severe hypoxia (SpO2 ≤65%)[5]	Critical	0/283 (0%)
Endotracheal tube obstruction[3,6]	Critical	0/126 (0%)[a]
Bradycardia (Heart rate <60)[7]	Critical	0/283 (0%)
Hypotension (Systolic BP ≤40 mmHg)[8]	Critical	5/283 (1.8%)
Critical hypoglycaemia (D'stix < 2)	Critical	1/283 (0.4%)
Severe acidosis (Arterial pH <7)[9]	Critical	0/85 (0%)[b]
Severe alkalosis (Arterial pH >7.55)[9]	Critical	1/85 (1.2%)[b]
Hypothermia (temp < 36.5)[10]	Serious	23/283 (8.1%)
Desaturation[11]	Serious	3/283 (1.1%)
Mild hypoglycaemia (D'stix 2–3.3 mmol/L)[12,13]	Serious	4/283 (1.4%)
Mild acidosis (Arterial pH 7–7.28)	Serious	26/85 (30.6%)[b]
Mild alkalosis (Arterial pH 7.48–7.55)	Serious	6/85 (7.1%)[b]
Hyperventilation (arterial pC02 <3.4kPa)	Serious	4/181 (2.2%)[c]
Loss of venous access	Serious	3/283 (1.1%)
Other equipment failure	Serious	8/283 (2.8%)

[a]126 patients required invasive ventilation during transport

[b]85 patients had pre and post transport arterial blood gas. More acidotic or alkalotic compared to baseline

[c]181 patients had access to an arterial line available during transport

Table 3: Number of interventions required. Number of intervention/ Total number of potentials cases requiring interventions. Count, (%)

Variables	CCT cohort (2019–2022)
Respiratory interventions during transport	
Perform manual bagging	1/283 (0.4%)
Respiratory interventions after transport	
Step up of respiratory support	3/283 (1.1%)
Requirement of change of endotracheal tube	0/126 (0%)
Cardiovascular interventions after transport	
Requirement of fluid resuscitation	24/283 (8.5%)
Commencement of inotropic support	5/283 (1.8%)
Metabolic intervention	
Correction of hypoglycaemia	5/283 (1.8%)
Equipment intervention	
Re-establishment of intravenous access	1/283 (0.4%)

Results

A total of 283 infants were transported by the CCT team during the collection dates. All the demographics and relevant details of transport are summarised in Table 4.

Table 4: Demographics and Relevant details of transport

Variables	CCT cohort (2019–2022)
	N = 283
Female, number (%)	120 (42.4%)
Male, number (%)	163 (57.6%)
Birth weight (gram), mean ± SD	2060 ± 984
Small for gestational age, number (%)	39 (13.8%)
Caesarean section, number (%)	147 (51.9%)
Apgar < 7 at 5mins, number (%)	40 (14.1%)
Gestational age at birth (week), mean ± SD	33.3 ± 5.1
•Extremely preterm (less than 28 weeks), n = 52	25.1 ± 1.2
•Very preterm (28 to 32 weeks), n=46	29.7 ± 1.0
•Moderate to late preterm (32 to 37 weeks), n = 82	34.2 ± 1.5
•Term ≥37 weeks, n = 103	38.5 ± 1.4
Age at transport (day), median (range)	7 (0–163)
•Extremely preterm (less than 28 weeks), n = 14	9 (0–163)
•Very preterm (28 to 32 weeks), n= 42	12 (0–57)
•Moderate to late preterm (32 to 37 weeks), n = 94	11 (0–71)
•Term ≥37 weeks, n = 133	5 (0–127)
Weight at transport (gram), mean ± SD	2268 ± 903
Indication at transport/ Specialty	
Cardiac assessment/Management	43 (15.2%)
Paediatric general surgical assessment/Management	182 (64.3%)
Required surgery during admission	115 (40.6%)
Emergency transport	167 (70%)[d]
Retrievals	235 (83%)
Day time transfers	218 (77%)
Transport duration (mins) mean ± SD	34 ± 16
Dispatch time (mins) mean ± SD	57 ± 43[e]
Transport distance (km) mean ± SD	11.6 ± 10.5
Any support during transport	190 (67.1%)[f]
•Invasive ventilation	126 (44.5%)
•Non-invasive ventilation	57 (20.1%)
•Inotropic support	39 (13.8%)
•IV Sedation	32 (11.3%)
•Prostaglandin infusion	16 (5.7%)
Central line	156 (55.1%)
Arterial line	181 (64.0%)
Monitoring during transport	283 (100%)
Escorted by doctors	283 (100%)

