

Clinical Outcome of Preterm Neonates with Respiratory Distress Syndrome on Continuous Positive Airway Pressure

Sijad-Ur-Rehman, Quratulain, Wahid Ali, Romana Bibi, Sohail Ashraf, Kulsoom Iqbal

ABSTRACT:

Objectives: To evaluate the clinical course in preterm neonates with Respiratory Distress Syndrome on bubble Continuous Positive Airway Pressure along with their outcome during stay in hospital.

Study Design and Setting: A descriptive case study at the NICU was carried out at Bacha-Khan Medical Complex Swabi from December 2020 to December 2021.

Methodology: Respiratory Distress Syndrome was diagnosed by following the criteria: tachypnea (> 60 breaths/min), subcostal retraction and saturation <92%. Clinical course was assessed by mean length of hospital stay from the day of admission to the day of discharge. Outcome was assessed by means of switching the baby to mechanical ventilation by failing CPAP therapy by not maintaining O₂ saturation > 92% and tachypnea > 60 breaths/min on 10cm maximum pressure of H₂O. CPAP response were noted.

Results: Total of 100 patients enrolled in our study, 56 patients were male and 44 patients were female. Mean age was 1.24+0.04days. Mean gestational age of babies was 31.18+0.170weeks. Mean weight of babies was 2.035+0.023kg. Mean hospital stay was 15.05+0.237days. Out of 100 patients included in study 76% babies needed ventilatory support during hospital stay and 24% babies recovered from respiratory distress syndrome without need of ventilator support.

Conclusion: Respiratory Distress Syndrome is a fatal complication in Preterm neonates in Neonatal Intensive Care Unit. Respiratory assistance done through continuous positive airway pressure has shown encouraging results in management by preventing complications, mechanical ventilation need, less hospital stay and preventing mortality.

Key Words: Respiratory Distress Syndrome, Continuous Positive Airway Pressure, Mechanical Ventilation.

How to cite this Article:

Rehman S, Ain Q, Ali W, Bibi R, Ashraf S, Iqbal K. Clinical Outcome of Preterm Neonates with Respiratory Distress Syndrome on Continuous Positive Airway Pressure J Bahria Uni Med Dental Coll. 2022; 12(4):186-90. DOI: <https://doi.org/10.51985/JBUMDC202228>

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non Commercial License (<http://creativecommons.org/licenses/by-nc/4.0>) which permits unrestricted non commercial use, distribution and reproduction in any medium, provided the original work is properly cited.

Sijad-Ur-Rehman

Associate Professor, Department of Pediatrics
Gujju Khan Medical College / Bacha Khan Medical Complex
Sawabi

Quratulain

Senior Registrar, Department of Pediatrics
HITEC Institute of Medical Sciences Taxila Cantt.

Wahid Ali

Assistant Professor, Department of Pediatrics
HBS Medical and Dental College / HBS General Hospital
Islamabad

Romana Bibi (Corresponding Author)

Resident, Department of Gynaecology/Obstetrics
Gynae A Unit, Khyber Teaching Hospital Peshawar
Email: romanawazir14@gmail.com

Sohail Ashraf

Associate Professor, Department of Pediatrics
Wah Medical College / National University of Medical Sciences

Kulsoom Iqbal

Assistant Professor, Department of Radiology
HITEC Institute of Medical Sciences Taxila Cantt.

Received: 24-Feb-2022

Accepted: 16-Sep-2022

INTRODUCTION:

Leading causes of infant death and morbidity is respiratory distress syndrome. The illness known as RDS (respiratory distress syndrome in newborns) affects infants whose lungs have not yet reached their fully developed. It could also be attributed to hereditary difficulties with lung development. RDS is most common in babies born before the ages of 34 weeks.¹ At least two of the following clinical signs are required to diagnosis respiratory distress syndrome (RDS): tachypnea (>60/min), dyspnea with flaring, and dyspnea with Nasal retractions, subcostal or intercostal retractions, and inspiratory subcostal or intercostal retractions In room air, there is flaring, expiratory grunting, and cyanosis.² Severe respiratory distress syndrome (RDS), which is more common in preterm babies of less than 34 weeks, is one of the most common causes of this respiratory failure. It is usually caused by meconium aspiration syndrome in term infants and surfactant deficiency in premature babies.³

