e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2022; 14(5); 693-701

Original Research Article

Clinicopathological Pattern and Outcome of Neonates Requiring Mechanical Ventilation in NICU

Latha S.P[1], S. V. Savaskar[2], Sachin Bandichhode[3], MoinTamboli[4]

[1]Senior Resident, Dept. of Paediatrics, Dr V. M. Govt. Medical College, Solapur.
[2]Professor and Hod, Dept. of Paediatrics, Dr V. M. Govt. Medical College, Solapur.
[3]Associate Professor, Dept. of Paediatrics, Dr V. M. Govt. Medical College, Solapur.
[4]Assistant Professor, Dept. of Paediatrics, Dr V. M. Govt. Medical College, Solapur.

Received: 15-03-2022 / Revised: 20-04-2022 / Accepted: 15-05-2022
Corresponding author: Dr. Sachin Bandichhode
Conflict of interest: Nil

Abstract

Introduction: Neonatal period carries the highest risk of mortality in childhood. Mechanical ventilation is an appropriate treatment for respiratory failure in sick neonates and it has drastically enhanced the final prognosis of their disease over the past two decades. The aim of the study is to find out the clinical profile and the indication of ventilation in NICU, to study the predictors of morbidity and mortality in ventilated neonates and to study the outcome of ventilated babies in NICU.

Materials and methods: The present observational study was done in NICU, Dr. V.M. Government Medical College, Solapur, Maharastra, India from July 2018 - August 2020. Sample size of the study included all ventilated neonates with gestational age > 28 weeks and birth weight >1000 grams and excluded neonates with gestational age < 28 weeks, birth weight < 1000 grams, multiple congenital anomalies and those who died within 6 hours of admission.

Results: In our present study, out of 300 ventilated newborns172 (57.34%) newborns survived, and 128 (42.67%) newborns died. Proportion of survival was significantly higher. RDS was the most common indication of ventilation. And complications were noted in 125 (41.67%) ventilated newborns, Ventilator associated pneumonia being the common complication.

Conclusion: In our present study, out of 300 ventilated newborns there were 173 (57.67%) male newborns and 127 (42.33%) female newborns and majority were inborn, delivered by LSCS, pre-term and had birth weight between 1.0-1.5 kg. Majority of the ventilated neonates had respiratory distress and tachypnea and indication in majority of neonates for mechanical ventilation were respiratory distress syndrome. Most common complication during the study period was ventilator associated pneumonia. Mortality was higher among outborn, preterm male, with birth weight of 1- 1.5 kg and those with acidosis, neutropenia, positive CRP, delayed capillary refill time and bradycardia and this study showed survival rate of 57.34%.

Introduction

The neonatal period— first 28 days of life—carries the highest risk of mortality per day than any other period during the childhood. The daily risk of mortality in the first 4 weeks of life is ~ 30 fold higher than the post-neonatal period.

Mechanical ventilation is an appropriate treatment for respiratory failure in sick neonates, which will reduce neonatal mortality [2,3]. The survival rate in neonates with mechanical ventilation differs from 24.5 to 67.9% in developing countries and 91% in developed countries in different studies [4,5]. Mechanical ventilation in neonates, especially in preterm neonates, has drastically enhanced the final prognosis of their disease over the past two decades [6,7]. The most important use of mechanical ventilation in neonates is respiratory failure because of respiratory distress syndrome (RDS), apnea, asphyxia, meconium aspiration syndrome (MAS), sepsis, pneumonia and transient tachypnea of the newborn (TTN), and persistent pulmonary hypertension of the newborn (PPHN), post resuscitation and after surgery in sick neonates [8,9].

Mechanical ventilation is an effective therapy to improve the neonatal survival rate and is one of the main components of the NICU. Different components, such as primary disease, gestational age, birth weight and related health conditions, depend on the need for mechanical ventilation. Identification of prognostic factors and their care is mandatory in order to increase survival in mechanically ventilated neonates. This research was therefore intended to assess the outcome of NICU admitted mechanically ventilated neonates, and we researched various factors like clinical profile, indications and tried to classify the risk factors responsible for death.

