Factors associated with failure of using high flow nasal cannula in children

Kanokkarn Sunkonkit | Supakanya Kungsuwan | Sukanlaya Seetaboot | Sanit Reungrongrat

Division of Pulmonary and Critical Care, Department of Pediatrics, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand

Abstract

Introduction: High flow nasal cannula (HFNC) has significantly success in treating acute respiratory distress while HFNC failure dramatically increases mortality and morbidity.

Objective: To describe factors associated with failure of HFNC use in children.

Methods: We performed a retrospective observational study using demographic and laboratory findings. We compared clinical and laboratory variables in both successful and failed HFNC groups. The correlations between factors and HFNC failure were constructed by binary logistic regression analysis.

Results: Between August 2016 and May 2018, 250 children receiving HFNC (median age 16 months; range 1–228 months, male 50.8%) were enrolled. Pneumonia was the most common cause of respiratory distress, and the median length of stay (LOS) in hospital was 11 days. HFNC failure was found 16.4% while HFNC complication was 4.8% including epistaxis, pressure sore, and gastric distension. Based on multivariable logistic regression analysis, factors associated with HFNC failure were children with congenital heart disease comorbidity (p = 0.005), HFNC use with maximum FiO2 > 0.6 (p = 0.021), lobar infiltration on chest X-ray (p = 0.012), the reduction of heart rate, and respiratory rate <20% after 1 h of HFNC use (p = 0.001 and p = 0.001, respectively).

Conclusion: HFNC is feasible to use for children with respiratory distress; however, patients with congenital heart disease, using HFNC with FiO2 > 0.6, lobar infiltration on chest X-ray should be closely monitored. Heart rate and respiratory rate are important parameters in addition to clinical assessment for evaluating HFNC failure in children.

Abbreviations: BiPAP, bi-level positive airway pressure; BW, body weight; CAP, community-acquired pneumonia; CBC, complete blood count; CPAP, continuous positive airway pressure; FiO2, fraction of inspired oxygen; GA, gestational age; HFNC, high flow nasal cannula; IQR, interquartile range; kg, kilograms; LOS, length of stay; LPM, liters per minute; NIV, non-invasive ventilation; OR, odds ratio; pCO2, partial pressure of carbon dioxide; PICU, pediatric intensive care unit; PRISM III, Pediatric Risk of Modified III scores; RR, relative risk; SLE, systemic lupus erythematosus; SpO2, oxygen saturation.

This work was conducted at Chiang Mai University Hospital, Chiang Mai, Thailand. All authors have seen and approved the manuscript. This has not been previously published.

© 2022 The Authors. The Clinical Respiratory Journal published by John Wiley & Sons Ltd.
1 | INTRODUCTION

High flow nasal cannula (HFNC) is extensively used as an important non-invasive respiratory support.\textsuperscript{1–4} Many studies show that most patients are more comfortable with HFNC than a face mask.\textsuperscript{1–3,5} A high flow system, depending on the size and type of nasal cannula, refers to flow rate \( \geq 2 \) L/min (LPM) despite a range from 4 to 70 LPM.\textsuperscript{5,6} HFNC is composed of a heated and humidified mixture of oxygen and airflow, which is greater than the inspiratory flow of the patient, so the patient can obtain fixed fraction of inspired oxygen (FiO\(_2\)).\textsuperscript{6,7} In regard to respiratory support, HFNC has reported plenty of advantages to reduce the intubation and improve both oxygenation and ventilatory status.\textsuperscript{1–6,8} Previous studies have mentioned the mechanisms of HFNC including decreased inspiratory resistance, washout rebreathing of carbon dioxide gas, decreased metabolic work, maintaining positive airway pressure, and improving mucociliary clearance.\textsuperscript{1,4,6,8–13} Consequently, HFNC can improve oxygenation, reduce the respiratory rate, work of breathing, and endotracheal intubation rate.\textsuperscript{14–16} On the other hand, some adverse effects of HFNC are air leak syndrome (pneumothorax and pneumomediastinum), nasal bleeding, noise emissions, abdominal distension, and delayed intubation.\textsuperscript{1,17,18}

Recent studies have demonstrated that the HFNC failure rate ranges from 6.0 to 24.4\%\textsuperscript{18–24}, however, a few studies demonstrated the risk factors of HFNC failure in children. This study aims to describe the factors associated with HFNC failure in children and complications in order to ensure and improve the management and outcome in the future.

1.1 | Objectives

The first objective of our study was identifying factors associated with HFNC failure in children. The second objective was to characterize the complications from HFNC use.