In Malawi, using the bCPAP to support newborns' ventilation is a very cost-effective method,⁴ treatment of infant respiratory distress with a low-cost B-CPAP system has been shown to improve overall survival. The benefits were higher for infants with a low birth weight and RDS.^{4,5} Bubble CPAP is a

significant advancement in the treatment of respiratory distress.^{6,7} There was a considerable improvement in the mean respiratory rate, mean oxygen saturation ($p=0.001$), and frequency of chest in-drawing after 24 hours of bubble CPAP ($p=0.001$). In a Pakistani study, therapeutic efficacy was shown to be 80 (84.2%), and bubble CPAP may be utilized as the first line of respiratory support for preterm and extremely preterm newborns with RDS.⁸ According to a recent study, this therapy is effective in avoiding respiratory problems in premature newborns.⁹ According to Simone Martin's study, the bubble CPAP had a decreased failure rate for CPAP in these same studies in terms of mortality and complications ($p=0.003$).¹⁰

The rationale of this study is to evaluate the clinical outcome on bubble CPAP of premature neonates with respiratory distress syndrome as in literature we could not find such study conducted in Pakistan. Due to resource limitation, most of hospitals in our country lack facility of mechanical ventilator. This study will help to improve management of preterm neonates with RDS at resource limited hospital. This study aimed to evaluate the clinical course in preterm neonates with RDS on bubble CPAP along with their outcome during stay in hospital.

METHODOLOGY:

A descriptive case study at the NICU was carried out at Bacha-Khan Medical Complex Swabi from December 2020 to December 2021. All premature infants admitted at gestational ages between 28-34 weeks included in inclusion criteria. NICU with RDS, birth weight <2500 grams, 3) either gender and exclusion criteria: babies with gross congenital anomalies, babies with gut and respiratory tract anomalies, Co-morbidities e.g. Infant of diabetic mother, hypoxic ischemic encephalopathy, preterm/premature rupture of membranes, antepartum hemorrhage.

Following institutional ethical approval from the Gajju Khan Medical College/Medical Complex Swabi 7-8/2022, 28038,

chairperson of the institutional ethical review board, informed consent from parents, in the study, patients at the neonatal Intensive Care Unit at Bacha Khan Medical Complex Hospital Swabi who met the inclusion criteria after a comprehensive history and examination were included. Diagnosis of RDS was done by observing tachypnea (> 60 breaths/min), chest retractions and cyanosis at room air. Clinical course was assessed by mean length of hospital stay from the day of admission to the day of discharge. Outcome was assessed by means of switching of the baby to mechanical ventilation after 72 hrs of bubble CPAP therapy based on following criteria of not maintaining O_2 saturation $> 92\%$ and tachypnea > 60 breaths/min.

Mean and standard deviation were calculated for age, period of gestation, weight in kg and duration of hospital stay, while frequency and percentages were calculated for gender and need of ventilator support.

RESULTS:

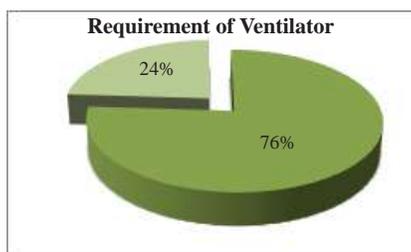
Total of 100 patients were enrolled in the study who presented in NICU, Bacha Khan Medical Complex Hospital after preterm birth. Among all the patients 56 patients were male and 44 patients were female. Descriptive statistics of age of all patients showed minimum age of 01 day and maximum age was 02 days. Mean age was $1.24+0.042$ days. Minimum gestational age of patients was 28 weeks and maximum gestational age was 34 weeks. Mean gestational age of babies was $31.18 + 0.170$ weeks.