Methodology

In this prospective observational study total patient selected were 300 intubated neonates in NICU, Dr. V.M. Government Medical College, Solapur, Maharastra, India from July 2018 - August 2020 i.e. 2 years. The study was approved by ethical committee of Dr. V.M. GMC and Shri. C. S. M General Hospital, Solapur, Maharastra, India. An informed consent was obtained from each of the parents to examine the cases for inclusion in this study. All ventilated neonates with gestational age > 28 weeks and birth weight >1000 grams were included in the study. Out of the 300 neonates 173 were male neonates and 127 were female neonates. Neonates with gestational age < 28 weeks, birth weight < 1000 grams, multiple congenital anomalies and those who died within 6 hours of admission were excluded from the study. The eligible neonates were registered for the study and were evaluated in the NICU. Initial stabilization of the patient including intubation when needed, fluid resuscitation, inotrope initiation was carried out accordingly. The following particulars were collected - Patient details, Cardiopulmonary status prior to intubation (heart rate, respiratory rate, oxygen saturation), Intubation details. Following details are taken into consideration like gestational age, gender, mode and place of delivery, indication & ventilation parameters. The neonates were monitored clinically, with periodic cardiopulmonary assessment, oxygen saturation and with arterial blood gases whenever indicated and feasible.

Complications like Ventilator associated pneumonia, Sepsis, Shock, DIC, Pulmonary hemorrhage, and Pneumothorax were recorded. Outcome were classified into two groups - Survivors and Non survivors.

Results

Out of total 7168 admissions during the study period 300 neonates were in intubated state and those were enrolled in the study.

Table 1: Sample distribution.

Parameters	Number of patients	Percentage
Total admissions	7168	100%
Ventilated neonates (n)	300	04.18%

Table 1: represents the total number of patients enrolled in the study, i.e. 300 ventilated neonates were included in this study.

Table 2: Distribution of cases according to different parameters.

Parameters	Number of patients	Percentage
Place of delivery		
Home	28	09.33%
Inborn	173	57.67%
Outborn	99	33.00%
Mode of delivery		
LSCS	172	57.33%
Vaginal	128	42.67%
Gestational age		
Pre-term	188	62.67%
Full-term	112	37.33%
Gender		
Male	173	57.67%
Female	127	42.33%
Birth weight		
1.0-1.5 kg	144	48.00%
1.5-2.5 kg	100	33.33%
> 2.5 kg	56	18.67%
APGAR SCORE		
>7	114	38.00%
<7	68	22.67%
Not known	118	39.34%
RESUCITATION		
Given	102	34.00%
Not Given	142	47.33%
Not known	56	18.67%

Table 3: Indicators of ventilation

INDICATION	CASES(n), 300	PERCENTAGE %
RDS	90	30.00
Birth asphyxia	76	25.34
Neonatal sepsis	65	21.67
MAS	45	15.00
Apnea of prematurity	17	05.67
PPHN	04	01.33
Meningitis	02	00.67
IVH	01	00.33

Table 4: Distribution according to Clinical signs

Clinical signs	Number of patients	Percentage
Tachypnea	156	52.00
Delayed Capillary refill time	110	36.67
SpO2 < 92%	98	32.67
Hypothermia	90	30.00
Bradycardia	54	18.00

Proportion of newborns with tachypnea was significantly higher followd by delayed capillary refill time.

Table 5: Distribution on basis of ABG Parameters

Parameters	Survivors (57.33%) Mean (range)	Non survivors (42.66%) Mean (range)
Initial arterial pH	7.25 (7.08-7.42)	7.10(6.95-7.25)
PaO2(mm of Hg)	68.20(31.50-104.9)	60.2(30.4- 90.0)
PaCO2(mm of Hg)	42.4(23.9-60.9)	44.84(22.04-67.64)
HCO3 (mmol/l)	19.4(12.1-26.7)	17.9(10.8-25.0)

The mean pH was 7.25 in survivors and 7.10 in non-survivors, mean PaO2 (mm of Hg) was 68.20 in survivors and 60.20 in non-survivors, mean PaCO2 (mm of Hg) was 42.40 in survivors and 44.84 in non-survivors and mean HCO3 (mm of Hg) was 19.40 in survivors and 17.90 in non-survivors.

