

# Early predictors of high-flow nasal cannula oxygen treatment failure in patients with respiratory distress admitted to the pediatric emergency department

Şule Demir<sup>1</sup>, Murat Anıl<sup>2</sup>, Gülşen Yalçın<sup>3</sup>, Şefika Bardak<sup>1</sup>, Gülşah Demir<sup>1</sup>,  
Emel Berksoy<sup>1</sup>, Gamze Gökalp<sup>1</sup>, Fulya Kamit<sup>4</sup>, Sema Bozkaya Yılmaz<sup>5</sup>,  
Ayşe Berna Anıl<sup>6</sup>

Departments of <sup>1</sup>Pediatric Emergency, <sup>5</sup>Pediatric Neurology and <sup>6</sup>Pediatric Intensive Care, University of Health Sciences, Tepecik Training and Research Hospital İzmir; <sup>2</sup>Department of Pediatric Emergency, Demokrasi University Faculty of Medicine, İzmir; <sup>3</sup>Department of Pediatric Emergency, Pediatric Hospital, Diyarbakır; <sup>4</sup>Department of Pediatric Intensive Care, Yeniüyüzyıl University Gaziosmanpaşa Hospital, İstanbul, Turkey.

## ABSTRACT

**Background.** High-flow nasal cannula (HFNC) therapy is a relatively new method used in patients with respiratory distress. The aim of the study was to evaluate the outcomes and to determine the baseline predictors of HFNC treatment failure in children with acute respiratory distress/failure in the pediatric emergency department.

**Methods.** Children with respiratory distress/failure aged 1 month to 18 years who underwent HFNC therapy with the pre-established protocol were retrospectively analyzed. HFNC therapy was used in respiratory and non-respiratory pathologies. HFNC failure was defined as the need for escalation to non-invasive ventilation or invasive mechanical ventilation. HFNC responders and non-responders were compared based on baseline clinical data.

**Results.** Of the 524 cases (median age:13 months; 292 males / 232 females), 484 (92.4%) had respiratory tract and 40 (7.6%) had non-respiratory tract pathologies. HFNC therapy was unsuccessful in 62 (11.8%) patients. The success rates were 81% and 55% in respiratory and non-respiratory diseases, respectively. In children with respiratory system pathologies, the pre-treatment venous pCO<sub>2</sub> level (p: 0.045; OR: 0.958; 95%CI: 0.821-0.990) and the clinically important radiological finding on chest X-ray (lobar infiltration, atelectasis, pleural effusion) (p: 0.045; OR: 3.262; 95%CI: 1.178-9.034) were the most significant parameters in predicting HFNC failure. In children with non-respiratory pathologies, the pre-treatment venous lactate level (p: 0.008; OR: 1.558; 95%CI: 1.125-2.158) was a significant predictor of HFNC failure. There were no cases of pneumothorax or any other reported adverse effects related to HFNC therapy.

**Conclusions.** HFNC treatment is a safe oxygen therapy in children with respiratory distress/failure due to various etiologies in the emergency department. The lower venous pCO<sub>2</sub> level increases and the clinically important radiological finding on chest radiograph decreases the success of HFNC treatment in respiratory pathologies. The higher venous lactate level is a predictor of HFNC treatment failure in non-respiratory pathologies.

**Key words:** pediatric emergency, oxygen therapy, respiratory distress, high-flow nasal cannula.

✉ Şule Demir  
sule287@hotmail.com

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High-flow nasal cannula (HFNC) oxygen therapy is one of the non-invasive methods of respiratory support therapy that is well tolerated by patients and has been used in neonates, infants, children, and adults in recent years.<sup>1-3</sup> The device consists of an air/oxygen

mixer, an active humidifier, a heated circuit, and a nasal cannula. Application and patient follow-up are extremely easy for healthcare providers. Reduction of anatomical dead space, positive end expiratory pressure effect, and the constant fraction of inspired oxygen are the physiological effects of HFNC. HFNC therapy decreases the work of breathing, improves oxygenation, and provides a continuous positive airway pressure (CPAP) effect for a range of respiratory distress pathologies.<sup>1,2,4,5</sup> However, non-invasive (NIV) and invasive mechanical ventilator (MV) support may be delayed if treatment is persisted even though no positive clinical effect is observed. This may adversely affect the patient's clinical outcomes. It is therefore important to predict the failure of HFNC oxygen therapy before and during treatment. However, there are very few studies to predict treatment failure, especially in the emergency department.<sup>2,5-7</sup>