Mean weight of babies was $2.03+0.023$ kg. Minimum weight of baby was 1.5 Kg and maximum weight was 2.4 Kg. Minimum days of hospital stay were 11 days and maximum duration of stay was 22 days. Mean hospital stay was $15.05+0.237$ days. Out of 100 patients included in study 76% babies needed ventilator support during hospital stay and 24% babies recovered from respiratory distress syndrome without needing ventilator.

DESCRIPTIVE STATISTICS

Gender	Frequency	Percentage	Probability	Requirement of Ventilator	Frequency	Percentage	Probability
Male	56	56%	0.56	Yes	76	76%	0.76
Female	44	44%	0.44	No	24	24%	0.24
Total	100	100%	1.00		100	100%	1.00

Pie Chart No. 01: Distribution of Patients Needing Ventilator Support



DISCUSSION:

Early detection of Respiratory Distress Syndrome (RDS) and management is key to prognosis of the disease. Marked tachypnea and low oxygen saturation are the main clinical indicators for diagnosis. Management is based on ensuring a secure airway and ventilation to improve on going pathology. Ventilation mainly invasive mechanical ventilation has been backbone of treatment for long but this method has been related to many complications and morbidity.

Alternate therapy in form of CPAP has been introduced in last few decades which can be in form of bubble CPAP and has shown improved results, less duration of stay in hospital and less need of invasive mechanical ventilation in patients receiving CPAP.¹¹ In a study conducted in Pakistan, successful treatment (efficacy) was found to be 80 (84.2%).⁸ A recent study shown that this therapy is useful in reducing respiratory issues in late preterm infants. In our study improved outcome following CPAP use was seen with average stay of patients was 15.05+0.237days. Out of 100 patients included in study 76% babies needed ventilator support during hospital stay and 24% babies recovered from respiratory distress syndrome without needing ventilator support.

In hospitalized infants aged 28 days, CPAP was used to treat respiratory distress. The study, Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) and Newcastle-Ottawa Quality Assessment Scale techniques were used to assess the quality of recommendations. In three studies, using bubble CPAP first, rather than oxygen treatment, and then if necessary, mechanical ventilation reduced the need for mechanical ventilation by 30%-50%. Despite the fact that a meta-analysis of CPAP failure demonstrated that an Additional three trials comparing bubble CPAP to ventilator CPAP found that both groups' mortality and complication rates were the same ($p=0.003$).¹¹

A retrospective analysis of neonates >32 weeks of gestation who were conveyed in Western Australian Neonatal Transport Service with acute respiratory distress. CPAP use grew dramatically from 33% in 2002 to 59% in 2004 over the study period. Overall, 10(29%) patients required endotracheal tube (ETT) ventilation, 166(45%) required nasal CPAP, and 95(26%) required cot oxygen. Within 24 hours, 22(13%) of the neonates in the CPAP group required ETT ventilation; these infants had a higher beginning those who were successfully transported on CPAP alone had lower oxygen requirements.¹²

In May 2006, a plan was created to encourage the use of bCPAP on a regular basis in neonates who require ventilator assistance to avoid intubation and Mechanical Ventilation. Intubation rates were found to be significantly different 72% ($p<0.000$). The proportion of patients treated only with bCPAP 27% ($p=0.0001$). Although the average duration of stay in the NICU increased (14.6 days in 2006 and 17.5 days in 2008, $p=0.0481$), the death rate was drastically lowered 40% ($p=0.0001$).¹³

Since it was initially introduced as an RDS is being treated with an interventional treatment, there have always been concerns about the increased labored breathing in neonates treated with nasal continuous PAP (n-CPAP). As a result, respiratory support systems such as nasal bi-level PAP (N-BiPAP) and sigh-PAP (SiPAP) were developed in the last ten years. From October 2012 to March 2014, a randomized clinical trial was conducted on 74 babies with RDS who

were admitted in the NICU at Al-Zahra Hospital. Patients were randomized to one of two respiratory support groups: N-BiPAP or SiPAP, at random. Each group consisted of 37 neonates who were compared in terms of noninvasive ventilation duration and demographic features. In terms of the average length of noninvasive respiratory support and the average duration of the need for oxygen supplementation, there was no significant difference between the groups.¹⁴