Table 6: Ventilator parameters in study cases

Parameter	Survivors mean (range)	Non – survivors mean (range)
PIP (cm of H2O)	13.52 (12 - 18)	15.56 (12-22)
PEEP (cm of H2O)	6.25 (5-8)	7.10(5-8)
Rate (/min)	38 (30-44)	40.46(32-50)
FiO2	0.67(0.3-1)	0.90(0.4-1)

Table 7: Relation of complications during the ventilated period to outcome

COMPLICATIONS	NO. OF PATIENTS	SURVIVAL (%)
Ventilator associated pneumonia	42	22 (12.79%)
Sepsis	38	27 (15.69%)
Shock	23	17 (09.88%)
DIC	10	4 (03.12%)
Pulmonary hemorrhage	08	01(05.71%)
Pneumothorax	04	02 (01.16%)
TOTAL	125	73 (42.44%)

Table 8: Relation of different parameters to outcome

PLACE	SURVIVAL	%	NON SURVIVAL	%
Home(28)	11	06.39%	17	13.28%
Inborn(173)	120	69.76 %	53	41.46%
Outborn(99)	41	23.83%	58	45.30%

GESTATION				
PRETERM(188)	87	50.58%	101	78.90%
FULLTERM(122)	85	49.41%	27	21.09%
GENDER				
MALE (n=173)	81	47.09%	92	71.87%
FEMALE(n=127)	91	52.91%	36	28.14%
WEIGHT				
1-1.5 Kg(144)	71	(41.27%)	73	(57.03%)
1.5 – 2.5 Kg(100)	62	(36.04%)	38	(29.68%)
> 2.5 Kg (56)	39	(22.67%)	17	(13.28%)
APGAR SCORE				
>7 (n=114)	68	39.53%	46	35.93%
<7 (n= 68)	38	22.09%	30	23.43%
Not known(118)	66	38.37%	52	40.62%
RESUCITATION				
Given (102)	64	37.20%	38	29.68%
Not Given (142)	78	45.34%	64	50.00%
Not known (56)	30	17.14%	26	20.31%
Clinical parameters				
Tachypnoea	83	53.20%	73	46.79%
Bradycardia	13	24.07%	41	75.92%
SpO2	38	38.78%	60	61.22%

Table 9: Relation of Investigations to Outcome.

PARAMETERS	NUMBER	SURVIVAL (%)	NON SURVIVAL(%)
POSITIVE CRP	55	21 (38.18%)	34 (61.81%)
THROMBOCYTOPENIA	57	32(57.14%)	25(43.85%)
POSITIVE BLOOD CULTURE	35	16(45.71%)	19(54.28%)
HYPOGLYCEMIA	22	15(68.18%)	07(31.81%)
NEUTROPENIA	28	13(46.42%)	15(53.57%)

Table 10: Outcome according to it Diagnosis.

FINDINGS	CASES	SURVIVAL, n=172 (%)	NON SURVIVAL, n=128 (%)
RDS	90	42 (46.67%)	48 (53.33%)
BIRTH ASPHYXIA	76	42 (55.26%)	34 (44.73%)
SEPSIS	65	32 (49.23%)	33 (50.76%)
MAS	45	40 (88.89%)	05 (11.11%)
APNEA OF PREMATURITY	17	11 (64.70%)	06 (35.29%)
PPHN	04	03 (75.00%)	01 (25.00%)
MENINGITIS	02	02 (100.00%)	00 (00.00%)
IVH	01	00 (00.00%)	01 (100.0%)

Table 11: Outcome

OUTCOME	NUMBER	PERCENTAGE
Survival	172	57.34%
Non survival	128	42.67%

Table 12: Predictors of Survival and Mortality in studied cases

PARAMETERS	VALUE	TOTAL	SURVIVAL (%)	DEATH (%)
Gestation	preterm	188	87 (46.27%)	101(53.72%)
Birth weight	<2.5 kg	244	133(54.5%)	111 (45.49%)
Gender	Male	173	81 (46.82%)	92 (53.17%)
Acidosis	< 7.1	145	40(27.58%)	105 (72.41%)
RDS	Yes	90	42 (46.67%)	48 (53.34%)
Asphyxia	Yes	76	42 (55.26%)	34 (44.73%)
Sepsis	Present	65	32 (49.23%)	33 (50.76%)
Meningitis	Present	0	02(100.00%)	00 (00.00%)
Thrombocytopenia	Present	42	24(57.14%)	18 (42.85%)
Neutropenia	Present	28	13(46.43%)	15(53.57%)
Hypoglycemia	Present	22	15(68.18%)	07 (31.81%)
CRP	Positive	65	25(40.00%)	40 (61.53%)
IVH	Present	01	00 (00.00%)	01 (100.0%)
Capillary Refill Time	Delayed	110	44 (40.00%)	66 (60.00%)
Tachypnoea	Present	156	83 (53.20%)	73 (46.79%)
SpO2	< 92%	98	38 (38.78%)	60 (61.22%)
Bradycardia	Present	54	13 (24.07%)	41 (75.92%)
Hypothermia	Present	90	35 (38.89%)	55 (61.11%)