2 | MATERIALS AND METHODS

2.1 | Study design

This was a single-center, retrospective chart review of children using HFNC in a tertiary care hospital in pediatric intensive care (PICU) and outside PICU between August 2016 and May 2018 at Pediatric Department, Faculty of Medicine, Chiang Mai University Hospital, Chiang Mai, Thailand. A retrospective review was approved by the Institutional Review Board at the Research Ethics Committee, Faculty of Medicine, Chiang Mai University Hospital (Study code: PED-2561-05570), with a waiver of informed consent granted.

2.2 | Patient population

Inclusion criteria was pediatric patients aged 1 month to 15 years of age who used HFNC at Chiang Mai University Hospital. Exclusion criteria was the pediatric patient who were on tracheostomy. The patient data including age, sex, date of admission and discharge from hospital, history of prematurity (defined as born prior to 37 weeks gestational age [GA]), history of intubation, underlying diseases, diagnosis, length of stay (LOS) in hospital, place where HFNC used, infiltration pattern on chest X-ray, initial vital signs, and vital signs after HFNC use were collected. HFNC data including maximum total flow, FiO\(_2\), duration, outcome, and complication of HFNC use were recorded. HFNCs are available in both pediatric general ward and PICU setting. HFNC initiation and monitoring in this study were based on Figure S1. HFNC failure was defined as need for intubation or non-invasive ventilation (NIV) support; however, continuous positive airway pressure (CPAP) and bi-level positive airway pressure (Bi-level PAP) were not available in our pediatric ward setting. Therefore, the pediatric patients who were prescribed HFNC and failed in our institute will be intubated and transfer to PICU.

2.3 | High flow nasal cannula devices

HFNC therapy in our institution uses the GGM HF-2900 Humidoflo\textsuperscript{®} HFT system (Great Group Medical, Changhwa, Taiwan). Enrollment for HFNC management was based on the decision of physicians following HFNC recommendations. The HFNC guidelines follow the Pediatric HFNC guideline at the Pediatric Pulmonary and Critical Care Division, Chiang Mai University Hospital (Figure S1). Regarding the guidelines, indications for using HFNC included hypoxemia with respiratory distress due to acute bronchiolitis or pneumonia, chronic lung disease, congestive heart failure, and respiratory support post-extubation. The guidelines also suggested that contraindications included pneumothorax, congenital lung cyst, severe upper airway obstruction, and no spontaneous breathing. The cannula size was chosen,
which did not occlude more than 50% of the internal diameter of each the nares. According to HFNC setting, the flow rate started at 2 L/min/kg and increased by 0.5 L/min/kg as work of breathing required or fair air entry, but not exceed total flow of 2 L/min/kg; FiO2 started at 0.6 and titrated as needed to achieve target oxygen saturation (SpO2); and set temperature at 34–37°C and was adjusted to the patient performance. After using HFNC, vital signs (heart rate, respiratory rate, and oxygen saturation [SpO2]), clinical status, work of breathing, chest X-ray, and blood gas were monitored. HFNC use was discontinued when patients needed more respiratory support such as intubation or NIV. In the other hand, if the patients improved from their respiratory distress, HFNC weaning protocol would be considered.

2.4 | Statistical analysis

Data analysis was carried out using IBM SPSS 23.0. The demographic data were evaluated by descriptive statistics. Normally distributed continuous variables were compared using Student’s t tests, and skewed continuous variables were compared using Mann–Whitney U test. Categorical data were evaluated by chi-square test or Fisher’s exact test. A p value less than 0.05 indicated statistical significance. The correlations between factors and HFNC failure were constructed by logistic regression analysis.