In four rural Ghana hospitals, In the first hour, The mean respiratory rate of children who received immediate CPAP decreased by 16 breaths per minute (CI 95%: 10-21), compared to no change in children who received CPAP one hour later (CI 95%: -2 to +5).¹⁵ A research was carried out in terms of demographics, CPAP failure (21.1 and 20.0% for VF and CF; $p=1.000$) did not differ between the groups, air leak syndrome (10.5 and 5.0%; $p = 0.605$), total CPAP time (median: 22.0 h, IQR: 8.00-31.00 h and median: 22.0 hour, IQR: 6.00-32.00 hour; $p = 0.822$).¹⁶

In a resource-limited situation, RDS in newborns were treated with a low-cost self-contained bubble System of bCPAP. In 2013, study in Blantyre, Malawi, patients experiencing respiratory distress weighing less than 10 kg were included in the study. 70% of those who were given bCPAP survived. Within 24 hr, 80% survivors showed signs of improvement. The use of bCPAP was judged to be beneficial by all treating physicians, resulting in a change in practice.¹⁷

CPAP was linked to a lower risk of treatment failure (typical risk ratio (RR) 0.64, 95 percent confidence interval (CI) 0.50 to 0.82; typical risk difference (RD) -0.19, 95% CI -0.28 to -0.09; decrease in the need for ventilator support (average RR 0.72, 95% CI 0.54 to 0.96; typical RD -0.13, 95% CI -0.25 to -0.02).¹⁸ 37 infants with RDS were divided into two groups and given CPAP alone or CPAP plus HFOV treatment. Compared to the HPA+CPAP group, the CPAP group had longer mean scores for the duration of CPAP and oxygenation, as well as for the length of hospitalization. However, the differences were only statistically significant for the duration of oxygenation ($P=0.05$).¹⁹

In Kenya prematurity/acute respiratory distress syndrome was the most common indication, and the overall mortality rate was 24%. 61% of premature with acute respiratory distress syndrome being the most common indication for CPAP²⁰. Prophylactic use of Bubble CPAP reduces the time it takes to alleviate respiratory distress (3.14+2.74 vs. 3.58+2.12 days, p -value > 0.05), as well as the incidence of RDS (40% vs. 46 %, p -value > 0.05), the need for surfactant (20% vs. 28 %), and the switch to mechanical ventilation (14% vs. 18 %, p -value > 0.05). Both groups had received prenatal steroids in about 80% of cases. BCPAP use as a preventive shortens hospital stays (28.34+12.18days vs. 30.74+12.24 days), increases sepsis frequency (22% vs. 18 %), and reduces the number of ROP (16% vs 22%).²¹

A study from Multan, Pakistan, Out of 172 newborns, 91 (52.9%) were malnourished, 89 (51.7%) had gestational ages between 31 and 32 weeks, and 97 (56.4%) were born weighing between 1000 and 1500 grams. The majority of the neonates, 97 (56.4%), had RDS that was radiological rated as moderate. 143 (83.1%) newborns experienced a successful outcome from early CPAP. There was no statistically significant difference in the results of the CPAP between the genders of research participants ($p=0.4990$). Birth weight, gestational age, and the degree of radiological grading of RDS were all substantially related to the effectiveness of CPAP ($p=0.00001$). Additionally substantially linked with CPAP outcomes among study participants were the arterial blood gas parameters PO₂, PCO₂, and HCO₃ ($p=0.0001$).²²