Discussion

In our study out of total 300 ventilated newborns 172 (57.34%) newborns survived, and 128 (42.67%) newborns died. Mortality in ventilated newborns was 42.67%, which is comparable to mortality of 43.3% reported by Srinivas N et al [41] 2016.

The outcome was affected by place of delivery, prematurity and birth weight of the neonate. Mortality is higher in outborn neonates, preterm neonates and birth weight of 1-1.5 kg. Similar to our study Dutt RD et al [32] 2014 showed higher mortality in these groups. Similar to Mullai Baalaaji AR et al [40] 2011, Dutt RD et al [32] 2014, mortality rate is higher in male gender. Proportion of newborns with tachypnea was significantly higher in our study, similar to study by Nirosha P et al [38] 2017 and Mullai Baalaaji AR et al [40] 2011. RDS was the most common indication of ventilation followed by birth asphyxia in our study very similar to study by Sharma R et al [6] 2017 but in contrast to Dutt RD et al [32] 2014 where septicemia was the most common indication followed by HMD. Mortality was significantly higher in newborns with diagnosis of RDS and followed by Birth asphyxia in similar to Srinivas N et al [41] 2016. Dutt RD et al [32] 2014 study, showed that Babies with birth asphyxia and septicemia have similar mortality rate. Mortality in IVH neonates was 100% in this study, similarly Saleh SM et al [35] 2019 study showed mortality in IVH were 100.00%. Srinivas N et al [41] 2016 study showed mortality in asphyxia, sepsis and meningitis were 22.22%, 57.33% and 50.00% in comparison to present study i.e. 44.73%, 50.76% and 00.00% respectively.

Neonates with positive CRP, Blood culture and neutropenia showed higher mortality in this study similar to Srinivas N et al [41] 2016 study.

The mean pH was 7.25 in survivors and 7.10 in non-survivors. Hossain MM et al [39] 2009 showed very similar results to present study i.e. The mean pH was 7.25 ± 0.17 in survivors

Ventilator associated pneumonia was the most common complication during the

course of study similar to Dekate P et al [34] 2019 but in contrast to Dutt RD et al [32] 2014 which showed septicemia as the major complication. Proportion of mortality was significantly higher in ventilator associated pneumonia complication, in contrast to present study Sultana SN et al [36] 2020, showed that Hospital acquired sepsis, shock was significantly associated with mortality.

Conclusion

In total number of admissions majorities were non ventilated children. Of those ventilated children majority were inborn, delivered by LSCS, pre-term and male neonates and had birth weight between 1.0-1.5 kg. Majority of the ventilated neonates had respiratory distress and tachypnea and indication in majority of neonates for mechanical ventilation were respiratory distress syndrome, birth asphyxia, neonatal sepsis and meconium aspiration syndrome. Complications in most number of ventilated neonates was ventilator associated pneumonia followed by sepsis. Mortality was higher among outborn, preterm male, with birth weight of 1- 1.5 kg and those with acidosis, neutropenia, positive CRP, delayed capillary refill time and bradycardia. Survival and mortality rate of the mechanically ventilated neonates were 57.34% and 42.67% respectively.