3 | RESULTS

3.1 | Demographic data

Two hundred and fifty pediatric patients using HFNC due to respiratory distress were admitted between August 1, 2016, and May 31, 2018. Table 1 demonstrated the information regarding demographic and clinical data between HFNC success and the failure groups. According to the information, the median age was 16 months (interquartile range [IQR]: 6–38.25), and half of the pediatric patients (127 patients; 50.5%) were males. Sixty-one of 250 patients (24.4%) were born prior to GA 37 weeks while 17 patients (6.8%) had a history of intubation. The most common cause of respiratory distress was pneumonia found in 6.8% had a history of intubation. The most common cause of respiratory distress was pneumonia found in 143 patients (57.2%). Other causes of respiratory distress were acute bronchiolitis in 53 patients (21.2%), post-extubation stridor in 44 patients (17.6%), and congestive heart failure in 10 patients (4%). Half of the patients (50%) had underlying diseases. For the underlying diseases, congenital heart disease were identified in 73 patients (29.2%), chronic lung disease occurred in 21 patients (8.4%), neuromuscular disorder occurred in 12 patients (4.8%), systemic lupus erythematosus (SLE) occurred in 6 patients (2.4%), thalassemia occurred in 5 patients (2.0%), hematologic malignancy occurred in 5 patients (2.0%), and short bowel syndrome occurred in 3 patients (1.2%). Overall, using HFNC at general pediatric ward was equivalent to 52.4% (n = 131), while the failure of HFNC use following with intubation was 16.4% (n = 41). The median of intubation time was 26 h (IQR: 0–144). The median of total flow rate and FiO2 used in both successful and failed groups were 1 L/min/kg (IQR: 1–2), 1.8 L/min/kg (IQR:1–2), FiO2 0.6 (IQR:0.6–0.6), and 0.6 (IQR:0.6–0.7), respectively. The median LOS in hospital was 11 days (IQR: 7.0–23.25) while the median duration of HFNC use was 48 h (IQR: 19.0–72.0). On chest X-ray, we found perihilar infiltration in 139 patients (55.6%), interstitial infiltration in 44 patients (17.6%), hyperinflation with atelectasis in 43 patients (17.2%), and lobar infiltration in 24 patients (9.6%). Most patients used HFNC without complication (95.2%); however, the complications from HFNC such as gastric distension in 7 patients (2.8%), nose pressure sore in 4 patients (1.6%), and epistaxis in 1 patient (0.4%) occurred.

The comparison of baseline characteristic of patients between HFNC success and failure groups was shown in Table 1. The patients using HFNC successfully had older age (117 months [56%] vs. 30 [73.2%], p = 0.041) and history of preterm (43 patients [20.6%] vs. 18 patients [43.9%], p = 0.001) compared with the other group. More than half of both groups had a diagnosis of pneumonia. The second most common diagnosis in the HFNC success group was acute bronchiolitis while the other group had congestive heart failure. Most patients in the HFNC group had no underlying disease while nearly one-third of the comorbidities of patients in the HFNC failure group had congenital heart disease comorbidity. Both patients in HFNC success and failure groups used HFNC at pediatric ward (116 patients [55.5%] vs. 15 patients [36.6%], p = 0.027). Moreover, baseline characteristics including maximum FiO2, duration of HFNC use, lobar infiltration on chest X-ray, and LOS in hospital were different between the HFNC success and failure group with statistical significance. However, our study found that there were no statistical differences between groups in terms of sex, body weight (BW), history of intubation, initial heart rate, initial respiratory rate, maximum total flow rate, complete blood count (CBC), electrolyte, and complications.