Most of the studies in HFNC were performed on respiratory system diseases, especially bronchiolitis.<sup>3,8-10</sup> There are a limited number of studies in the literature on non-respiratory pathologies that may cause respiratory distress such as sepsis, heart failure, and metabolic diseases. Finally, the clinical studies were generally conducted in intensive care units.<sup>2,5-7</sup>

The aim of the study is to evaluate the clinical outcomes and to determine the baseline predictors of HFNC treatment failure for children with respiratory distress/failure in the pediatric emergency department.

## Material and Methods

The patients aged 1 month to 18 years who underwent HFNC oxygen treatment with a pre-established protocol between the dates of 01.01.2016 and 01.04.2018 in the pediatric emergency department of Tepecik Teaching and Research Hospital were retrospectively analyzed. Children transferred to another hospital for any reason were excluded from the study. The study was approved by the Ethics

Committee of Tepecik Training and Research Hospital (2018/6-1).

Tepecik Teaching and Research Hospital is a tertiary pediatric referral hospital, which is located in a populous and low socio-economic district of Izmir. The pediatric emergency department has a pediatric emergency sub-specialty fellowship program and approximately 165.000 pediatric cases visit per year.

Respiratory distress is typically characterized by signs of increased work of breathing, such as tachypnea, use of accessory muscles, nasal flaring, and/or retractions. The diagnosis of respiratory failure requires at least two clinical signs of respiratory distress and one laboratory criterion (arterial  $\text{PaCO}_2 > 50$  mmHg and  $\text{PaO}_2 < 50$  mm Hg in room air;  $\text{PaCO}_2 > 50$  mm Hg and  $\text{pH} < 7.30$ ; arterial  $\text{PaCO}_2 > 60$  mmHg and  $\text{PaO}_2 < 60$  mm Hg when  $\text{FiO}_2$  0.60 in patients without cyanotic heart disease; oxygen saturation  $< 90\%$  when  $\text{FiO}_2$  0.60). Oxygenation of the patients was monitored by pulse oximetry and lower than 94% was accepted as hypoxemia.<sup>2</sup>

In our retrospective study group, oxygen support was started with a simple mask, nonrebreathing mask or HFNC according to the pathology that causes respiratory distress, clinical severity, and clinician decision. Treatment failure is defined if three following criteria are met and an escalation of treatment or level of care is required: Heart rate remains unchanged or increased compared to admission, respiratory rate remains unchanged or increased compared to admission, oxygen requirement in HFNC support exceeds  $\text{FiO}_2 \geq 50\%$  to maintain a targeted oxygen-saturation level. If the patient is not hemodynamically (heart rate, capillary refill time, quality of central and peripheral pulses, level of consciousness, etc.) stable at the end of the first hour of HFNC support, it is considered as a treatment failure criterion alone. We have used a pre-established HFNC protocol since 2013. According to this protocol, the initial flow rate is 5-10 L/min in infants and 15-20 L/min in children. If the oxygen saturation is  $< 94\%$

initial FiO<sub>2</sub> level is set as 1.00; if the oxygen saturation is >93%, FiO<sub>2</sub> is set as 0.30. When the target oxygen saturation level is reached, FiO<sub>2</sub> is reduced by 0.05-0.10 every 3-5 minutes. The flow rate is reduced by 1 L/min in infants, 5 L/min in young children and 5-10 L/min in older children at one-hour intervals when the FiO<sub>2</sub> level is below 0.50. According to our HFNC protocol, the patient is escalated to NIV or MV, if there is any clinical deterioration (increase in oxygen requirement, work of breathing, respiratory rate, or heart rate) in the first 30 min. If there is no change in clinical findings in the first 30 min, the patients are followed for at least an additional 30 min.<sup>2</sup> If the patient does not improve clinically, the maximum follow-up time is 2 hours under HFNC support.<sup>2,5-7</sup>

The demographic, clinical and laboratory findings of the patients were recorded by the same person on a standard form. Venous blood gas analysis is routinely used in our department. Arterial blood sample is taken in patients considered to have respiratory failure. Three pediatric emergency specialists evaluated chest X-rays retrospectively. The presence of at least one of the clinical manifestations of lobar infiltration, atelectasis, traumatic pulmonary contusion, pleural effusion, and pulmonary edema was accepted as a clinical important radiographic finding. The duration of HFNC therapy was recorded as days. In the hospital medical registration system, HFNC treatments lasting less than one day are recorded as one day. The patients were divided into two main groups as patients with respiratory system pathologies and non-respiratory system pathologies.

