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Heated Humidified High Flow Nasal Cannula for Non-Invasive Primary Respiratory Support in Neonates: Experience of a Referral Neonatal Level III Facility in South-South Nigeria

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ABSTRACT:

Background: Heated humidified high flow nasal cannula (HHHFNC) is an increasingly used tool for non-invasive ventilation (NIV) in neonates and children needing advanced respiratory support.[1] In neonates, common indications for HHHFNC therapy include: respiratory distress syndrome (RDS), post extubation from mechanical ventilation; and other causes of respiratory distress. Its use in Nigeria is not widespread. The aim of this study is to assess the indications, clinical characteristics, outcome and determinants of the successful use of HHHFNC for providing primary respiratory support for neonates referred and needing NIV in a Level III NICU in Nigeria.

Methods: This was a retrospective study. All neonates in this study were referred to our facility, Med-Vical Medical Centre, Benin City, Edo State, Nigeria and received HHHFNC for primary respiratory support.

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Results: The highest indication for primary use of HHHFNC for neonates was respiratory distress syndrome (50.0%). The success rate of HHHFNC in this study was high (70.0%). Although not statistically significant, a higher proportion of neonates in the failure group weighed less than 1kg, while in the successful group, a higher proportion was delivered after 28 weeks. All infants who stayed longer than 7days on admission belonged to the successful group, and none failed HHHFNC therapy. This difference was statistically significant (p=0.011).

In conclusion, this study revealed that the success rate of HHHFNC therapy as primary respiratory support in neonates with respiratory distress is high (70.0%), thus it can be used confidently in neonates needing NIV. Length of hospital stay was the only significant factor associated with the successful use of HHHFNC as primary respiratory support.

KEYWORDS: Heated humidified high flaw nasal cannula, preterm, neonates, respiratory distress syndrome, non-invasive ventilation, Neonatal advanced respiratory support in Nigeria.

INTRODUCTION

Heated humidified high flow nasal cannula (HHHFNC) is an increasingly used tool for non-invasive ventilation (NIV) in neonates and children admitted in neonatal intensive care units (NICUs) and Emergency rooms/paediatric intensive care units (PICUs) respectively of developed countries.[1] Its use in low and medium income countries, especially Nigeria is not as widespread compared to developed countries.

Indications for its use vary from one age group to the other, as it is also used in adults.[2] In older infants and children it is commonly used for children in respiratory distress with bronchiolitis, bronchopneumonia, and asthma exacerbations.[3-4] In neonates, similar to nasal bubble continuous positive airway pressure (NBCPAP), common indications for HHHFNC include: respiratory distress syndrome (RDS) in neonates above 30 weeks gestational age (as primary respiratory support); post extubation from mechanical ventilation; and other causes of respiratory distress, such as sepsis, transient tachypnea of the newborn (TTNB), pneumonia, mild to moderate perinatal asphyxia.[5] In addition, studies have shown that the efficacy of HHHFNC in providing NIV is non-inferior to that of other methods of NIV, such as non-invasive posititve pressure

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ventilation (NIPPV) and NBCPAP.[6-10] In addition, studies have documented several advantages of HHHFNC over NBCPAP. HHHFNC is less cumbersome, with no bulky nasal interfaces like that seen in NBCPAP; HHHFNC causes less nasal trauma, it is easier to use and set up (with an inbuilt gas mixer in some devices, like that seen in Fisher and paykel, airvo 2); and HHHFNC is preferred by nurses and parents compared to NBCPAP, as it does not interfere with parental bonding and oral feeds (including breastfeeding).[11-13] There are variable outcomes following the use of HHHFNC especially when used as primary respiratory support in neonates with RDS. However, more studies have reported favourable outcome in bigger preterms (≥ 28 weeks gestation) or term neonates, compared to smaller preterm neonates (especially those delivered less than or equal to 28 weeks gestation).[7-10,14-18] Infact, in many NICUs, the use of HHHFNC as primary respiratory support in neonatal RDS is usually restricted to neonates ≥ 30 weeks gestational age (GA).[14] In preterm neonates delivered less than 28 weeks GA and weighing less than 1kg, the use of HHHFNC has been controversial;[15,-18] a few studies, including a case report by Enato et al, have reported favourable outcome in this group of neonates with no increased risk of necrotizing enterocolitis, bronchopulmonary dysplasia and sepsis associated with the use of HHHFNC in ELBW infants.[15,17-19]