3.2 | Clinical parameters associated with HFNC failure

From the multivariable logistic regression analysis, patients being younger than 2 years of age, history of preterm birth, and using HFNC in PICU were not associated with HFNC failure. Among all the results, the presence
| Parameters                                                                 | HFNC outcome |           |           | p value  |
|---------------------------------------------------------------------------|--------------|-----------|-----------|----------|
|                                                                           | Success (n = 209) | Failure (n = 41) |           |          |
| Age < 2 years old, n (%)                                                  | 117 (56.0)   | 30 (73.2)  |           | 0.041*   |
| Sex (Male: Female)*                                                       | 0.95: 1      | 1.56: 1    |           | 0.154    |
| Body weight (kg)                                                           | 8 (5.0, 12.0)* | 7 (4.0, 10.0)* |           | 0.075    |
| History of preterm (GA < 37 weeks), n (%)                                 | 43 (20.6)    | 18 (43.9)  |           | 0.001*   |
| History of intubation, n (%)                                              | 12 (5.7)     | 5 (12.2)   |           | 0.168    |
| Diagnosis                                                                 |              |           | 0.006*    |          |
| Pneumonia, n (%)                                                           | 115 (55.0)   | 28 (68.3)  |           |          |
| Acute bronchiolitis, n (%)                                                | 49 (23.4)    | 4 (9.8)    |           |          |
| Post-extubation stridor, n (%)                                            | 40 (19.1)    | 4 (9.8)    |           |          |
| Congestive heart failure, n (%)                                           | 5 (2.4)      | 5 (12.2)   |           |          |
| Underlying disease                                                         |              |           | <0.001*   |          |
| No underlying disease, n (%)                                              | 125 (59.8)   | 0 (0.0)    |           |          |
| Chronic lung disease, n (%)                                               | 19 (9.1)     | 2 (4.9)    |           |          |
| Congenital heart disease, n (%)                                           | 44 (21.1)    | 29 (70.7)  |           |          |
| Others, n (%)                                                              | 21 (10.0)    | 10 (24.4)  |           |          |
| HFNC use                                                                   |              |           | 0.027*    |          |
| at ward, n (%)                                                             | 116 (55.5)   | 15 (36.6)  |           |          |
| in PICU, n (%)                                                             | 93 (44.5)    | 26 (63.4)  |           |          |
| Initial heart rate (/min)                                                 | 145 (130.0, 160.0)* | 150 (140.0, 155.0)* |           | 0.514    |
| Initial respiratory rate (/min)                                           | 48 (40.0, 52.0)* | 48 (40.0, 54.0)* |           | 0.629    |
| Max. total flow rate (L/min/kg)                                           | 1 (1.0, 2.0)* | 1.8 (1.0, 2.0)* |           | 0.053    |
| Max. FiO₂                                                                  | 60 (60.0, 60.0)* | 60 (60.0, 70.0)* |           | < 0.001* |
| Duration of HFNC use (hour)                                               | 48 (28.0, 84.0)* | 4 (2.5, 9.0)* |           | < 0.001* |
| Hemoglobin (g/dl)                                                          | 11 (9.8, 12.6)* | 10.7 (9.2, 11.2)* |           | 0.064    |
| White blood cell count (cells/mm³)                                        | 10 160 (7780, 14 395)* | 12 100 (8635, 16 205)* |           | 0.156    |
| Platelet count (cells/mm³)                                                | 253 000 (212 000, 316 000)* | 267 000 (195 000, 312 000)* |           | 0.550    |
| Sodium (mmol/L)                                                            | 136 (133.0, 138.0)* | 135 (132.5, 138.0)* |           | 0.255    |
| Potassium (mmol/L)                                                         | 3.8 (3.5, 4.2)* | 3.7 (3.2, 4.2)* |           | 0.109    |
| Chloride (mmol/L)                                                          | 100 (97.0, 103.0)* | 98 (96.0, 103.0)* |           | 0.471    |
| Total CO₂ (mmol/L)                                                         | 20 (18.0, 25.0)* | 20 (18.0, 27.0)* |           | 0.761    |
| Chest X-ray                                                                |              |           | <0.001*   |          |
| Lobar infiltration, n (%)                                                 | 8 (3.8)      | 16 (39.0)  |           |          |
| Others, n (%)                                                              | 201 (96.2)   | 25 (61.0)  |           |          |
| LOS in hospital (days)                                                     | 8 (6.0, 21.0)* | 22 (16.0, 41.5)* |           | <0.001* |
| Complication                                                               |              |           |          |          |
| No complications, n (%)                                                    | 199 (95.2)   | 39 (95.1)  |           | 0.933    |
| Epistaxis, n (%)                                                           | 1 (0.5)      | 0 (0.0)    |           |          |
| Pressure sore, n (%)                                                       | 3 (1.4)      | 1 (2.4)    |           |          |
| Gastric distension, n (%)                                                 | 6 (2.9)      | 1 (2.4)    |           |          |

Abbreviations: dl, deciliter; FiO₂, fraction of inspired oxygen; g, grams; GA, gestational age; HFNC, high flow nasal cannula; kg, kilograms; L, liter; LPM, liter per minute; LOS, length of stay; mm³, cubic millimeter.

*Median (interquartile range; IQR).

*Statistically significant p < 0.05.
of congenital heart comorbidity (RR 6.36, 95% CI, 1.74–23.17; \( p = 0.005 \)), using HFNC with maximum FiO\(_2\) > 0.6 (RR 4.23, 95% CI, 1.24–14.37; \( p = 0.021 \)), presence of lobar infiltration on chest X-ray (RR 5.85, 95% CI, 1.48–23.18; \( p = 0.012 \)), and reduction of heart rate and respiratory rate less than 20% after HFNC use for 1 h (RR 16.69, 95% CI, 3.39–82.27; \( p = 0.001 \) and RR 8.79, 95% CI, 2.47–31.26; \( p = 0.001 \), respectively) were dramatically associated with HFNC failure (Table 2).