The patients were classified into five sub-groups according to the pathophysiology of the underlying disease in terms of diagnostic groups: Respiratory system (bronchiolitis, pneumonia, asthma attack, croup syndrome, foreign body aspiration, whooping cough, chest trauma, carbon monoxide intoxication), cardiovascular system (heart failure), central nervous system (head trauma, status epilepticus), gastrointestinal system (acute

pancreatitis), hematologic/oncologic diseases, and metabolic/endocrine diseases (inherited metabolic disease, sepsis, diabetic ketoacidosis). In each main group, patients were divided into two groups: HFNC responders (success) and non-responders (unsuccessful, failure). HFNC failure was defined as the need for escalation to NIV or MV.

The HFNC system (Fisher & Paykel Healthcare Airvo 2) comprises a humidifier (MR290) and a continuous-flow circuit (900PT531 for infants, 900PT501 for children). We selected the nasal prong size that best fit each patient's nostrils (Optiflow, OPT318, OPT842, OPT844, OPT846).

### Statistical Analysis

In the statistical analysis, the numerical data were expressed as the median and interquartile range (IQR) when they were not normally distributed. Normally distributed data was expressed as mean ± standard deviation (SD) and minimum and maximum values. The categorical data were expressed in numbers (n) and percentages (%). Mann-Whitney U test or Student's t-test was used to compare the numerical data in two independent groups, and Chi-square or Fischer's Exact Test was used to compare the categorical data, whichever was appropriate. Multivariable logistic regression analysis was used to identify risk factors for HFNC failure. The odds ratio (OR) and 95% confidence interval (CI) were calculated.

Statistical analyzes were performed using SPSS for Mac (IBM Statistical Packages for the Social Sciences; Armonk, NY, USA) 20.0 and p<0.05 was considered statistically significant.

### Results

In the present study, the medical records of 529 patients were analyzed. Five cases were excluded from the study because they were transferred to another hospital. Finally, 524 patients (median age: 13 months; IQR: 6-30 months; minimum: 1 month, maximum: 231 months; 292 boys/232 girls) were included

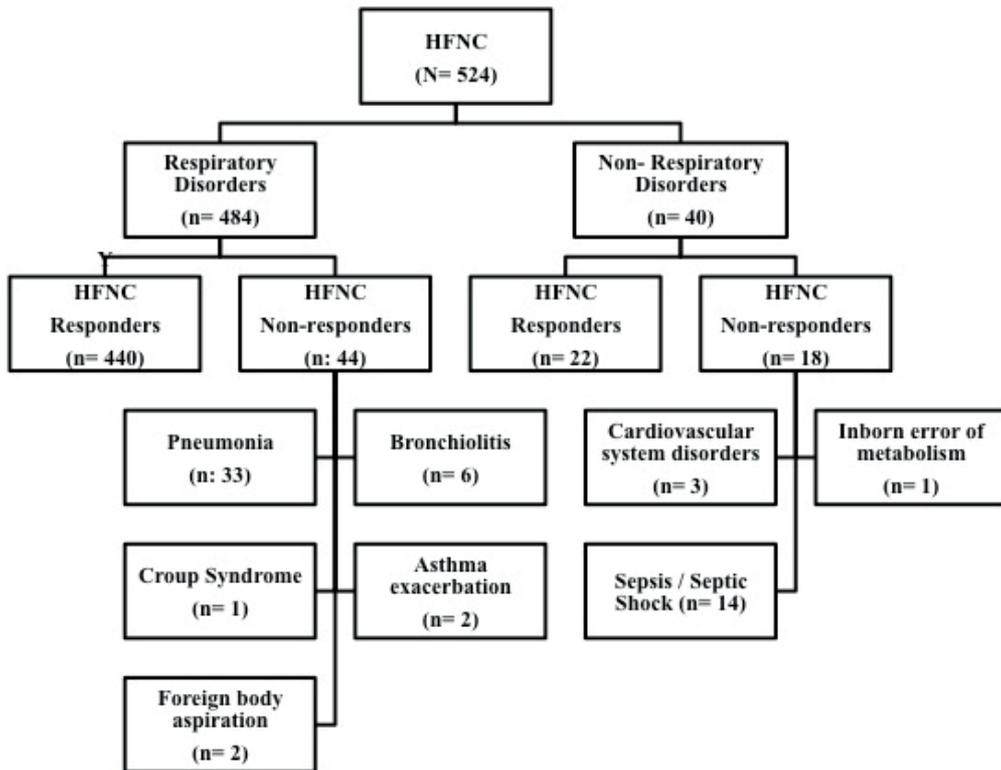
**Table I.** Diagnosis and treatment indications of patients receiving high-flow nasal cannula oxygen therapy.

