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The demographic profile, clinical spectrum, and outcome of term neonates requiring continuous positive airway pressure in a tertiary care teaching hospital

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ABSTRACT

Background: Respiratory distress is the major cause of neonatal intensive care unit (NICU) admission of full-term neonates for which they require different levels of mode of ventilation. **Aims and Objectives:** The objective of this study was to determine the demographic profile, clinical spectrum, and outcome of term neonates, requiring continuous positive airway pressure (CPAP) in tertiary care teaching hospitals. **Materials and Methods:** The study was a prospective observational study conducted from December 2020 to November 2022 in the neonatal section of the department of pediatrics. **Results:** A total of 261 neonates were included in the study. The male-to-female ratio was 1.7:1, the range of birth weight was between 2.1 kg and 3 kg (60.91%), the gestation age was 38 weeks (59.2%), and 73.6% were lower-segment cesarean section born. The age of starting CPAP in most of the newborns was at admission to NICU (in 69.73% of cases). The success rate of CPAP therapy was high (60.9%) and the rest 39.08% of patients did not settle with CPAP and required higher modes of respiratory support such as nasal intermittent positive pressure ventilation (IPPV) (5.89%) and IPPV (94.11%). **Conclusion:** In the resource-limiting settings, due to the non-availability of higher levels of ventilatory gadgets, the early use of CPAP as a mode of ventilation in full-term babies with transient tachypnea of newborns is well-documented and it can be safely used in other common neonatal conditions which can cause respiratory distress in full-term neonates. The low-middle-income countries are facing challenges to improve comprehensive neonatal care; there is a dire need for simple and cost-effective methods of respiratory support. Bubble CPAP is one such promising ventilatory support intervention, which may reduce the need for costly mechanical ventilators.

Key words: Bubble continuous positive airway pressure; Full term; Respiratory distress; Transient tachypnea of newborns; MAS

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INTRODUCTION

Respiratory distress immediately after birth is common and is typically caused by abnormal respiratory function during the transition from fetal to neonatal life. It is manifested by tachypnea, nasal flaring, intercostal or subcostal retractions, audible grunting, and cyanosis. The most common reason for a neonate to get admitted to the neonatal intensive care unit (NICU) is respiratory distress.

The successful transition from fetal to neonatal life at delivery requires a series of rapid physiologic changes in the cardiorespiratory system. These changes result in the redirection of gas exchange from the placenta to the lung and comprise replacement of alveolar fluid with air, the onset of regular breathing, and an increase in pulmonary blood flow as a result of increased systemic vascular resistance and decreased pulmonary vascular resistance.[1] It has been observed that around 15% of full-term

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infants and 29% of late preterm infants who get admitted to the NICU develop significant respiratory morbidity, and that is even higher for infants born before 34 weeks gestation.[2] The most common cause of respiratory distress in preterm infants is transient deficiency of surfactant leading to hyaline membrane disease (respiratory distress syndrome). This condition becomes less common as gestational age approaches to term and other causes of respiratory distress become more common.[3] These include transient tachypnea of the new-born; early neonatal sepsis; meconium aspiration syndrome; perinatal asphyxia leading to pulmonary hypertension of the new-born; and pneumothorax or other pulmonary air leak disorder, congenital diaphragmatic hernia, tracheoesophageal fistula, and congenital pulmonary airway malformation.[3] There are certain known risk factors that individually or collectively increase the likelihood of neonatal respiratory disease. These factors include prematurity, meconium-stained amniotic fluid, cesarean section delivery, gestational diabetes, maternal chorioamnionitis, or prenatal ultrasonographic findings, such as oligohydramnios or structural lung abnormalities.[3,4] Regardless of the etiology of respiratory distress, it is essential to provide early respiratory support, and supplemental oxygen to maintain a targeted peripheral oxygen saturation (SpO_2) between 90 and 95%. The choice of respiratory support depends on the infant's initial respiratory effort and pattern of breathing. For infants with a strong respiratory drive (i.e., sustained regular respirations), non-invasive positive pressure is initially provided to prevent and reduce atelectasis. Nasal continuous positive airway pressure (CPAP) and nasal intermittent positive pressure ventilation (NIPPV) are both reasonable options for non-invasive support. CPAP refers to the application of prewarmed humidified oxygen and positive pressure to the airways of a spontaneously breathing infant throughout the respiratory cycle.[5] The overuse of mechanical ventilation in newborn babies can contribute to pulmonary baro and volutrauma and the subsequent development of chronic lung disease. The CPAP is less injurious to the lungs of newborn infants and is therefore the initial choice of ventilatory management in NICU.[6] The CPAP can be used in the ventilatory management of full-term infants as an alternative to mechanical ventilation in resource-limited countries. The clinical goals of CPAP are to maintain the functional residual capacity of the lungs and support gas exchange to reduce apnea, work of breathing (WOB), and lung injury. However, CPAP has also been used to treat infants with other respiratory disorders, including transient tachypnea of the newborn, meconium aspiration syndrome, primary pulmonary hypertension, pulmonary hemorrhage, patent ductus arteriosus (PDA), and consequent pulmonary edema. Further, CPAP is also useful for treating obstructive and central apnea of prematurity. It is contraindicated in patients with upper airway abnormalities (i.e., cleft palate, choanal atresia, and tracheoesophageal fistula), unrepaired diaphragmatic hernia, severe cardiovascular instability, and recurrent apneic episodes.[6]