### 4 | DISCUSSION

This study demonstrates that HFNC is an effective non-invasive respiratory support in children. Overall, our study provides the information that HFNC use is favorable for respiratory distress in children starting age from 1 to 228 months, especially pneumonia and acute bronchiolitis without outstanding complications such as pneumothorax or pneumomediastinum. Our study found that patients without underlying disease had a greater HFNC success rate. We found that HFNC failure rate was 16.4%, compared with other studies ranging from 6 to 24.4%.\(^{18-24}\) Our study had two times higher HFNC failure rate than the data by Better et al.\(^{21}\) who studied 231 pediatric patients using HFNC outside PICU, retrospectively (HFNC failure rate was 6%). Vareesunthorn et al.\(^{23}\) described in a 3-year retrospective study of 99 pediatric patients aged <5 years, admitted to a pediatric ward with the diagnosis of community-acquired pneumonia (CAP) using modified HFNC with a failure rate of 7%. In contrast, our HFNC failure rate was less than Kallappa et al.\(^{24}\) who studied HFNC use in bronchiolitis patients for 3 years and found that intubation rate was 24.4%, approximately 1.5 times higher than our study. On the other hand, Bressan et al.\(^{25}\) who demonstrated in a prospective observational pilot study in 27 infants with acute bronchiolitis treated with HFNC in a general ward showed no negative outcome from HFNC. This study excluded infants with cardiac history, recurrent wheezing, chronic lung disease, neuromuscular disease, home oxygen dependence, and history of a tracheostomy, but our study included all of patients treated with HFNC with several underlying diseases, which caused our study to have a higher failed HFNC rate.\(^{23}\) Furthermore, this difference is due to local factors from physician decision, progression of disease, underlying diseases, and availability of resources such as nurse to patient ratio.

Based on the multivariable logistic regression analysis, we found that the presence of congenital heart comorbidity (\( p = 0.005 \)), HFNC use with maximum FiO\(_2\) > 0.6 (\( p = 0.021 \)), lobar infiltration on chest X-ray (\( p = 0.012 \)), and the reduction of heart rate and respiratory rate less than 20% after 1 h HFNC use (\( p = 0.001 \) and \( p = 0.001 \), respectively) were associated with increasing HFNC failure. However, our finding found no differences of HFNC failure rate in younger children than 2 years of age, preterm, using HFNC at ward or PICU, initial heart rate, and respiratory rate. Comparing with other studies, Better et al. retrospectively examined patients using HFNC outside PICU concluding that higher FiO\(_2\) requirement (OR = 38.3, 95% CI: 4.0–366.3; \( p = 0.002 \)), diagnosis less likely to be bronchiolitis (OR = 0.3, 95% CI: 0.1–0.9; \( p = 0.048 \)), history of intubation (\( p = 0.046 \), and cardiac comorbidities (\( p = 0.026 \)) are related with HFNC failure.\(^{21}\) Vareesunthorn et al. with a 3-year retrospective study in children <5 years implied that the SpO\(_2\)/FiO\(_2\) ratio <264 and higher FiO\(_2\) requirement are associative predictors of HFNC failure.\(^{23}\) Abboud et al. studied 113 patients with viral bronchiolitis using HFNC in PICU found HFNC failure 18.6%, which was associated with initial respiratory rate (\( p < 0.001 \)), pCO\(_2\) before and after HFNC use (\( p < 0.001 \)) and (\( p < 0.001 \), respectively, and higher Pediatric Risk of

| Parameters                              | HFNC outcome | Relative risk (95% CI) | \( p \) value |
|-----------------------------------------|--------------|------------------------|---------------|
| **Age <2 years old**                    | Success (n = 209) | 117 (56.0) | 30 (73.2) | - | 0.950 |
| History of preterm                      | 43 (20.6) | 18 (43.9) | - | 0.809 |
| Congenital heart disease comorbidity    | 44 (21.1) | 29 (70.7) | 6.36 (1.74–23.17) | 0.005* |
| HFNC use in PICU                        | 93 (44.5) | 26 (63.4) | - | 0.284 |
| Max FiO\(_2\) > 0.6                     | 32 (15.3) | 14 (34.1) | 4.23 (1.24–14.37) | 0.021* |
| Decrease heart rate <20% after HFNC use | 4 (1.9) | 22 (53.7) | 16.69 (3.39–82.27) | 0.001* |
| Decrease respiratory rate <20% after HFNC | 10 (4.8) | 28 (68.3) | 8.79 (2.47–31.26) | 0.001* |
| Lobar infiltration on chest X-ray       | 8 (3.8) | 16 (39.0) | 5.85 (1.48–23.18) | 0.012* |

**TABLE 2** Factors associated with HFNC failure in children (n = 250)

Abbreviations: FiO\(_2\), fraction of inspired oxygen; HFNC, high flow nasal cannula; PICU, pediatric intensive care unit.