Diagnosis, n, (%)	Indications, n, (%)
Pneumonia, 206 (39,3)	
Bronchiolitis, 171 (32,6)	Respiratory system pathology, 484 (92,4)
Asthma exacerbation, 76 (14,5)	Non-Respiratory system pathology, 40 (7,6)
Sepsis, 23 (4,4)	Metabolic/endocrine disorders, 24 (4,6)
Croup Syndrome, 20 (3,8)	Cardiovascular, 8 (1,5)
Heart failure, 6 (1,1)	Central nervous system, 5 (1)
Foreign body aspiration, 4 (0,8)	Hematologic/oncologic disorders, 2 (0,4)
Trauma, 4 (0,8)	Gastrointestinal system, 1 (0,2)
Poisoning, 4 (0,8)	
Inborn errors of metabolism, 3 (0,6)	
Pertussis, 3 (0,6)	
Status epilepticus, 2 (0,4)	
Pulmonary edema, 1 (0,2)	
Acute pancreatitis 1 (0,2)	

in the study. A total of 210 patients (40.1%) had a chronic disease. Respiratory failure was determined in 96 patients (18.3%). In general, HFNC was used in 484 (92.4%) patients with respiratory pathologies and in 40 (7.6%) patients with non-respiratory pathologies (Table I). One patient died in the emergency department (6-month-old girl, heart failure, hypertrophic cardiomyopathy), 102 patients (19.5%) were admitted to the pediatric intensive care unit and 376 patients (71.8%) were admitted to pediatric wards. A total of 45 patients (8.6%) were discharged from the emergency department at the end of the follow-up. In the follow-up, three patients were transferred from the wards to the pediatric intensive care unit. Thus, a total of 105 (20%) patients were followed in the pediatric intensive care unit. HFNC treatment was unsuccessful in 62 patients (11.8% of 524 patients: 60% in sepsis, 50% in cardiovascular disease; 16% in pneumonia, 3.5% in bronchiolitis, 2.6% in asthma) (Fig. 1). Among 62 patients in HFNC non-responder group, 33 patients were escalated to MV, and 28 were escalated to NIV (Fig. 2). A total of 7 patients (1.3%) died (3 sepsis, 3 heart failure and 1 inborn error of metabolism (Table II). The clinically significant radiologic findings on chest X-ray were determined in 54 (10.3%) patients (28 lobar infiltration, 24 atelectasis, 1 lobar infiltration