Table 1: Existing case definitions of respiratory distress in the neonate[9]

WHO	Respiratory rate of more than 60 or <30 breaths/min, grunting on expiration, chest indrawing, or central cyanosis (blue tongue and lips), apnea (spontaneous cessation of breathing for more than 20 s).
NCI/NICHD	Increased work of breathing with tachypnea and retractions.
2016 ICD-10 CM diagnosis code	A condition of the newborn marked by dyspnea with cyanosis, heralded by such prodromal signs as dilatation of the nasal alae, expiratory grunt, and retraction of the suprasternal notch or costal margins, most frequently occurring in premature infants, children of diabetic mothers, and infants delivered by cesarean section, and sometimes with no apparent cause.
Swiss society of Neonatology definition in Ersch et al. Acta Paediatrica 2007	Presence of at least two of the following criteria: Tachypnea (>60 breaths/min), central cyanosis in room air, expiratory grunting, subcostal, intercostal, or jugular retractions, and nasal flaring.

WHO: World Health Organization

The non-invasive application of CPAP is also a form of positive-pressure ventilation and, therefore, some complications that arise during mechanical ventilation can also occur with CPAP. Air leak, although not reported frequently, is still a concern, especially when an inappropriately high CPAP level is used. Pneumothorax, pulmonary interstitial emphysema, pneumomediastinum, pneumatocele, and vascular air embolism have been described in infants receiving CPAP. CPAP has also been associated with increased intracranial pressures decreased urine output and glomerular filtration rate. Bowel distention is often a mild complication noted with CPAP, due to swallowing of air and can be relieved using an orogastric tube.[7]

Assessment of respiratory distress in the neonate

Initial assessment of an infant with respiratory distress should focus on the physical examination and rapid identification of life-threatening conditions.[8,9] The assessment for respiratory distress should include at least some of the following clinical parameters: (1) measurement of respiratory rate; (2) WOB determined by inspiratory sternal, intercostal, and subcostal recession/indrawing; (3) keen hearing to airway or respiratory noises such as expiratory grunting or inspiratory stridor; (4) nasal flaring or head bobbing; and (5) bluish tinge of mucus membranes or cyanosis. The use of pulse oximetry should be routine and SPO_2 is an important parameter when there is concern about color/cyanosis. Apnea should prompt urgent medical assessment and actions. Further, respiratory distress may be accompanied by increased, decreased, or normal respirations depending on the level of respiratory fatigue that the infant is experiencing at the time of assessment. Therefore, assessing respiratory rate alone may not be indicative of respiratory compromise in a fatigued neonate. Hence, utilizing a validated scoring system can improve the sensitivity of assessment and implementation of subsequent management.[10] Several scoring systems are specifically used for the assessment of respiratory distress in the neonate. Among them, the World Health Organization provides the most simplified scoring system, which classifies breathing difficulty by assessing respiratory rate, grunting, and chest in-drawing.[11] The other scoring systems that are utilized to classify respiratory distress in newborns include the Acute Care of at-risk Newborns Respiratory Score, the Silverman Scoring System, and Downe's Respiratory Distress Score.