The indications and outcome of HHHFNC across GA has not been reported in the Country, despite adequate literature search, the authors did not find any article from Nigeria concerning the use of HHHFNC. The aim of this study is to assess the indications, clinical characteristics of neonates on HHHFNC, their clinical outcome, and determinants of the successful use of HHHFNC for providing primary respiratory support for neonates referred and needing NIV in a Level III NICU in Benin City, Edo State, Nigeria.

METHOD

This was a retrospective study involving 20 preterm and term neonates. All neonates in this study were referred to our facility, Med-Vical Medical Centre, Benin City, Edo State, Nigeria between January 2023 and May 2024, for acute advanced respiratory support. They were commenced on HHHFNC as primary non-invasive respiratory support for respiratory distress. The HHHFNC

used in this study was the Optiflow System (Fisher & Paykel Optiflow System, Healthcare, Auckland, New Zealand), and short binasal prongs were used as the interface with different sizes. Infants received an initial gas flow of upto 8 L/min, which was then regulated down to between 2 and 7 L/min according to the patients' conditions. Also, FiO_2 of upto 0.8 was started and was titrated against the oxygen saturation, until SpO_2 of 90–95% was achieved.

The eligibility criteria for this study were: 1) Neonates who required non-invasive ventilation using HHHFNC as primary respiratory support irrespective of the GA. 2) Neonates with no known or obvious congenital heart diseases (CHD). A total of 22 patients received HHHFNC as primary respiratory support, after excluding the newborns with CHD, only 20 were included in this study.

The primary outcome of HHHFNC in neonates was classified as either successful treatment or failed treatment with HHHFNC.[14] Secondary outcomes include: length of hospital stay, duration of HHHFNC, incidence of bronchopulmaonary dysplasia (BPD), and necrotizing enterocolitis (NEC).

Definition of terms

Primary respiratory support using HHHFNC is defined as the use of only HHHFNC for non-invasive ventilation following delivery or at presentation in children with respiratory distress. Successful HHHFNC is defined as neonates who were successfully weaned off HHHFNC to low flow nasal cannula; while HHHFNC treatment failure is defined as requiring intubation and mechanical ventilation or other non-invasive respiratory support, because of worsening or continuous respiratory distress, persistent desaturations, requiring repeated stimulation or bag-and-mask ventilation, or apnea.[14]

Data collection

A proforma was used to collect information about the mother's level of education, pregnancy, infant demographics, primary and secondary outcome, and clinical indications for HHHFNC (such as: respiratory distress syndrome (RDS), transient tachypnea of newborn (TTN), and perinatal asphyxia).

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Statistical Analysis

Data collected was entered into SPSS, version 22 (IBM Corp., Armonk, NY, USA). The clinical characteristics, indications and outcome of neonates on HHHFNC were presented as frequency, and percentage. We compared and analysed the baseline characteristics, indications and patient outcomes of the successful and failure groups as categorical variables using Chi-square test/Fischer's exact test. $P < 0.05$ was considered significant.

RESULTS

A total of 20 infants were involved in the study. There were more male neonates (70.0%) in the study than female neonates [Table 1]. Preterm neonates were more (65.0%) than term neonates. Majority of referred neonates were products of singleton gestation (95.0%). Only 15.0% of neonates placed on HHHFNC as primary respiratory support weighed less than 1000g, and 25.0% were delivered at less than 28 weeks GA. More than half of the infants presented within 24 hours of life and the duration of their illness was less than 24 hours [Table 1]. Seventy five percent (75.0%) of them had HHHFNC therapy for less than or equal to seven days, while 30% stayed more than 14 days in the hospital. Only 15% of the babies had mothers with tertiary level of education. Most of the babies (95.0%) did not receive surfactant [Table 1].