*Statistically significant \( p < 0.05 \).
Based on our study, younger age and history of preterm were not associated with HFNC failure, which was similar to Betters and Abboud et al. studies. Betters et al. found that maximum flow (ml/kg) of HFNC was not different between HFNC success and the failure group (median 714.3 [IQR: 487.8–1041.7] vs. 629.1 [IQR: 476.2–1041.7], p = 0.787), and Vareesunthorn et al. revealed that maximum total flow rate per kilogram was not different between the success and failure groups (1.3 ± 0.4 vs. 1.5 ± 0.4, p = 0.358). Optimal total flow rate and FiO2 adjusted following clinical signs and symptoms bring about effective respiratory support. Higher FiO2 requirement is another factor associated with HFNC failure, which were found in Betters and Vareesunthorn et al. studies as well as our study. Moreover, those studies appeared that a high maximum FiO2 could predict HFNC failure (FiO2 0.4 [IQR: 0.3–0.6] vs. FiO2 1.0 [IQR: 0.6–1.0], p < 0.001 and FiO2 0.38 ± 0.08 vs. FiO2 0.53 ± 0.11, p < 0.001, respectively). Patients having more severity of disease or progression of disease require higher oxygen requirement or higher respiratory support such as invasive ventilation. Our study revealed that the total flow rate was not related to HFNC failure; thus, FiO2 might be a substantial predictor for HFNC failure.

Children with congenital heart disease comorbidity and lobar infiltration on chest X-ray both revealed significant values in the logistical regression analysis, and may demonstrate significance in the setting of more patients. Children with congenital heart disease may present with increased work of breathing and hypoxia which might be concealed by positive airway pressure and high FiO2 by HFNC. Thus, this patient group required close monitoring and frequent reassessment after HFNC initiation.

Although initial heart rate and respiratory rate were not associated with HFNC failure in our study, the reduction of heart rate and respiratory rate less than 20% after 1 h HFNC use were associated with increasing HFNC failure significantly. This emphasizes that vital signs including heart rate and respiratory rate are important parameters in addition to clinical assessment for evaluating HFNC failure in children especially in the first hour after HFNC initiation.

This study shows the LOS in hospital was 11 days, however, with multifactorial issues impacting the duration, namely, clinical signs and symptoms of patients, progression of disease, cause of respiratory distress, other comorbidities, and different physician management. We illustrated that the failure group had less duration of HFNC use than the success group with statistical significance, which was similar to Betters et al. study (p = 0.015) because of early further intervention. The complications from HFNC in our study, unrelated to HFNC failure, such as gastric distension, nose pressure sore, and epistaxis, were comparable with Slain et al. study.

Our current study suggested that HFNC is still an effective treatment in respiratory distress in children in order to improve the work of breathing and decrease intubation rates. HFNC can ameliorate the work of breathing with the mechanisms of HFNC such as inspiratory resistance reduction, washout rebreathing gas, decreased metabolic work, providing positive airway pressure, and improving mucociliary clearance. In addition, HFNC is easy to use, comfortable, and tolerable, which makes HFNC is attractive and broadly used in children and adults. However, we suggested that close monitoring should be considered in HFNC use, especially in high-risk groups for early detection for non-responders and not to delay intubation. The failure of HFNC and delaying intubation results in higher morbidity, mortality, and prolonged mechanical ventilation.

There are some notable limitations to our study that require consideration. First, this is a retrospective study, so some laboratory data such as electrolytes and some management were not available for analysis. Second, time of initiation, initial flow, and discontinuing HFNC are highly changeable based on clinical status of patients and dependent on physician experience, pleasure, and preference. Third, NIV was not available in our pediatric ward setting. The patients who were prescribed HFNC and failed will be intubated and transfer to PICU. So, the data regarding comparison of effectiveness and duration of CPAP and bi-level PAP were not available. Finally, co-treatment such as sedation techniques, feeding during HFNC, and IV fluid therapy, which may impact on decision making and HFNC failure, is unable to address in this current study design. Therefore, future prospective studies are required to illustrate the outcome of the HFNC guidelines, effects of co-treatment, cost-effectiveness, safety concerns, long-term benefits, and socio-economic impact in pediatric patients.