Another study from India was reported, 245/330 newborns were weaned from CPAP ventilation and released, while 85 babies passed away from the sickness. Infants with septicemia had a higher mortality rate. 25.75 percent of B-CPAP users had a Downes score of 4, 33.03 percent had a score of 5, and 41.21 percent had a score of 6. With the use of B-CPAP, all parameters, including cyanosis, grunting, tachypnea, chest indrawing, and air entry, improved. Asphyxia, RDS, prematurity-related apnea, meconium aspiration syndrome (MAS), and bronchopneumonia sepsis were some of the causes of respiratory distress.²³ According to another study, delivery room CPAP was linked to respiratory problems and the highest likelihood of NICU admission (9.3 times the risk of those without delivery room positive pressure).²⁴ Jordan published a different study that 143 infants in all (mean birth weight: 2,770–1,800 g) were enrolled. A newborn's brief tachypnea (42%), followed by a lengthy respiratory transition, was the most frequent underlying cause of respiratory distress (34%). Only nine newborns failed bCPAP, giving the therapy a success rate of 93.7%.²⁵

In a research by Ramin Iranpour et al,²⁶ 4/34 (11.8%) preterm newborns who were treated with NCPAP for respiratory distress syndrome required a ventilator. Only 8 (13.3%) newborns needed mechanical ventilation, according to a study done in Pakistan. Overall, 52 babies were successfully weaned off of nCPAP. RDS (65%) was the main indicator of CPAP use.²⁷ 90 infants with a clinical diagnosis of RDS were studied in Islamabad. Starting CPAP for the treatment of RDS occurred at a mean age of 5.27+2.66 hours of life. Chest X-ray results for 11/90 newborns (11.22%) indicated severe RDS, while the results for the remaining 79 babies (88.78%) indicated mild to moderate RDS.²⁸ In another Pakistani study, At 24 hours, the B-CPAP had 100% of the projected survival rates. Following 48 hours, the comparable outcomes were all positive.²⁹ Another study carried out in Multan, Out of 172 newborns in total, 97 (56.4%) had radiological RDS to be moderate, 143 (83.1%) newborns showed successful results with early CPAP.³⁰

Limitations of our study were single centered study data collected from the neonates admitted in our department and poor maternal efforts. Majority of the neonates who were born premature in periphery were presented late and were not treated properly by getting the appropriate dose of treatment they needed. The mortality and morbidity of infants who are born premature and with low birth weights should all be prevented by using CPAP and timely treatment if they experience respiratory distress syndrome.

CONCLUSION:

Respiratory Distress Syndrome is frequent and fatal condition seen in Preterm neonates in NICU. Early and prompt treatment is main stay of management. Respiratory assistance done through continuous positive airway pressure has shown encouraging results in management by preventing complications like need of mechanical ventilation, less hospital stay and preventing mortality. More studies need to be done with larger population size to extensively see the long terms outcome of this mode of treatment.

Authors Contribution:

Sijad-Ur-Rehman: Manuscript Writing, Concept of Study and Data Collection

Quratulain: Literature Review, Data Analysis

Wahid Ali: Manuscript Writing

Romana Bibi: Manuscript Writing, Data Analysis, Critical Review and Corresponding Author

Sohail Ashraf: Results Interpretation and Discussion Writing

Kulsoom Iqbal: Study Designing, Study Conduction

REFERENCES:

1. Groenendaal F, De Vries LS, Martin RJ, Fanaroff AA, Walsh MC. Hypoxic-ischemic encephalopathy. Fanaroff and Marfin's neonatal/perinatal medicine. Diseases of the fetus and infant. 2015;904-26.
2. Balamkar R and Shrikhande D (2015) Surfactant Replacement Therapy in Neonatal Respiratory Distress Syndrome: Case Control Study in Rural Hospital, Loni, India. Resea J of Pharma, Biol and Chemi Sci, 2015 6(5): 1123-28
3. Pooniya V. Management of neonatal respiratory distress syndrome by indigenous CPAP in a resource poor setting. J Pediatr Care 2015;1:1.
4. Kawaza K, Machen HE, Brown J, Mwanza Z, Iniguez S, Gest A, et al. Efficacy of a low-cost bubble CPAP system in treatment of respiratory distress in a Neonatal Ward in Malawi. PLoS ONE 2014;9(1):e86327. DOI: <https://doi.org/10.1186/s12887-014-0288-1>
5. Dewez JE, van den Broek N. Continuous positive airway pressure (CPAP) to treat respiratory distress in newborns in low-and middle-income countries. Tropical Doctor 2017; 47(1):19-22.
6. Chen A, Deshmukh AA, Richards-Kortum R, Molyneux E, Kawaza K, Cantor SB. Cost-effectiveness analysis of a low-cost bubble CPAP device in providing ventilatory support for neonates in Malawi – a preliminary report. BMC Pediatr 2014; 14:288. doi: 10.1186/s12887-014-0288-1.