[d]From 240 patients (after the 43 cases prior to the introduction of the transfer urgency form in 2020 were excluded)

[e]Dispatch time calculated for all possible patients, 283 patients excluding 48 repatriates, 43 patients prior to the transfer urgency form creation in 2020, 13 patients with unavailable referral times and 12 patients with elective transfer urgency classifications. Total number 167 available.

[f]Number of support each patient required – 93 required 0, 137 required 1, 31 required 2, 17 required 3, 5 patients required 4 (Invasive ventilation or non-invasive ventilation counted as one type of support)

Demographics

There were slightly more male infants transported (n = 163; 57.6%) compared with female infants (n = 120). The mean birth weight was 2060 ± 984 g. About 13.8% of infants were born SGA (n = 39). About 51.9% were born via Caesarean section (n = 147) and 14.1% of infants had an Apgar score of <7 at 5 min of age (n = 40). The mean gestational age at birth was 33.3 ± 5.1 weeks. The mean weight at transport was 2268 ± 903 g.

The main indication for the transfer of patients was for surgical assessment and management (n = 182; 64.3%), with cardiac assessment being the second most common indication (n = 43; 15.2%). In total, 232 surgical procedures were performed on 115 patients from 283 (40.6%). From the 115 patients, over half required a second surgical procedure or more (61/115; 53%). Thirty-one patients required a second surgical procedure, 12 patients required a third surgical procedure, 10 patients required a fourth surgical procedure, 5 patients required a fifth surgical procedure, and 3 patients required a sixth surgical procedure during their hospital admission.

Clinical support

Close to 70% (n = 190) of patients were critically ill during transport; 44.5% (n = 126) were invasively intubated, 20.1% (n = 57) required non-invasive ventilation, 13.8% (n = 39) required inotropic support, 11.3% (n = 32) required intravenous sedation and 5.7% (n = 16) required prostaglandin infusion. Close to 40% of all cardiac referred patients required prostaglandin infusion during transport, (n = 16). The remaining transport details can be found in Table 4.

Complications

A total of 84 complications were documented in 71 patients (25.1%), with 13 patients (18.3%) affected by >1 complication (12 patients having two complications and 1 patient having three complications). The most common complication encountered was 30.6% mild acidosis, followed by 8.1% hypothermia, and 7.1% mild alkalosis. The remaining number of critical and serious complications immediately after transport are summarised in Table 2.

Interventions

Thirty-six patients required interventions during transport or within 1 hr of admission. Six patients required two interventions during transport or within 1 hr of admission. A total of 39 interventions were required from 36 patients (12.7%), with over 60% requiring interventions in fluid resuscitation (61.5%), followed by correction of hypoglycaemia (12.8%) and commencement of inotropic support (12.8%), respectively. The remaining interventions are described in Table 3.

Table 5: Dispatch time. Calculated for all possible patients and comparison to the agreed transfer urgency status

Transfer urgency,	Day time n, (%) n = 123	Out of hours n, (%) n = 56	Total Number n, (%) n = 179	Mean ± SD (hours: mins)	Number, (%) over transfer urgency time
TC	30 (65.2)	16 (34.8)	46 (25.7)	00:33 ± 00:15	1 (2.2)[g]
U	73 (66.4)	37 (33.6)	110 (61.5)	00:59 ± 00:33	2 (1.8)[h]
P	9 (81.8)	2 (18.2)	11 (6.1)	02:04 ± 01:37	0 (0)
E	11 (91.7)	1 (8.3)	12 (6.7)[i]	04:27 ± 04:35	n/a (n/a)

TC – Time critical ≤ 1-h dispatch from our hospital, U – Urgent ≤ 2-h dispatch from our hospital, P Priority < 8-h dispatch from our hospital, E – Elective