5 | CONCLUSIONS

HFNC, a useful non-invasive respiratory treatment, is practicable in children with respiratory distress. However, patient who have congenital heart disease comorbidity, using HFNC with FiO2 > 0.6, lobar infiltration on chest X-ray, heart rate, and respiratory rate decreased less than 20% after HFNC use for 1 h should be closely
monitored because of higher risk of HFNC failure. Heart rate and respiratory rate are important parameters in addition to clinical assessment for evaluating HFNC failure in children.

ACKNOWLEDGMENTS
The authors would like to thank all patients who participated in this study. The authors also wish to acknowledge the contribution of the staff of Division of Pulmonary and Critical Care, Department of Pediatrics, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand.

AUTHOR CONTRIBUTIONS
Kanokkarn Sunkonkit, M.D., was responsible for the study concept, study design, interpretation of results, data collection, preparation of the first draft of the manuscript, data analysis, editing of manuscript drafts, and approval of the final version of the manuscript. Supakanya Kungsuwan, M.D., was responsible for the editing of manuscript drafts and approval of the final version of the manuscript. Sukanlaya Seetaboot, M.N.S., was responsible for the data collection and approval of the final version of the manuscript. Sanit Reungrongrat, M.D., was responsible for the editing of manuscript drafts and approval of the final version of the manuscript.

CONFLICT OF INTEREST
The authors declare no conflict of interest.

ETHICS STATEMENT
This study was approved by the Ethics Committee of the Faculty of Medicine, Chiang Mai University, Thailand (study code: PED-2561-05570). The requirement of informed consents was waived by the Ethics Committee of the Faculty of Medicine, Chiang Mai University, Thailand.

DATA AVAILABILITY STATEMENT
Data are available on request due to privacy/ethical restrictions.

ORCID
Kanokkarn Sunkonkit https://orcid.org/0000-0003-2725-4636
Sanit Reungrongrat https://orcid.org/0000-0002-4056-3911

REFERENCES
1. Mikalsen IB, Davis P, Øymar K. High flow nasal cannula in children: a literature review. Scand J Trauma Resusc Emerg Med. 2016;24(1):1-12. doi:10.1186/s13049-016-0278-4
2. Milésí C, Boughal M, Jacquot A, et al. High-flow nasal cannula: recommendations for daily practice in pediatrics. Ann Intensive Care. 2014;4(1):1-7. doi:10.1186/s13613-014-0029-5
3. Roca O, Riera J, Torres F, Masclans JR. High-flow oxygen therapy in acute respiratory failure. Respir Care. 2010;55(4):408-413.
4. Kwon JW. High-flow nasal cannula oxygen therapy in children: a clinical review. Clin Exp Pediatr. 2020;63(1):3-7. doi:10.3345/kjp.2019.00626
5. Mayfield S, Jauncey-Cooke J, Hough JL, Schibler A, Gibbons K, Bogossian F. High-flow nasal cannula therapy for respiratory support in children. Cochrane Database Syst Rev. 2014;2014 (3):Cd009850.
6. Chao KY, Chien YH, Mu SC. High-flow nasal cannula in children with asthma exacerbation: a review of current evidence. Paediatr Respir Rev. 2021;40:52-57. doi:10.1016/j.prrv.2021.01.003
7. Nishimura M. High-flow nasal cannula oxygen therapy devices. Respir Care. 2019;64(6):735-742. doi:10.4187/respcare.06718
8. Slain KN, Shein SL, Rotta AT. The use of high-flow nasal cannula in the pediatric emergency department. J Pediatr (Rio J). 2017;93(Suppl 1):36-45. doi:10.1016/j.jped.2017.06.006
9. Dysart K, Miller TL, Wolfsen MR, Shaffer TH. Research in high flow therapy: mechanisms of action. Respir Med 2009;103(10):1400-1405. doi:10.1136/jor.2009.04.007
10. Hasani A, Chapman TH, McCool D, Smith RE, Dilworth JP, Agnew JE. Domiciliary humidification improves lung mucociliary clearance in patients with bronchiectasis. Chron Respir Dis. 2008;5(2):81-86. doi:10.1177/14799723070787190
11. Williams R, Rankin N, Smith T, Galler D, Seakins P. Relationship between the humidity and temperature of inspired gas and the function of the airway mucosa. Crit Care Med. 1996;24(11):1920-1929. doi:10.1097/00003246-199611000-00025
12. Lampland AL, Plumm B, Meyers PA, Worwa CT, Mammel MC. Observational study of humidified high-flow nasal cannula compared with nasal continuous positive airway pressure. J Pediatr. 2009;154(2):177-182. doi:10.1016/j.jpeds.2008.07.021
13. Spence KL, Murphy D, Kilian C, McGonigle R, Kilani RA. High-flow nasal cannula as a device to provide continuous positive airway pressure in infants. J Perinatol. 2007;27(12):772-775. doi:10.1038/sj.jp.7211828
14. Wing R, James C, Maranda LS, Armsby CC. Use of high-flow nasal cannula support in the emergency department reduces the need for intubation in pediatric acute respiratory insufficiency. Pediatr Emerg Care. 2012;28(11):1117-1123. doi:10.1097/PEC.0b013e31827122a9
15. McKieran C, Chuas LC, Visintainer PF, Allen H. High flow nasal cannulae therapy in infants with bronchiolitis. J Pediatr. 2010;156(4):634-638. doi:10.1016/j.jpeds.2009.10.039
16. Schibler A, Pham TM, Dunster KR, et al. Reduced intubation rates for infants after introduction of high-flow nasal prong oxygen delivery. Intensive Care Med. 2011;37(5):847-852. doi:10.1007/s00134-011-2177-5
17. Inoue S, Tamaki Y, Sonobe S, Egawa J, Kawaguchi M. A pediatric case developing critical abdominal distension caused by a combination of humidified high-flow nasal cannula oxygen therapy and nasal airway. JA Clin Rep. 2018;4(1):1-3. doi:10.1186/s40981-017-0143-0
18. Kang BJ, Koh Y, Lim CM, et al. Failure of high-flow nasal cannula therapy may delay intubation and increase mortality. *Intensive Care Med*. 2015;41(4):623-632. doi:10.1007/s00134-015-3693-5