7. Brown J, Machen H, Kawaza K, Mwanza Z, Iniguez S, Lang H. A high-value, low-cost bubble continuous positive airway pressure system for low-resource settings: technical assessment and initial case reports. *PLoS One* 2013; 8(1):e53622. doi.org/10.1371/journal.pone.0053622. doi.org/10.1371/journal.pone.0090972
8. BANO I, HAROON F, MALIK KB, Bari A, Rathore AW. Efficacy of Nasal Continuous Positive Airway Pressure by Bubble CPAP in Neonates with Respiratory Distress Syndrome. *Pak Pediatr J*. 2021;45(4):384-88.
9. Gyamfi-Bannerman C, Thom EA. Antenatal Betamethasone for Women at Risk for Late Preterm Delivery. *N Engl J Med*. 2016;375(5):486-7. pmid:27518669. DOI: 10.1056/NEJMoA1516783
10. Martin S, Duke T, Davis P. Efficacy and safety of bubble CPAP in neonatal care in low and middle income countries: a systematic review. *Arch Dis Child Fetal Neonatal Ed*. 2014; 99: 495-504. doi.org/10.1136/archdischild-2013-305519
11. Jobe AH, Ikegami M. Biology of surfactant. *Clin Perinatol*. 2001; 28:655. doi.org/10.1016/S0095-5108(05)70111-1
12. Resnick S, Sokol J. Impact of introducing binasal continuous positive airway pressure for acute respiratory distress in newborns during retrieval: Experience from Western Australia. *J Paediatr Child Health*. 2010; 46:754-9. doi.org/10.1111/j.1440-1754.2010.01834.x
13. Rezzonico R, Caccamo LM, Manfredini V, Cartabia M, Sanchez N, Paredes Z, et al. Impact of the systematic introduction of low-cost bubble nasal CPAP in a NICU of a developing country: a prospective pre- and post-intervention study. *BMC Pediatr*. 2015;15:26.
14. Sadeghnia A, Danaei N, Barkatein B. A Comparison of the Effect of Nasal bi-level Positive Airway Pressure and Sigh-positive Airway Pressure on the Treatment of the Preterm Newborns Weighing Less than 1500 g Affiliated with Respiratory Distress Syndrome. *Int J Prev Med*. 2016;7:21. doi: 10.4103/2008-7802.173930
15. Wilson PT, Morris MC, Biagas KV, Otupiri E, Moresky RT. A randomized clinical trial evaluating nasal continuous positive airway pressure for acute respiratory distress in a developing country. *J Pediatr*. 2013; 162:988-92. doi.org/10.1016/j.jpeds.2012.10.022
16. Yagui AC, Vale LA, Haddad LB, Prado C, Rossi FS, Deutsch AD, et al. Bubble CPAP versus CPAP with variable flow in newborns with respiratory distress: a randomized controlled trial. *J Pediatr*. (Rio J). 2011; 87:499-504.
17. Machen HE, Mwanza ZV, Brown JK, Kawaza KM, Newberry L, Richards-Kortum RR, et al. Outcomes of patients with respiratory distress treated with bubble CPAP on a pediatric ward in Malawi. *J Trop Pediatr*. 2015;6:421-7. doi.org/10.1093/tropej/fmv052
18. Ho JJ, Subramaniam P, Davis PG. Continuous positive airway pressure (CPAP) for respiratory distress in preterm infants. *Cochrane Database of Systematic Reviews*. 2020(10). doi.org/10.1002/14651858.CD002271.