Why it was important to conduct this study

For extremely preterm neonates, CPAP is an effective early intervention for ventilatory support and is used as an alternative and or to prevent mechanical ventilation and subsequent complications of invasive ventilation. Similarly, in full-term neonates, CPAP may be an effective alternative to head-box or Prong oxygen therapy for the recruitment of alveoli in low-middle-income countries. The use of CPAP in full-term neonates may help in the early discharge from the hospital and prevent the need for higher ventilatory methods, which are frequently not available in resource-limited hospitals.

The use of CPAP in the preterm population is now a widely used and accepted mode of early ventilation support, but its use and efficacy in full-term neonates have not been widely researched.

Aims and Objectives

The aim was to study the clinical profile and outcome of term neonates requiring CPAP in resource-limited settings. The objective of this study was demographic profile, clinical spectrum, and outcome of term neonates, requiring CPAP in tertiary care teaching hospital Kashmir India.

MATERIALS AND METHODS

The approval of the Institutional Ethical Board was obtained from Govt. Medical College, Srinagar. Kashmir vide order No: F(Minutes-BOPGS) Acad/KU/22 Dated February 02, 2022. The study was a prospective observational study conducted from December 2020 to November 2022. The study was conducted in the neonatal division of the Department of Pediatrics, an associated hospital of Government Medical College Srinagar.

Sample size

Based on 15% mortality; 2% absolute error; and 95% confidence, a total sample size of 261 was taken.

Data collection

Two hundred and sixty-one neonates brought to our hospital requiring inpatient management were stabilized first and then admitted to the neonatology unit. On arrival, the neonate's vitals were assessed followed by stabilization and documentation of demographic data about the baby and mother. Respiratory distress was documented by fast breathing (Respiratory rate >60/min) and any one of the following: Low O_2 saturation (SPO_2 < 90%), chest retraction, grunting, and nasal flaring.

Downe's scoring assessed the severity of the respiratory distress. The final score was classified into mild (<5), moderate (5–7), and severe (>7) to indicate the severity of distress. Details of birth history, type of delivery along with maternal variables, for example, multiple births, pregnancy-induced hypertension, and prolonged rupture of membrane were recorded. The different variables of babies, for example, birth weight, gestational age, and crying immediately after birth, Apgar score at 1 min and 5 min, delivery room management (oxygen, tactile stimulation, bag and mask ventilation, and intubation), and Downe's scoring before were recorded on predesigned pro forma. Following were the parameters observed during the study period: Time of starting CPAP, respiratory rate before, during, and after CPAP, total duration required to wean off CPAP, and any case of CPAP failure requiring mechanical ventilation. The other clinical data recorded were PDA, atrial septal defect and ventricular septal defect (clinical and Echo proven), pneumothorax, culture-positive sepsis, and duration of hospital stay among the survivors.

Table 2: Downe's score for grading severity of respiratory distress

Feature	Score 0	Score 1	Score 2
Cyanosis	None	In-room air	In 40% FiO_2
Retractions	None	Mild	Severe
Grunting	None	Audible with stethoscope	Audible without stethoscope
Air entry	Normal	Decreased	Barely audible
Respiratory rate	<60	60–80	>80 or apnea

Inclusion criteria

Full-term neonates with respiratory distress were included in the study study.

Exclusion criteria

All preterm neonates and full-term neonates with dysmorphism, gross congenital malformations including congenital heart diseases, neonatal shock, and some major interventions were excluded from the study.

Statistical analysis

The recorded data were compiled and entered into a spreadsheet (Microsoft Excel) and then exported to the data editor of SPSS Version 20.0. Frequency and percentages were determined.

RESULTS

As shown in Table 1, there are various existing case definitions of respiratory distress in a neonate. For uniformity and simplification, we use the case definition of the World Health Organization in this research. Further to grade the severity of respiratory distress, the Downes Score was assessed at the outset in all the neonates as depicted in Table 2.