References

1. Sankar MJ, Neogi SB, Sharma J, Chauhan M, Srivastava R, Prabhakar PK, Khera A, Kumar R, Zodpey S, Paul VK. State of newborn health in India. Journal of Perinatology. 2016 Dec;36(3):S3-8.
2. Mathur NB, Garg P, Mishra TK. Predictors of fatality in neonates requiring mechanical ventilation. Indian pediatrics. 2005 Jul 1;42(7):645.
3. Monsef AR, Eghbalian F, Sabzehei MK, Khanlarzade E. Evaluating the Short-Term Outcome of Mechanically Ventilated Neonates Admitted to the Neonatal Intensive Care Unit of Besat Hospital, Hamadan, Iran. International Journal of Pediatrics. 2019;7(9):10029-34.
4. Prabha P, Georg R, Francis F. Profile and outcomes of neonates requiring ventilation: The Kerala Experience. Current Pediatric Research. 2014 Oct 1;18(2):5762.
5. Iqbal Q, Younus MM, Ahmed A, Ahmad I, Iqbal J, Charoo BA, Ali SW. Neonatal mechanical ventilation: Indications and outcome. Indian journal of critical care medicine: peer-reviewed, official publication of Indian Society of Critical Care Medicine. 2015 Sep;19(9):523.
6. Sharma R, Baheti S. Outcome of neonatal ventilation: a prospective and cross-sectional study in tertiary care Centre. International Journal of Contemporary Pediatrics. 2017;4(5):1820.
7. Sabzeie MK, Sabouri T, Sokri M, Basiri B, Khazaei M. The Study of Pulmonary Complication of Neonatal Mechanical Ventilation in NICU.
8. Riyas PK, Vijayakumar KM, Kulkarni ML. Neonatal mechanical ventilation. The Indian Journal of Pediatrics. 2003 Jul 1;70(7):537-40.
9. Eghbalian F. A comparison of supine and prone positioning on improves arterial oxygenation in premature neonates. Journal of neonatal-perinatal medicine. 2014 Jan 1;7(4):273-7.
10. Chatburn RL. Fundamentals of mechanical ventilation: a short course in the theory and application of mechanical ventilators. Mandu Press; 2003.
11. Bunnell JB. High-Frequency Ventilation: General Concepts. InManual of Neonatal Respiratory Care 2012 (pp. 301-317). Springer, Boston, MA.
12. Zimová-Herknerová M, Plavka R. Expired tidal volumes measured by hot-wire anemometer during high-frequency oscillation in preterm infants.

Pediatric pulmonology. 2006 May;41(5):428-33.
13. Rimensberger PC, Schulzke SM, Tingay D, Von Ungern-Sternberg BS. Pediatric and neonatal mechanical ventilation. From Basics to Clinical. 2015.
14. Schulze A. Respiratory gas conditioning and humidification. In Manual of Neonatal Respiratory Care 2012 (pp. 99-106). Springer, Boston, MA.
15. Donn SM, Sinha SK. Minimising ventilator induced lung injury in preterm infants. Archives of Disease in Childhood-Fetal and Neonatal Edition. 2006 May 1;91(3):F226-30.
16. Attar MA, Donn SM. Mechanisms of ventilator-induced lung injury in premature infants. In Seminars in Neonatology. WB Saunders. 2002 Oct 1: 7(5):353-360.
17. Donn SM, Boon W. Mechanical ventilation of the neonate: Should we target volume or pressure? Respiratory care. 2009 Sep 1;54(9):1236-43.
18. Cannon ML, Cornell J, Tripp-Hamel DS, Gentile MA, Hubble CL, Meliones JN, Cheifetz IM. Tidal volumes for ventilated infants should be determined with a pneumotachometer placed at the endotracheal tube. American Journal of Respiratory and Critical Care Medicine. 2000 Dec 1;162(6):2109-12.
19. Oca MJ, Becker MA, Dechert RE, Donn SM. Relationship of neonatal endotracheal tube size and airway resistance. Respiratory care. 2002 Sep;47(9):994-7.
20. Donn SM, Kuhns LR. Mechanism of endotracheal tube movement with change of head position in the neonate. Pediatric radiology. 1980 Mar 1;9(1):37-40.
21. Donn SM, Blane CE. Endotracheal tube movement in the preterm neonate: oral versus nasal intubation. Annals of Otology, Rhinology & Laryngology. 1985 Jan;94(1):18-20.
22. Aziz HF, Martin JB, Moore JJ. The pediatric disposable end-tidal carbon dioxide detector role in endotracheal intubation in newborns. Journal of Perinatology. 1999 Mar;19(2):110-3.
23. Jarreau PH. Gross air leaks. In Pediatric and Neonatal Mechanical Ventilation. Springer, Berlin, Heidelberg: 2015:947-960.
24. Sinha SK, Donn SM. Advances in neonatal conventional ventilation. Archives of Disease in Childhood Fetal and Neonatal edition. 1996 Sep;75(2):F135.
25. Donn SM, Sinha SK. Newer modes of mechanical ventilation for the neonate. Current opinion in pediatrics. 2001 Apr 1;13(2):99-103.
26. Donn SM, editor. Neonatal and pediatric pulmonary graphics: principles and clinical applications. Futura Publishing Company; 1998.
27. Carlo WA, Ambalavanan N, Chatburn RL. Classification of mechanical ventilation devices. In Manual of neonatal respiratory care. Springer, Boston, MA. 2012:87-91.
28. Hummler HD, Gerhardt T, Gonzalez A, Bolivar J, Claure N, Everett R, Bancalari E. Patient-triggered ventilation in neonates: comparison of a flow-and an impedance-triggered system. American journal of respiratory and critical care medicine. 1996 Oct;154(4):1049-54.
29. Prinianakis G, Kondili E, Georgopoulos D. Effects of the flow waveform method of triggering and cycling on patient-ventilator interaction during pressure support. Intensive care medicine. 2003 Nov 1;29(11):1950-9.
30. Greenough A, Morley C. Pneumothorax in infants who fight ventilators. The Lancet. 1984 Mar 24;323(8378):689.
31. Perlman JM, Goodman S, Kreusser KL, Volpe JJ. Reduction in intraventricular hemorrhage by elimination of fluctuating cerebral blood-flow velocity in preterm infants with respiratory distress syndrome. New England