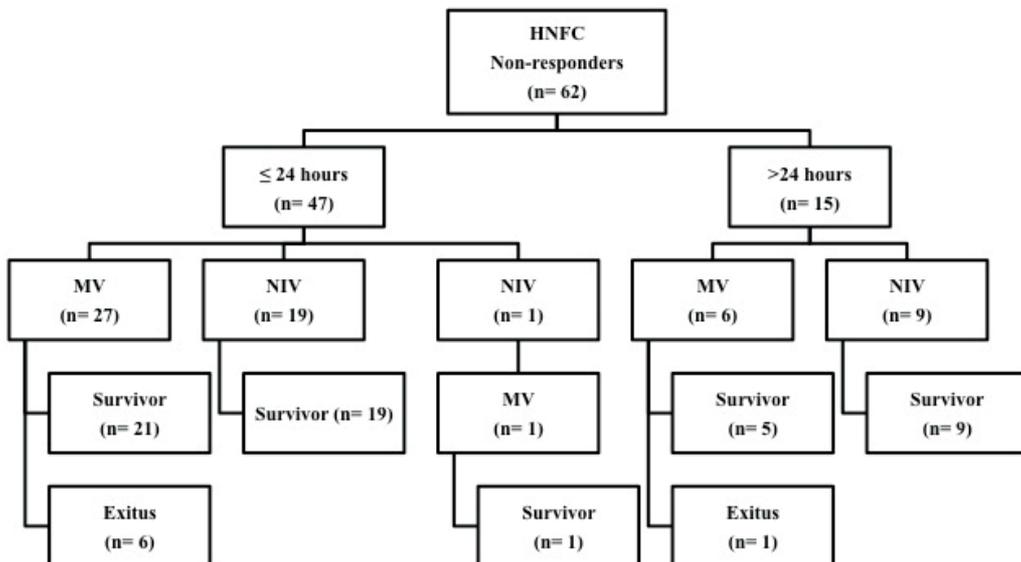
and pleural effusion, 1 pulmonary edema). The median duration of HFNC was 2 days (IQR: 1-4 days; minimum: 1 day, maximum: 30 days).

The HFNC failure rate was 44/484 (9%) in children with respiratory pathologies, 18/40 (45%) in children with non-respiratory pathologies. We compared HFNC responders and non-responders in children with respiratory pathologies. Age of patient, initial venous pH and pCO<sub>2</sub>, leukocyte and neutrophil counts in peripheral blood, and existence of clinically important finding on chest X-ray were significantly different between the two groups (p<0.05). According to the logistic regression analysis, existence of a clinically important finding on chest X-ray (p: 0.045; OR: 3.262; 95%CI: 1.178-9.034) was found to predict HFNC failure. Conversely, lower initial venous PCO<sub>2</sub> level (p: 0.045; OR: 0.958; 95%CI: 0.821-0.990) decreased the HFNC failure risk (Table III). Among patients with non-respiratory pathologies, initial venous lactate and C-reactive protein levels were significantly higher in non-responder group (p<0.05) (Table IV). Higher venous lactate level (p: 0.008; OR: 1.558; 95%CI: 1.125-2.158) was determined as a predictor of HFNC failure in logistic regression analysis. During the study, none of the identified adverse effects were related to HFNC therapy.



HNFC: High-flow nasal cannula oxygen therapy, n: number of patients

Fig. 1. Etiological distribution of patients on high-flow nasal cannula oxygen therapy.



HNFC: High-flow nasal cannula oxygen therapy; MV: Mechanical ventilation; NIV: Non-invasive ventilation; n: number of patients

Fig. 2. Clinical outcomes of patients who high-flow nasal cannula oxygen therapy failed.

**Table II.** Clinical features of deceased patients.

Diagnosis	Age	Gender	Chronic disease, pathology, congenital anomaly	Results
Heart Failure	5 Months	Female	Ventricular Septal Defect, Congenital Mitral Insufficiency	Intubation (Day 7) Exitus (Postoperative day 8)
Heart Failure	6 Months	Female	Hypertrophic Cardiomyopathy	Intubation (Day 1) Exitus (Day 1)
Heart Failure	4 Months	Male	Ventricular Septal Defect,	Intubation (Day 1) Exitus (Day 32)
Sepsis	2 Months	Female	Truncus Arteriosus	Intubation (Day 1) Exitus (Day 7)
Sepsis	16 Months	Male	Cerebral Palsy	Intubation (Day 1) Exitus (Day 5)
Sepsis	2 Months	Female	None	Intubation (Day 1) Exitus (Day 13)
Metabolic Disorders	2 Months	Female	Inborn error of metabolism	Intubation (Day 1) Exitus (Day 14)