As revealed in Table 3, most full-term newborns who were admitted with respiratory distress had a gestation age of 38 to 39 weeks (Table 3a), and male babies outnumbered females (Table 3b). The birth weight of babies ranges from 2000 to 2999 grams (Table 3c) and in 87.4% of babies did not have any significant maternal risk factor for adverse neonatal outcomes (Table 3d). The most common mode of delivery was the lower segment cesarian section 73.6% (Table 3e) and 82.8% of babies cried immediately after the birth (Table 3f). It further shows that a history of neonatal resuscitation was present in 17.2% of babies (Table 3g). Furthermore, the table depicts that 65.5% of these newborns were admitted to the level 3 NICU within 6 h of birth (Table 3h), with complaints of fast breathing, subcostal retractions, grunting and cyanosis (Table 3i). Most of the admitted newborns (88.5%) had oxygen saturation at room air less than 90% Table 3j).

As depicted in Table 4a, around 68.85% of the babies had a Downes Score of more than 5 on the initial assessment before starting bubble CPAP. Therefore, most newborns 69.73% required CPAP on admission to the Neonatal Intensive Care Unit as shown in Table 4b.

Table 4c shows that 58.6% of the babies required PEEP (positive end-expiratory pressure) of 6 or 7 and FiO2 of more than 40% (Table 4d) on admission and in 88.50% of babies, ventilatory settings were escalated over some time (Table 4e). 51.7% of babies were weaned from CPAP within 24 h as shown in Table 4f.

Table 3: Demographic, clinical, and risk profile of neonates

(a) Gestation age: The majority of infants, accounting for 59.2%, had a gestation age of 38 weeks, as indicated in the table		
Gestation age	**Number of cases**	**Percentage**
38 weeks	154	59.2
39 weeks	95	36.3
40 weeks	12	4.5
Total	261	100
(b) Gender: Illustrates that the percentage of male newborns was 63.2%		
Male	165	63.2
Female	96	36.8
(c) Birth weight: Shows that 60.91% of babies fell within the weight range of 2000–2999 g		
1000–1999 g	5	1.9
2000–2999 g	159	60.91
3000–3999 g	85	32.56
4000–5000 g	12	4.5
(d) Maternal risk factors: Illustrates that 87.4% of mothers did not exhibit any significant risk factors		
Not significant	228	87.4
Pregnancy Induced Hypertension	21	8.0
Gestational diabetes Miletus	21	8.0
Premature rupture of membranes >24 h	12	4.6
(e) Mode of delivery: This Table depicts that most common mode of delivery was lower-segment cesarean section		
Lower-segment cesarean section	192	73.6
Normal vaginal delivery	69	26.4
(f) Cried immediately at the time of Birth: The table depicts that 82.8% babies cried immediately after the birth		
Cried immediately	216	82.8
Not cried	45	17.2
(g) Resuscitation is required at birth: This table depicts that 82.8% babies did not require neonatal resuscitation		
No	216	82.8
Yes	45	17.2
(h) Age at the time of admission in hours: This table depicts that 65.5% were admitted within 6 h of birth		
1–6 h	171	65.5
7–12 h	42	16.1
13–18 h	12	4.6
19–24 h	36	13.8
(i) Presenting complaint: The table depicts that fast breathing, subcostal retractions and Grunt were the common presentations		
Fast breathing	261	100
Subcostal retractions	213	81.6
Grunt	186	71.3
Cyanosis	12	4.6
(j) SPO_2 room air on admission: The table depicts that 88.5% babies were having SPO_2 <90% on admission		
<80%	93	35.6
80–90%	138	52.9
>90%	30	11.5

Table 5 reveals that around 39% of babies required a higher mode of ventilatory support during hospital stays, and