[g]One patient exceeded the Time critical transfer urgency time of ≤ 1-h dispatch, time 01:10. It was an out of hours transfer

[h]Two patients exceeded the Urgent transfer urgency time ≤ 2-h dispatch, times 02:02 and 04:47. The 04:47 h dispatch time was delayed as the CCT team was already out on transfer earlier in day and had to return to our hospital and pre-prepare again for this retrieval. This was an out of hours transfer

[i]Means and SD calculated from the 12 patients with all available data. 13 patients had missing referral times so unable to calculate their dispatch times. In total 25 patients were transferred as an elective case

Dispatch times

The dispatch times were calculated for each transfer. Only three cases exceeded their respective transfer urgency classification (n = 3); the CCT team was able to leave our hospital within 98.3% of their agreed-upon dispatch time. The means and standard deviations (SD) are described in Table 5.

Seventy percent of transfers were emergency transports (n = 167). Unsurprisingly, most transfers were retrievals (n = 235) and most transfers occurred during daytime hours (n = 218). The two cross-border retrievals with China and Macao; one case initially referred from Shanghai but retrieved at the Shenzhen–Hong Kong border in 2021 and the other case was retrieved at the Hong Kong–Zhuhai–Macao Bridge in 2022. The mean transport time was 34 ± 16 minutes. When comparing out of hours versus daytime mean transport times, it was 31 ± 14 and 34 ± 16 minutes, respectively (P = 0.17). The mean dispatch time for priority, urgent and time critical transfers were calculated which was 57 ± 43 minutes, and when comparing out-of-hours versus daytime dispatch time 50 ± 24 and 59 ± 49 minutes, respectively, there is no statistical significance (P = 0.20)

Mortalities

A total of three cases (1.1%) were non-transport-related deaths within 7 days of admission/transfer. Each of the cases was the withdrawal of care secondary to their underlying disease.

Discussion

To the author's best knowledge, this is the first-ever review of data from a designated and specialised paediatric CCT team in our city. These results provide a good baseline of information and may help shape the future planning for further services at our hospital as the service of the CCT team expands in the workforce to cover more clusters and regional hospitals within our city.

During the 3-year study with centralised tertiary care, on average 94 cases per year were retrieved or repatriated to/from our hospital, this is comparable to a previous similar local study (n = 85/year) over 3 years of data collection NICU/cardiac intensive care unit at another regional hospital in our city.[14] This study was before the relocation of central services and transports were not performed by a designated specialised CCT team.

Our city has a land area of approximately 1100 km^2, however, the distribution of clusters, hospitals, and the CCT service currently meant the average distance travelled in this study was only 11.6 km, with an average transport time of 34 min. This is considerably lower when compared with other geographic regions like Australia; whose Victoria State Neonatal retrieval service between July 2014 and December 2016 retrieved a total of 118 patients receiving high flow in which road distance median was 24 km (range 1–320 km) and 262 km (75–753 km) via air fixed-wing transport.[15] When compared with a 5-year review of Singapore, a country with a land area of 724 km^2; their transport team Children's Hospital Emergency Transport Service (CHETS), which also covers neighbouring Malaysia found that 98% were land transfers. A total of 164 neonates were transferred (~32 infants/year). Unfortunately, due to unavailable data close to 40% of the transport times from the CHETS study were incomplete, secondary analysis of the data to benchmark or compare the quality of CHETS to our data was unobtainable.[16]

Our findings of 60% of cardiac patients transferred requiring cardiothoracic surgery (26 of 43), was comparable to the Singaporean data of 64% requiring cardiothoracic surgery (11 of 17). This highlights one of the benefits of a centralised tertiary centre with skilled paediatric cardiologists and paediatric cardiothoracic surgeons all being under one roof. Before the centralisation of services, ~46% (n = 117/256) were referred for a cardiac assessment, however, within this study, participants came

from both private and public regional hospitals and the authors are unsure how many of the cardiac referrals required cardiothoracic surgery.[14]

Regarding overall complications, our study revealed we had a complication occurrence rate of 25% from a total of 84 complications documented in 71 patients, which is lower than data reported around the world. A study from Western Australia comparing neonatal specialist and non-neonatal specialist transport teams found their total unintended events ranging between 57% (28/49) versus 77% (54/70).[17]