The highest indication for primary use of HHHFNC for neonates was respiratory distress syndrome (50.0%), followed by perinatal asphyxia (30.0%). Only one neonate (5.0%) received HHHFNC for TTNB [Table 2]. The success rate of HHHFNC in this study was high (70.0%), while failure rate was 30.0% [Table 3].

In comparing the two groups of infants (failure and successful groups) based on their clinical characteristics, a higher proportion of neonates in the failure group were males, delivered at term, weighed under 1kg, and presented late (more than 3 days since onset of illness) compared to the successful group [Table 4]. In the successful group, a higher proportion was delivered after 28 weeks and had longer use of HHHFNC. More neonates in the successful group had mothers with at least a secondary level of education; the only product of multiple gestation was successful with HHHFNC. Although the proportion of those who received surfactant seemed

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higher in the successful group, the use of surfactant within each of the groups was comparable and had no significant impact on the outcome of HHHFNC. All these differences based on clinical characteristics between the successful and failure group were not significant. However, all infants who stayed longer than 7days on admission belonged to the successful group, and none failed HHHFNC therapy [Table 4]. This difference was statistically significant (p=0.011) Table 4.

The proportion of infants with RDS who had successful HHHFNC therapy, was similar to that of infants with Perinatal asphyxia [Table 5]. None of the neonates had complications of BPD, pneumothorax or NEC.

DISCUSSION

Only few studies on the clinical characteristics, outcome and determinants of HHHFNC therapy as primary respiratory support in newborn infants with respiratory distress have been published. Most studies compared the outcome and efficacy of HHHFNC with other non-invasive respiratory support, such as NIPPV and NBCPAP. This study focused on the clinical characteristics, outcome and determinants of HHHFNC as primary respiratory support for neonates referred for advanced care.

The higher proportion of male and preterm neonates in this study is not surprising as more male preterm neonates tend to require respiratory support compared to their female counterparts.[20-21]

The proportion of preterm neonates weighing less than 1kg and delivered before 28 weeks was low, compared to those weighing more than 1kg and delivered at 28 weeks or more. This is expected as our centre is a referral Level III, NICU; coupled with the poor referral system and method in our locale, most of these very small preterm babies do not present early enough to our centre and thus they either arrive in respiratory failure (thereby needing mechanical ventilation) or they expire before arrival. Another reason for the low number of extreme premature infants in this study could be due to the fact that most parents decide not to spend their resources on very small premature babies, as they believe the baby will not survive and it will be a waste of their resources in the midst of worsening financial and economic crises in the country. In addition,

some health care workers in peripheral facilities, especially in the rural or semi-urban areas share this same belief, thus they make little or no effort to salvage these babies in the first place.

It is worthy to note that although, Edo State has a very effective health insurance scheme for older children and adults, that for very sick or small preterm newborns has not been well established. The availability of only few NICUs that can provide advanced care in the State and The country as a whole is a significant challenge in reducing neonatal mortality. The State Government-owned Hospitals can only provide basic to moderate neonatal care services (Level I/II). At the time of this study only our facility, in addition to The Federal Government Teaching Hospital provide advanced neonatal care services.

RDS and perinatal asphyxia were the highest indications of HHHFNC. This is a reflection of the group of neonates who need or are referred for advanced care; as a higher proportion of neonates in this study were preterm neonates and RDS is a common feature in preterm neonates. TTNB was seen in only one (1) neonate. This is unlike that seen in a study by Lee et al, 2019, where TTNB was the most common indication for HHHFNC. This disparity can be explained by the fact that most cases of TTNB in Nigeria can be managed in peripheral NICUs with improvised bubble continuous positive air way pressure (IBCPAP), which is low cost compared to conventional NBCPAP and HHHFNC.[22]

The successful rate of HHHFNC (70.0%) was high, while the failure rate was low (30.0%) in this study. A similar finding was seen by Lee et al in South Korea, with a failure rate of 30.0%.[14] Other studies on the use of HHHFNC as primary respiratory support have documented failure rates of between 12.9% and 38.0%. Murki et al. found that the failure rate of HHHFNC was 26.3% for the preterm infants with GA ≥28 weeks and birth weight ≥1000g; Shin et al. and Ciuffini et al. found that the failure rate of HHHFNC was 38.0% and 12.9%, respectively.[23-25]