Table 4: Efficacy, safety and outcome of CPAP in full-term neonates

(a) Downe's score before using Bubble CPAP: The table shows that 68.8% of infants had a Downe's score exceeding 5		
4	78	29.8
5	126	48.2
6	57	20.6
(b) Age at which Bubble CPAP* was started after admission: The table illustrates that a significant majority of newborns, accounting for 69.73%, needed CPAP on admission		
On admission	182	69.73
1–12 h of admission	61	23.3
13–24 h of admission	4	1.53
25–36 h of admission	6	2.29
37–48 h of admission	7	2.68
49–60 h of admission	0	0
61–72 h of admission	0	0
73–84 h of admission	0	05
85–96 h of admission	2	0.76
(c) PEEP# utilized at the outset: The table indicates that over 58.6% of babies needed PEEP 6		
PEEP#	**Cases**	**Percentage**
5	96	36.78
6	153	58.6
7	12	4.59
(d) FIO2& used at the outset: This table illustrates that 63% of infants necessitate an FIO_2 of more than 40%		
30%	96	36.78
40%	60	22.98
50%	78	29.8
60%	27	10.34
(e) Number of patients in which CPAP settings were escalated: This table illustrates that 88.50% of infants necessitated an escalation in PEEP, FIO_2, or both		
PEEP	84	32.1
FIO2	90	34.4
PEEP+FIO_2	57	21.83
Total	231	88.50
(f) The total duration of bubble CPAP in hours: This table illustrates that 51.7% needed CPAP for a duration of <24 h		
1–12	64	24.5
13–24	71	27.2
25–36	22	8.4
37–48	51	19.5
49–60	6	2.29
61–72	29	11.11
73–84	0	0
85–96	0	0
97–108	9	3.4
109–120	6	2.29
121–132	0	0
133–144	3	1.14

*CPAP Continuous positive airway pressure. #PEEP Positive end-expiratory pressure. &FIO2 Fractional inhaled oxygen

36.7% were put on invasive positive pressure ventilation. 5.74% developed pneumothorax on CPAP.

Table 6 shows that the most common cause of respiratory distress in full-term babies was transient tachypnea of the newborn (TTN), followed by early neonatal sepsis, meconium aspiration syndrome, and perinatal asphyxia. It further reveals that 78.65 were discharged successfully and the rest 21.83% died.

Table 5: The tables depicts that around 39% babies who were put on CPAP required higher ventilation support, 5.74% developed pneumothorax

Number of babies who required higher ventilation support out of 261		
Non-invasive ventilation	6	2.29
Invasive positive pressure ventilation	96	36.7
Number of babies who developed a pneumothorax		
Developed	15	5.74
Not developed	246	94.25

CPAP: Continuous positive airway pressure

Table 6: This table depicts that 78.16% babies were discharged successfully and 21.83% died

The outcome of babies who required CPAP and or higher ventilation		
Outcome	**Number of cases**	**Percentage**
Discharged	204	78.16
Expired	57	21.83
(a) Causes of respiratory distress requiring CPAP: This table depicts that the most common cause of respiratory distress in full term babies was transient tachypnea of newborn		
Causes	**No. of cases**	**Percentage**
Transient tachypnea of newborn	69	26.4
Transient tachypnea of newborn with sepsis	16	6.1
Transient of tachypnea pneumothorax	7	2.68
Transient tachypnea of newborn with ASD with increased PA pressures	2	0.76
Congenital pneumonia	2	0.76
Bronchopneumonia	10	3.83
Meconium aspiration syndrome	26	9.9
Meconium aspiration syndrome with sepsis	23	8.8
Meconium aspiration pneumothorax	9	3.44
Meconium aspiration syndrome with severe PPHN	14	5.3
Meconium aspiration syndrome with PDA with increased PA pressures	2	0.76
Term with respiratory distress syndrome	13	4.9
Term with respiratory distress syndrome with sepsis	17	6.5
Term with respiratory distress syndrome with pneumothorax	3	1.14
Perinatal asphyxia with HIE 1	15	5.7
Perinatal asphyxia with HIE 2	11	4.2
Neonatal sepsis	19	7.2

PDA: Patent ductus arteriosus, ASD: Atrial septal defect, CPAP: Continuous positive airway pressure

DISCUSSION

In our study, a total of 261 neonates were included with male-female ratio of 1.7:1. Majority of the neonates were of birth weight between 2.1 kg and 3 kg (60.91%) and born mostly at 38 weeks (59.2%). In our study, most of the babies were born by cesarean section (73.6%) and that was a major risk factor for respiratory distress in term infants. Zanardo et al.,[12] and Stutchfield et al.,[13] in their studies, have also revealed a highly significant association between CS delivery and RD in full-term newborns (P=0.0049).