**Table III.** Comparison of responders and non-responders receiving HFNC treatment for respiratory pathology.

Parameter	HFNC		P value	Logistic Regression	
	Responder (N= 440)	Non-responder (N= 44)		P value	OR (%95 CI)
Age, (month), median (IQR)	14 (7-30)	10 (2-30)	0.027*	>0.05	-
Male Gender, n (%)	249 (56,6)	30 (68,2)	0.138**	-	-
Chronic disease, n (%)	171 (38,9)	17 (38,6)	0.976**	-	-
Clinically important findings on chest x-ray, n (%)	37 (8,4)	13 (29,5)	<0.001**	0.045	3,262 (1,178-9,034)
Oxygen saturation (%), n (%)	89 (87-91)	88 (82-90)	0.377*	-	-
Body temperature (°C)	37.3±0.8	37±0.6	0.103***	-	-
Median±SD (Min-Max)	(36-38.5)	(36-38.2)			
Leucocyte (/mm <sup>3</sup> ), median (IQR)	13700 (10200-18600)	10600 (8100-14300)	0.002*	>0.05	-
Neutrophil (/mm <sup>3</sup> ), median (IQR)	8300 (5100-12700)	5900 (3100-9000)	0.001*	>0.05	-
Hemoglobin (gr/dL), median (IQR)	11 (10.3-12.1)	10.4 (9.7-11.8)	0.115*	-	-
C-reactive protein (mg/ml), median (IQR)	11.7 (4-30.2)	16.9 (7.1-36.7)	0.070*	-	-
pH (mmHg), median (IQR)	7.37 (7.32-7.41)	7.34 (7.27-7.40)	0.044*	>0.05	-
HCO <sub>3</sub> <sup>-</sup> (mmol/L), median (IQR)	22.1 (20.7-24)	21.6 (19.8-24.3)	0.498*	-	-
pCO <sub>2</sub> (mmHg), median (IQR)	39.2 (34.2-44.5)	42.7 (35.5-49.3)	0.033*	0.045	0,958 (0,821-0,990)
Lactate (mmol/L), median (IQR)	1.9 (1.4-2.7)	1.9 (1.3-2.7)	0.974*	-	-

HFNC: High-flow nasal cannula therapy, IQR: Interquartile range, SD.: Standard deviation, HCO<sub>3</sub><sup>-</sup>: Bicarbonate; pCO<sub>2</sub>: Carbon dioxide, \*:Mann-Whitney U Testi; \*\*: Chi Square Test, \*\*\*: Student's t Test, OR: Odds Ratio, CI: Confidence Interval, Min: minimum, Max: maximum

**Table IV.** Comparison of responders and non-responders receiving HFNC treatment for non-respiratory pathology.

Parameter	HFNC		P value	Logistic Regression	
	Responder (N= 22)	Non-responder (N= 18)		P value	OR (%95 CI)
Age (month), median (IQR)	13.5 (6-45)	8.5 (2-36)	0.270*	-	-
Male Gender, n (%)	9 (40.9)	4 (22.2)	0.209**	-	-
Chronic disease, n (%)	11 (50)	10 (55.6)	0.726**	-	-
Clinically important findings on chest x-ray, n (%)	1 (4.5)	3 (16.7)	0.310**	-	-
Oxygen saturation (%), n (%)	89 (86-94)	93 (87-97)	0.235*	-	-
Body temperature (°C), median (IQR)	36.7 (36-37)	36.7 (36-38)	>0.999*	-	-
Leucocyte (/mm <sup>3</sup> ), median (IQR)	14800 (7800-22200)	12400 (3900-29100)	0.463*	-	-
Neutrophil (/mm <sup>3</sup> ), median (IQR)	7000 (5000-14100)	7000 (2200-18900)	0.723*	-	-
Hemoglobin (gr/dL), median (IQR)	10.4 (9.2-10.8)	10.6 (8.8-11.8)	0.770*	-	-
C-reactive protein (mg/ml), median (IQR)	1.2 (0.2-3.2)	41.4 (4.3-90.7)	0.007*	>0.05	-
pH (mmHg), median (IQR)	7.29 (7.17-7.36)	7.19 (7.06-7.37)	0.211*	-	-
HCO <sub>3</sub> <sup>-</sup> (mmol/L), median (IQR)	17.6 (10-22.2)	19 (9-27)	0.221*	-	-
pCO <sub>2</sub> (mmHg), median (IQR)	36 (25-42)	31 (25-56)	0.924*	-	-
Lactate (mmol/L), median (IQR)	2.2 (1.2-4.8)	4.5 (2.2-8.5)	0.001*	0.008	1,558 (1,125-2,158)