A Taiwanese study comparing the outcome of transported neonates between two study periods; following the establishment of a transport neonatal network and the implementation of National Health Insurance found a statistical significance in a decrease in infant mortality (19.7% vs. 9.3%, $P < 0.01$). This individual study highlighted the importance of a specialised and trained transport team and outcomes in infant mortality. However, despite the statistically significant decrease in infant mortality, complications during transport like hypothermia remained similar (20.7% vs. 19.8%), but there was a marked improvement in the incidence of hypoglycaemia (26.8% vs. 13%, $P < 0.01$) and acidaemia (35.3% vs. 26%, $P < 0.01$).[18]

Our results, when benchmarked to the Taiwanese study showed an improvement in the areas of hypothermia (8.1%) and any hypoglycaemia (critical or serious) (1.8%) complications.

One of the thoughts, regarding our result of mild acidosis (30.6%) is comparable with existing data, which is due to the patient cohort being transferred with over 40% requiring surgery. The mild acidosis may reflect the underlying disease or patient's condition. The patients were transferred to a predominant neonatal surgical and cardiothoracic centre for surgery.

While, a Cochrane review by Chang *et al.*[19] did not find any reliable evidence to support or refute the efficacy and clinical outcomes of the specialised neonatal transport team, our data when compared with Yan Leung et al.,[14] a similar retrospective study in the same geographic area following the centralisation of tertiary services and the introduction of a standardised workflow and designated CCT team showed, in general, a decrease in both the number of complications encountered (n = 71/283, 25.1% vs. n = 113/256, 44%) and interventions required (n = 36/283, 12.7% vs. 59/256, 23%); validating and re-enforcing the requirement and need for a specialised CCT team in our city.

The dispatch time when compared with the transfer urgency classification was reassuring and markedly high when compared to international standards (98.3% of cases from 179 were able to dispatch within their time allocation). In comparison to all the neonatal transfer teams within the UK in 2019/2020, the percentage of time-critical transfers dispatched within 60 min by their respective specialised neonatal transfer teams ranged from 38% to 100%.[20] Our result has set the bar high for the future which may or may not decrease as the scope of the services increases in terms of hospital service coverage to other clusters or as the number of cases being referred for transfer increases.

The limitations of this study are that it was a retrospective single-centre study, despite the best efforts of electronic and going through handwritten documentation; there was missing data, especially on referrals time, which meant it was difficult to calculate the dispatch time. Another limitation due to the retrospective nature of the study is the lack of gauging the true disease severity of the patient diagnosis via a validated subjective scoring system like the Paediatric Risk of Mortality score, specifically when considering comparing with a similar population cohort.[21] There can be a consideration for selection bias, however, our study includes only transfers by the CCT team. The remaining transfers to NICU by other regional hospital teams were excluded as their regional hospital at the time was not in the current workflow design. Subsequently, post-design of this study the CCT coverage for neonatal transfers to date now includes seven of the eight NICUs in the city.

The repatriated cases; although more stable following their intervention at our hospital, were included as they were still requiring intensive care and transported back to their respective regional NICUs for further rehabilitation.

Conclusions

This study has shown 3 years of data on the first designated CCT team in our city. Over a total of 283 transports, the total number of complications was 25.1% and the total number of interventions required was 12.7%. While, it is difficult at the best of time to truly compare transport teams for outcomes due to multiple confounders such as the patient cohorts, geographical distances, and even the mode of transport; this study provides a good benchmark for the introduction of a designated and standardised workflow for a CCT team at a centralised tertiary level children's hospital. This study also identifies areas of enhancement for subsequent quality improvement projects in the future.

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Conflicts of interest
There are no conflicts of interest.

Author contributions
YY Chee designed the study, supervised all aspects of the research, supervised analyses, interpreted the results and reviewed and approved the final version. YW Tan collected the data, conducted interpreted analyses, wrote the initial draft, and reviewed and approved the final version. AWM Choi, M Behera, A Dudi, ZGK Hung, E Man, BKY Ng, SW Yim, and RMS Wong all assisted in data collection, data analysis and reviewed and approved the final version.

Data availability statement
Data is available upon reasonable request made to the corresponding author.

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