19. Choupani Dastgerdi R, Hamidi M, Khalili Dehkordi M. Comparison of the Effectiveness of Continuous Positive Airway Pressure (CPAP) Therapy with a Combination of High-Frequency Oscillations and CPAP in the Treatment of Respiratory Distress Syndrome in Infants. *IJN*. 2022;13(1):13-7. https://ijn.mums.ac.ir/article_19523.html
20. Olayo B, Kirigia CK, Oliwa JN, Agai ON, Morris M, Benckert M, Adudans S, Murila F, Wilson PT. Effective training-of-trainers model for the introduction of continuous positive airway pressure for neonatal and paediatric patients in Kenya. *Paedr inter child health*. 2019 ;39(3):193-200. doi.org/10.1080/20469047.2019.1624007
21. Shaheen M, Jahan I, Hossain MI, Rahaman MM. Use of bubble continuous positive airway pressure (bCPAP) for prevention of respiratory distress in preterm infants; *Eur J Pharm Med Resea*:2021,8(4), 643-648
22. Rehman A, Quddusi AI, Nadeem A, Fatima N, Iqbal I. Early nasal continuous positive airway pressure in preterm neonates with Respiratory Distress Syndrome. *The PMJ*. 2021; 28(07):957-62. DOI:https://doi.org/1 0.29309/TPMJ/2021.28.07.5707
23. Slain KN, Rotta AT, Martinez-Schlurmann N, Stormorken AG, Shein SL. Outcomes of children with critical bronchiolitis meeting at risk for pediatric acute respiratory distress syndrome criteria. *Pediatr Crit Car Med*. 2019;20(2):e70-6. DOI:10.4103/jpai.jpai_11_21
24. Spillane NT, Macalintal F, Nyirenda T, Golombek SG. What happens to 35 week infants that receive delivery room continuous positive airway pressure?. *Journal of Perinatology*. 2021 ;41(7):1575-82. doi.org/10.1038/s41372-020-00883-w
25. Al-Lawama M, Alkhatib H, Wakileh Z, Elqaisi R, AlMassad G, Badran E, Hartman T. Bubble CPAP therapy for neonatal respiratory distress in level III neonatal unit in Amman, Jordan: a prospective observational study. *Int J Gen Med*. 2019;12:25. doi: 10.2147/IJGM.S185264
26. Iranpour R, Armanian AM, Abedi AR, Farajzadegan Z. Nasal high-frequency oscillatory ventilation (nHFOV) versus nasal continuous positive airway pressure (NCPAP) as an initial therapy for respiratory distress syndrome (RDS) in preterm and near-term infants. *BMJ Paediatr Open*. 2019; 14;3(1):e000443. doi: 10.1136/bmjpo-2019-000443. PMID: 31414062; PMCID: PMC6668751.
27. Anwaar O, Hussain M, Shakeel M, Baig MM. Outcome of use of nasal continuous positive airway pressure through infant flow drivers in neonates with respiratory distress in a tertiary care hospital in Pakistan. *Journal of Ayub Medical College Abbottabad*. 2018; 26;30(4):511-5.
28. Zia J, Zaman N, Zafar A, Mumtaz H, Fazal S. Early Bubble Continuous Positive Airway Pressure Therapy for Premature Neonates with Respiratory Distress Syndrome. *Annals of PIMS*. 2022; 28;18(1):41-5.
29. Khan G, Imtiaz S, Farooq K, Hamza A, Roy S, Imran M. Comparison of Bubble Continuous Positive Airway Pressure Versus Conventional Ventilation In Neonates with Respiratory Distress Syndrome. *PJMHS*. 2022 26;16(04):811-.
30. Rehman A, Quddusi AI, Nadeem A, Fatima N, Iqbal I. Early nasal continuous positive airway pressure in preterm neonates with Respiratory Distress Syndrome. *The PMJ*. 2021; 10;28(07):957-62.