HFNC: High-flow nasal cannula therapy, IQR: Interquartile range, SD: Standard deviation, \*:Mann-Whitney U Test, \*\*: Chi Square Test, OR: Odds Ratio, CI: Confidence Interval

## Discussion

HFNC oxygen treatment with the pre-established protocol was used in 524 patients aged 1 month to 18 years with various etiologies of respiratory distress/failure in the pediatric emergency department. The overall success rate was 88.2%. The rate of HFNC failure was 9% in children with respiratory pathologies and 45% in children with non-respiratory pathologies. No adverse effects related to HFNC treatment were observed. In children with respiratory pathologies, existence of a clinically important finding on chest X-ray increased and lower initial venous PCO<sub>2</sub> level decreased the risk of HFNC treatment failure. Higher venous lactate level was a risk factor for HFNC treatment failure in children with non-respiratory pathologies.

Most of the clinical studies on HFNC oxygen treatment were conducted in children with bronchiolitis and lower respiratory tract infections. High-flow nasal cannula oxygen therapy is a more effective treatment option than standard nasal oxygen therapy.<sup>3,6,8,9,11</sup> In a prospective study from Australia, Keproetes et al.<sup>10</sup> showed that the therapy failure rates were 14% in HFNC group and 33% in the standard nasal oxygen group among patients aged lower than 24 months with moderate bronchiolitis. Additionally, more than half of the children who experienced treatment failure on standard therapy were rescued with HFNC. They concluded that HFNC is safe and effective as a rescue therapy to reduce the pediatric intensive care unit admission in children with moderate bronchiolitis.<sup>10</sup> In a multicenter randomized

controlled study, Franklin et al.<sup>3</sup> evaluated the effectiveness of early HFNC therapy during hospital admission among infants with bronchiolitis if they had a need for supplemental oxygen therapy to keep the oxygen-saturation level in an acceptable range. The therapy failure rates were 12% in HFNC group and 23% in the standard nasal oxygen group.<sup>3</sup> In the limited number of studies, HFNC was used in children with non-respiratory diseases, most of them conducted in pediatric intensive care unit.<sup>2,5-7</sup> The risk of HFNC failure was increased in children with cardiovascular pathology, sepsis, extrapulmonary pediatric acute respiratory distress syndrome, trauma-induced lung contusion, neuromuscular disease.<sup>2</sup> The success of HFNC depends on its operating principle, such as reducing respiratory workload and inspiratory resistance, eliminating anatomic dead space in the nasopharynx, increasing mucociliary activity due to heated and highly humidified air, and a limited increase in positive end-expiratory pressure. As expected, the positive effect in the respiratory distress related to a circulatory pathology is more limited.<sup>12,13</sup> In our study, we assessed all children receiving HFNC oxygen treatment. Most of the children had respiratory tract pathologies and 7.6% of them had non-respiratory tract pathologies. The HFNC oxygen treatment was successful in 81% of children with respiratory disease and 55% of children with non-respiratory disease. The HFNC failure risk was higher in pneumonia among respiratory diseases and in sepsis among non-respiratory diseases. Similar to the literature, the success rate of HFNC in bronchiolitis is high. Although there is very limited information in the literature, we observed that HFNC is a reliable option in croup syndrome and pediatric asthma exacerbation in our daily practice. Nevertheless, we believe that HFNC is a reliable oxygen therapy option for children in pediatric emergency departments.