19. Lee M Jr, Nagler J. High-flow nasal cannula therapy beyond the perinatal period. *Curr Opin Pediatr*. 2017;29(3):291-296. doi:10.1097/MOP.0000000000000494

20. Frat JP, Thille AW, Mercat A, et al. High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. *N Engl J Med*. 2015;372(23):2185-2196. doi:10.1056/NEJMoa1503326

21. Betters KA, Gillespie SE, Miller J, Kotzbauer D, Hebar KB. High flow nasal cannula use outside of the ICU; factors associated with failure. *Pediatr Pulmonol*. 2017;52(6):806-812. doi:10.1002/ppul.23626

22. Abboud PA, Roth PJ, Skiles CL, Stolfi A, Rowin ME. Predictors of failure in infants with viral bronchiolitis treated with high-flow, high-humidity nasal cannula therapy*. *Pediatr Crit Care Med*. 2012;13(6):e343-e349. doi:10.1097/PCC.0b013e31825b546f

23. Vareesunthorn I, Preuthiphan A. Modified high-flow nasal cannula in young children with pneumonia: a 3-year retrospective study. *Pediatr Respiril Crit Care Med*. 2018;2(3):45-50. doi:10.4103/prcm.prcm_2_18

24. Kallappa C, Hufton M, Millen G, Ninan TK. Use of high flow nasal cannula oxygen (HFNCO) in infants with bronchiolitis on a paediatric ward: a 3-year experience. *Arch Dis Child*. 2014;99(8):790-791. doi:10.1136/archdischild-2014-306637

25. Bressan S, Balzani M, Krauss B, Pettenazzo A, Zanconato S, Baraldi E. High-flow nasal cannula oxygen for bronchiolitis in a pediatric ward: a pilot study. *Eur J Pediatr*. 2013;172(12):1649-1656. doi:10.1007/s00431-013-2094-4

26. Carter C, Aedy H, Notter J. COVID-19 disease: non-invasive ventilation and high frequency nasal oxygenation: clinics in integrated care. *Clin Integr Care*. 2020;100006. doi:10.1016/j.intcar.2020.100006 PMID: Epub 2020 Jul 17.

27. Ohshimo S. Oxygen administration for patients with ARDS. *J Intensive Care*. 2021;9(1):1-14. doi:10.1186/s40560-021-00532-0

28. Drake MG. High-flow nasal cannula oxygen in adults: an evidence-based assessment. *Ann Am Thorac Soc*. 2018;15(2):145-155. doi:10.1513/AnnalsATS.201707-548FR

**SUPPORTING INFORMATION**

Additional supporting information can be found online in the Supporting Information section at the end of this article.

**How to cite this article:** Sunkonkit K, Kungsuan S, Seetaboot S, Reungrograt S. Factors associated with failure of using high flow nasal cannula in children. *Clin Respir J*. 2022;16(11):732-739. doi:10.1111/crj.13533