The failure rate of HHHFNC reduced progressively with increase in GA and weight, with a marked decrease (though not statistically significant) from 60.0% at ≤28 weeks to 25% at 28-36 weeks GA and 14.3% at >36 weeks GA. Lee et al, 2019 had similar findings of lesser failure rates as GA increases, with failure rate of 13.6% for ≥38 weeks, 16.2% for ≥36 weeks, 19.3% for ≥34 weeks, and 22.1% for ≥33 weeks. Although there are no clear guidelines for the use of

HHHFNC as primary respiratory support, most studies have shown that the use of HHHFNC should be recommended in neonates ≥ 28 weeks GA.[14,26-28] Concerning weight at presentation, the higher the weight of neonates at presentation, the lower the failure rate; failure rate dropped from 66.7% in those weighing <1kg to 33.3% and 12.5% in neonates weighing 1-2.4kg and >2.4kg respectively. Murki et al doucumented similar findings.[23] However, most studies have documented that GA instead of birth weight is a stronger predictor of failure/success rate of HHHFNC.[14,27-28]

Failure of HHHFNC was influenced by age at presentation and duration of illness, as those who presented after 3 days of life had a higher failure rate than the others who presented earlier. In addition, the use of surfactant within each of the groups was comparable and had no significant impact on the outcome of HHHFNC.

Majority of neonates who had a longer duration of HHHFNC of more than 7 days had successful HHHFNC therapy. A similar finding was seen in Salim et al, where patients who responded to HHHFNC treatment had a longer duration of HHHFNC treatment.[29]

The only significant factor contributing to the successful use of HHHFNC in our study was length of hospital stay, all neonates who spent more than 7 days on admission, had successful HHHFNC therapy with zero failure rate (p=0.011). This can easily be explained by the fact that those who had successful HHHFNC had a longer duration on HHHFNC and thus a longer duration of admission. In addition, some of the neonates were small preterm infants, including neonates delivered at less than 28 weeks GA and less than 1kg, who spent a long time on admission to allow for maturity before discharge, even after HHHFNC was discontinued. Longer length of hospital stay is usually a negative predictor of treatment in most studies; however, in our study the contrary is the case, as successful use of HHHFNC in small preterm babies is associated with long hospital stay.[15]

In conclusion, our study revealed that the success rate of HHHFNC therapy as primary respiratory support in neonates with respiratory distress is high (70.0%), thus it can be used confidently in neonates needing NIV. Also this study, has demonstrated the clinical characteristics, clinical outcome and determinants associated with the successful use of

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HHHFNC therapy as primary respiratory support in a referral NICU in Southern Nigeria. This study serves as a baseline study, as it is the first of its kind in Edo State and probably, the sub-region. As seen in other studies, the success of HHHFNC therapy as primary respiratory support increases with gestational age and weight of infants. Length of hospital stay was the only significant factor associated with the successful use of HHHFNC as primary respiratory support; as all neonates spending more than 7 days on admission had 100% successful use of HHHFNC. This was statistically significant.

The limitation of this study is that it was an observational single-center retrospective study. Although our study did not have sufficient statistical power to detect significant differences between the successful and failure groups in the clinical characteristics of neonates, outcome and indications of HHHFNC, our study has demonstrated that HHHFNC therapy as primary respiratory support can be used successfully in referred neonates with respiratory distress such as RDS and perinatal asphyxia. Nation- wide large-scale studies should be performed in order to set up the guidelines for using HHHFNC as the primary respiratory support in neonates with respiratory distress in the Country.

The referral system in the district and the State for sick neonates and awareness of facilities that can provide advanced respiratory support for neonates in The State need to be improved and strengthened so as to encourage proper and timely referral of these infants. There is a huge need to expand neonatal care services in State-owned district and secondary health care facilities in The State and Country as a whole.