Inability to identify patients who will fail NIV early may cause a delay in intubation, which can lead to clinical deterioration and increased morbidity and mortality.<sup>14</sup> Therefore, it is

important to predict the HFNC treatment failure to prevent morbidity and mortality caused by receiving HFNC treatment longer than necessary.<sup>2,8,11</sup> According to studies conducted in pediatric intensive care units, respiratory distress caused by congenital heart disease<sup>7,11</sup>, oxygen need caused by non-respiratory diseases<sup>5</sup>, previous endotracheal intubation<sup>11</sup>, age greater than 10 years, high mortality and respiratory scores, and low SpO<sub>2</sub>/FiO<sub>2</sub> ratio have been reported as predictors for HFNC failure.<sup>7,11</sup> There are limited studies on this subject in pediatric emergency departments. Significant tachypnea, hypercapnia and acidosis were reported as predictors of HFNC treatment failure in patients younger than two years with respiratory disease.<sup>6</sup> In adults, HFNC has been found to be less successful in patients with severe parenchymal damage such as bacterial pneumonia.<sup>12,13</sup> The main limitation of the oxygen treatment via HFNC is its inability to create sufficient pressure in patients older than one month of age. Although it cannot be measured routinely, HFNC generates some flow dependent positive end-expiratory pressure. However, these pressure levels are probably not sufficient for some patients with parenchymal damage or hypercarbia. In pathologies such as bronchiolitis, delivering heated and humidified oxygen via HFNC device is often sufficient to correct pathology.<sup>3,6,8-13</sup> The mechanism of respiratory distress is different in non-respiratory pathologies. In circulatory failure, blood lactate level is an indicator of tissue perfusion. In these situations, HFNC provides the only safe and comfortable oxygen supply.<sup>15,16</sup> Unlike other studies in the literature, we investigated the predictors of HFNC failure in children with respiratory and non-respiratory pathologies, separately. In children with respiratory disease, existence of significant radiological finding on chest X-ray increased the likelihood of HFNC therapy failure. We determined that venous PaCO<sub>2</sub> was significantly higher in HFNC non-responders than HFNC-responders. Statistically, lower venous PaCO<sub>2</sub> level decreased the risk of HFNC therapy failure. In children with non-respiratory

pathologies, higher blood lactate level increased the risk of HFNC treatment failure. When the results are evaluated in general, both PaCO<sub>2</sub> and lactate levels were high in HFNC non-responders. This result suggests that HFNC success is lower in later stages of the diseases. Our results are consistent with HFNC device working principle.

In the literature, HFNC is generally described as a safe oxygen delivery method. Few studies have reported air leakage syndromes.<sup>9,17</sup> In our pediatric emergency department, we used HFNC with a pre-established protocol. We did not see any adverse effects related to HFNC therapy in the study period.

This study has several limitations. Firstly, this is a single center study giving the results of special pediatric emergency settings in a special region with distinctive necessities and also limited by the retrospective data. Secondly, there was no control group to compare the efficacy. Thirdly, we did not record the vital parameters, blood gas analysis on the follow-up. Fourthly, the exact time interval between initiation of HFNC and initiation of further respiratory support for respiratory failure in patients could not be obtained from hospital records as the study design was retrospective. According to the protocol used in the pediatric emergency department, the maximum follow-up period of patients whose clinical picture does not improve under HFNC support is two hours. However, the study has got some positive contributions to the literature. The total number of patients in the study is quite high when compared to other single-center studies. We evaluated the outcomes of HFNC treatment with pre-established protocol in children with respiratory distress/failure due to various etiologies. In the literature, there are very few studies evaluating HFNC outcomes in non-bronchiolitis diseases in pediatric patients

older than one month. Lastly, there are limited studies to evaluate the predictors of HFNC failure in pediatric emergency setting.

In conclusion, HFNC is a reliable oxygen delivery method in children with respiratory distress due to many different etiologies in the pediatric emergency department. The efficacy of HFNC is higher in children with respiratory pathologies than in children with non-respiratory pathologies. The presence of clinically important radiological findings on chest X-ray decreases and lower PaCO<sub>2</sub> increases HFNC success in children with respiratory pathologies. The higher blood lactate level increases the risk of HFNC failure in children with non-respiratory pathologies.

#### **Ethical approval**

The study has been approved by the Ethics Committee of Tepecik Training and Research Hospital (2018/6-1).

#### **Author contribution**

The authors confirm contribution to the paper as follows: study conception and design: MA; data collection: ŞD, GY, SBY, EB, GG; analysis and interpretation of results: ABA, MA, FK, ŞB, GD; draft manuscript preparation: ŞD, ŞB, GD. All authors reviewed the results and approved the final version of the manuscript.

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#### **Conflict of interest**

The authors declare that there is no conflict of interest.

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