In our study, we observed that around 216 (82.8%) newborn babies did not require any form of resuscitation at birth, and only 45 (17.2%) babies did require some form of neonatal resuscitation at birth. The most common presentation of respiratory distress in full-term newborns was fast breathing (100%), followed by subcostal retractions (81.6%) and grunting (71.3%). In our study, we used the Downes score as a severity scale for the assessment of respiratory distress, and in the majority of babies, the Downes score was 5 (58.6%) before starting CPAP. The age of starting CPAP in most of the newborns was at admission to the hospital (in 69.73% of cases). This finding of delayed use of CPAP was consistent with the study conducted by Manandhar, and Sunil Raja in a tertiary care hospital.[14] In our study, most patients required initial CPAP settings of PEEP 6 (153 cases) and FIO_2 30% (96 cases). Most neonates required 13–24 h of B-CPAP for stabilization and settling of respiratory distress. In our study, we found that the success rate of CPAP therapy was high (60.9%) and 39.08% of patients did not settle with the CPAP mode of ventilation and required another mode of respiratory support such as NIPPV (5.89%) and IPPV (94.11%). The frequency of CPAP failure as a primary mode of ventilation in full-term babies with respiratory distress was consistent with the study conducted at Government General Hospital Guntur, a tertiary care hospital. In their study, the success rate was 64% and the failure rate was 36% (36 cases).[14]

The CPAP though the noninvasive form of ventilation also works on the principle of positive-pressure ventilation. Therefore, there are some complications of CPAP like air leak syndromes, although not reported so frequently, a matter of concern, especially when inappropriately high pressures in CPAP are used to maintain PaO_2 and 0r SPO_2 levels in neonates.[15] In our study, we observed that 5.70% of cases developed air leaks.

The different etiologies of respiratory distress in full-term babies in our study were variable and like different studies previously conducted in different geographical areas of the world. Transient tachypnea of newborns (TTN) was the most common cause (26.4%) of respiratory distress in full-term babies particularly who were born by lower-segment cesarean section followed by meconium aspiration syndrome in 9.9% of cases. The main reason for TTN is the delayed absorption of fetal lung fluid, which is usually triggered by the rapid endocrine changes and activation of many active transport channels occurring perinatally and main activating factor for such physiological changes which help in the absorption of lung fluid are labor pains. Hence, these physiological changes do not occur in babies born by cesarean section; therefore, the majority of babies who are born by cesarean section develop TTN. Further, the most common mode of delivery in our study was the cesarean section; subsequently, a large number of full-term babies developed respiratory distress due to TTN. The overuse and misuse of the lower segment cesarean section in Kashmir explain that TTN is the most common etiology of respiratory distress in full-term babies. Instead of its high frequency, the advantages of CPAP as a mode of ventilation and its advantages are therapy well-documented in different studies.[16]

Limitations of the study

The limitations of our study were that all of the babies were outborn and presented to the hospital at different hours of postnatal age with different comorbidities and baseline metabolic environments on admission to tertiary care hospital.

CONCLUSION

In our study, 204 (78.16%) babies out of 261 patients survived and 57 (21.83%) babies expired. The most common cause of death was septicemia (52.6%) followed by MAS with severe PPHN (21.05%).

The early use of CPAP as a mode of ventilation in full-term babies with TTN is well-documented and it can be safely used in other common neonatal conditions which can cause respiratory distress in full-term neonates. The low-middle-income countries are facing challenges to improve comprehensive neonatal care, and there is a dire need for simple and cost-effective methods of respiratory support. Bubble CPAP is one such promising ventilatory support intervention, which may reduce the need for costly mechanical ventilators. Further, the CPAP can be applied by appropriately trained nursing staff even in delivery rooms and during the transport of sick babies. However, there is a need for more research to know the exact impact of bubble CPAP compared with standard oxygen therapy on neonatal morbidity, mortality, and reducing the duration of hospital stay. Furthermore, it is imperative to know the impact of early use of CPAP in delivery rooms of rural health-care delivery systems and during transportation to tertiary care hospitals. The different stakeholders and neonatal forums should frame the guidelines for effective implementation methods of CPAP, especially in non-tertiary hospitals and during the transportation of sick newborns.

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Authors' Contributions:
SH- Literature survey, data collection, data analysis, definition of intellectual content, preparation of figures and tables, implementation of the study protocol, manuscript preparation; **SAN-** Concept, manuscript preparation, editing, manuscript revision; **ST-** Design of study, statistical analysis and interpretation, coordination, manuscript revision.

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