Journal of Medicine. 1985 May 23;312(21):1353-7.
32. Dutt RD, Dutt C, Ambey R. Neonatal mechanical ventilation-early experiences in central India. Int J Med Res Rev. 2014; 2:319-23.
33. Yadav M, Chauhan G, Bhardwaj AK, Sharma PD. Clinicoetiological pattern and outcome of neonates requiring mechanical ventilation: Study in a tertiary care centre. Indian journal of critical care medicine: peer-reviewed, official publication of Indian Society of Critical Care Medicine. 2018 May;22(5):361.
34. Dekate P, Damke S, Meshram R, Sawangi W. Clinical Profile and Short-Term Outcome of Neonates Requiring Assisted Mechanical Ventilation. facilities. 2019 Jan; 2:3.
35. Saleh SM, El-Mazary AA, Mohammed ER. Analytical study for neonates with respiratory distress on mechanical ventilation admitted to NICU-Minia University Hospital. Annals of Neonatology Journal. 2019 Jun 29;1(2):49-58.
36. Sultana SN, Khan MM, Islam MT, Afroze S, Jahan I, Dey SK, Mannan MA, Shahidullah M. Clinical Profile and Outcome of Neonates Requiring Mechanical Ventilation. Birth.;37(11):20-8.
37. Shrestha P, Basnet S, Shrestha L, Shrestha P, Kathmandu N. Clinical Profile and Outcome of Mechanically Ventilated Neonates in a Tertiary Level Hospital. Journal of Nepal Paediatric Society. 2016;35(3):218-3.
38. Nirosha P. A Study of Respiratory Distress in Term Neonates in Early Neonatal Period (Doctoral dissertation, Government Theni Medical College, Theni).
39. Hossain MM, Shirin M, Al Mamun MA, Hasan MN, Sahidullah M. Predictors of mortality in ventilated neonates in intensive care unit. Bangladesh Journal of Child Health. 2009;33(3):77-82.
40. Mullai Baalaaji AR. Profile of Children Ventilated in Paediatric Intensive Care Unit of a Tertiary Care Hospital (Doctoral dissertation, Madurai Medical College, Madurai).
41. Srinivas N, Oommen RA, Shriyan A. Neonatal Mechanical Ventilation: Indications and Outcome. IJSR - International Journal Of Scientific Research, June 2016:5(6)69.48.
42. Trivedi SS, Chudasama RK, Srivastava A. Study of early predictors of fatality in mechanically ventilated neonates in NICU. Online Journal of Health and Allied Sciences. 2009 Nov 15;8(3).
43. Manfred, D. May There Exist Healthy Diseases? Journal of Medical Research and Health Sciences, 2022:5(3), 1801–1803.