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TABLE 1: Neonatal Baseline Socio-Demographic and Clinical Characteristics

Neonatal Demographic Characteristics	Frequency (N=20)	Percentage (%)
GENDER		
Male	14	70.0
Female	6	20.0
DURATION OF PREGNANCY		
Preterm	13	65.0
Term	7	35.0
TYPE OF GESTATION		
Singleton	19	95.0
Multiple	1	5.0
WEIGHT		
< 1000g	3	15.0
1000-2400g	9	45.0
>2400g	8	40.0
AGE AT PRESENTATION		
<24hours	11	55.0
1-3 days	4	20.0
>3 days	5	25.0

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GESTATIONAL AGE		
<28 weeks	5	25.0
28-36 weeks	8	40.0
>36weeks	7	35.0
DURATION OF ILLNESS		
<24 hours	12	60.0
1-3days	5	25.0
>3days	3	15.0
DURATION OF HHHFNC		
≤7 Days	15	75.0
>7 Days	5	25.0
MOTHER'S LOE		
None	2	10.0
Primary	6	30.0
Secondary	9	45.0
Tertiary	3	15.0
Length of hospital stay		
<7 Days	9	45.0
7-14 Days	5	25.0
>14 Days	6	30.0
SURFACTANT		
Yes	5	15.0
No	15	75.0

Table 2: Clinical Indication of Heated Humidified High Flow nasal Cannula

Clinical Indication	**Frequency (N=20)**	**Percentage (%)**
Severe respiratory distress syndrome	10	50.0
Perinatal Asphyxia	6	30.0
Transient Tachypnoea of the Newborn	1	5.0
Congenital pneumonia	2	10.0
Acute bilirubin encephalopathy	1	5.0
Total	20	100

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Table 3: Outcome of HHHFNC in neonates

Clinical Indication	Frequency (N=20)	Percentage (%)
Successful	14	70.0
Failure	6	30.0
Total	20	100.0

Table 4: Comparison Between Successful and Failed use of HHHFNC for Primary Respiratory Support in Neonates According to Neonatal Baseline Characteristics

Neonatal Characteristics	Successful n(%)	Failure n(%)	Total N	p-value
GENDER				
Male	9(64.3)	5(35.7)	14	0.613*
Female	5(83.3)	1(16.7)	6	
DURATION OF PREGNANCY				
Preterm	6(85.7)	1(14.3)	7	0.354*
Term	8(61.5)	5(38.5)	13	
TYPE OF GESTATION				
Singleton	13(68.4)	6(31.6)	19	1.000*
Multiple	1(100.0)	0(0)	1	
WEIGHT				
<1kg	1(33.3)	2(66.7)	3	0.209
1-2.4kg	6(66.7)	3(33.3)	9	
>2.4kg	7(87.5)	1(12.5)	8	
AGE AT PRESENTATION				
< 1 day	8(72.7)	3(27.3)	11	0.850
1-3 days	3(75.0)	1(25.0)	4	
>3 days	3(60.0)	2(40.0)	5	
GESTATIONAL AGE				
<28 weeks	2(40.0)	3(60.0)	5	0.216
28-36 weeks	6(75.0)	2(25.0)	8	
>36weeks	6(85.7)	1(14.3)	7	
DURATION OF ILLNESS				
≤24 hours	8(61.5)	5(38.5)	13	0.354*
>24 hours	6(85.7)	1(14.3)	7	
DURATION OF HHHFNC				
≤7 Days	8(61.5)	5(38.5)	13	0.260*
>7 Days	6(85.7)	1(14.3)	7	

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MOTHER'S LOE				
Less than Secondary LOE	3(60.0)	2(40.0)	5	0.613
Secondary and above LOE	11(73.3)	4(26.7)	15	
Length of hospital stay				
≤7 Days	4(40.0)	6(60.0)	10	0.011*
>7 Days	10(100)	0(0)	10	
SURFACTANT				
No	10(66.7)	5(33.9)	15	
Yes	4(80.0)	1(20.0)	5	1.000*

Table 5: Comparison between Successful and Failed use of HHHFNC for Primary Respiratory Support in Neonates according to Clinical Indication of HHHFNC.

Indication for HHHFNC	**Successful n(%)**	**Failure n(%)**	**Total**	**p-value**
Respiratory distress syndrome	6(60.0)	4(40.0)	10	0.329
Perinatal asphyxia	4(66.7)	2(33.3)	6	
Others	4(100.0)	0(0)	4	