

Peripheral Neutrophil- Lymphocyte Ratio as a Predictor of Seizure in Preterm Infants with Intra-Ventricular Hemorrhage

Heba Ibrahim Ashraf^{1*}, Mai Rabie El-Sheikh¹ and
Abd El-Rahman Mohamed El-Mashad¹

¹Department of Pediatrics, Tanta University, Tanta, Egypt.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/AJPR/2021/v6i130185

Editor(s):

(1) Dr. Emmanouil (Manolis) Magiorkinis, General Hospital for Chest Diseases, Greece.

Reviewers:

(1) Vidhi Shah, University in Pimpri-Chinchwad, India.

(2) Merdaci Slimane, University Djillali Liabès of Sidi Bel Abbès, Algeria.

Complete Peer review History: <http://www.sdiarticle4.com/review-history/70828>

Original Research Article

Received 01 May 2021

Accepted 06 July 2021

Published 08 July 2021

ABSTRACT

Background: Preterm infants with Intra-Ventricular Hemorrhage (IVH) are at risk for developing significant complications, including post hemorrhagic hydrocephalus and seizures. Neonatal seizures are the most common overt manifestation of neurological dysfunction in the newborn, and is associated with short- and long-term adverse effects.

Objective: The aim of the study is to evaluate the value of Peripheral Neutrophil- lymphocyte ratio (NLR) as a predictor of seizure in preterm infants with intra-ventricular hemorrhage.

Methods: This prospective cohort study that comprised 60 Preterm infants with IVH admitted at NICU pediatric department Tanta university hospital from November 2019 to May 2020, Preterm infants were divided into two groups according to incidence of seizure.

Preterm infants in this study subjected to Careful history taking, clinical examination and investigations (laboratory and Trans-cranial ultrasound) as well as analysis of result and follow up clinical status for development of seizure.

Results: There was a statistically highly significant difference regarding NLR and development of seizure with p value <0.001 (NLR \geq 2.3 with sensitivity 96%, specificity 93%, Area under the curve 0.849 and accuracy 84.9%).

Conclusion: NLR is a predictor of seizure in preterm infants with intra-ventricular hemorrhage.

Keywords: Preterm infants; intra-ventricular hemorrhage; peripheral neutrophil- lymphocyte ratio; seizure.

1. INTRODUCTION

A premature birth is defined as babies born alive before 37 weeks of pregnancy are completed [1]. IVH remains a major complication of prematurity, affecting 20–25% of premature infants of very low birth weight [2].

IVH is described in four grades [3]:

- Grade I - bleeding occurs just in the germinal matrix.
- Grade II - bleeding also occurs inside the ventricles, but they are not enlarged.
- Grade III - ventricles are enlarged by the accumulated blood.
- Grade IV - bleeding extends into the brain tissue around the ventricles.

Preterm infants with IVH are at risk for developing significant complications, including post hemorrhagic hydrocephalus and seizures [4].

A seizure is a paroxysmal behavior caused by hyper synchronous discharge of a group of neurons. Neonatal seizures are the most common overt manifestation of neurological dysfunction in the newborn [5].

Neutrophils are a type of white blood cell that helps heal damaged tissues and resolve infections. Neutrophil blood levels increase naturally in response to infections, injuries, and other types of stress. They may decrease in response to severe or chronic infections, drug treatments, and genetic conditions [6].

Lymphocytes are white blood cells that are also one of the body's main types of immune cells. They are made in the bone marrow and found in the blood and lymph tissue [7].

NLR measured from a peripheral blood complete blood count (CBC) provides a simple, cost-effective index of inflammation [8].

NLR has proven to be a reliable prognostic marker of morbidity, functional outcomes, and all-cause mortality in cancers, cardiovascular disease, renal disease, and cerebrovascular disease [9, 10].

Multiple studies have reported an association between the NLR in peripheral blood and outcomes after acute intracranial hemorrhage in adults [11, 12].

The aim of the study is to evaluate the value of Peripheral Neutrophil- lymphocyte ratio (NLR) as a predictor of seizure in preterm infants with intra-ventricular hemorrhage.

2. PATIENTS AND METHODS

This prospective cohort study was carried out at NICU Pediatric Department Tanta University Hospital from November 2019 to May 2020.

This study included 60 Preterm infants with IVH. Studied patients were divided into two groups according to presence of seizure as follows:

- Group I: contain 30 preterm infants with IVH without development of seizure.
- Group II: contain 30 preterm infants with IVH with development of seizure.

2.1 The Inclusion Criteria

Preterm infants (from 28 week to 34 week EGA) with IVH with criteria of diagnoses including ^[8]:

- frontal-occipital ratio (FOR)>0.55
- bulging fontanel
- sutures splayed>3 mm
- trans-cranial ultrasound

2.2 Exclusion Criteria

- Premature infants <28 or >34-week EGA
- Premature infants with multiple congenital anomalies
- Premature infants with sepsis.

All Premature infants in this study subjected to the following:

1. Full medical history includes:

- Personal history (name, age, sex and consanguinity)
- Present history
- Past history (past history of affected sibling)

- Maternal medical history of any acute or chronic illness before or during pregnancy)

2. Clinical examination includes:

- Gestational age
- Full general examination
- Anthropometrical measurements (body weight, length, head circumference)

3. Investigations includes:

I. Trans-cranial ultrasound

Cranial ultrasound uses reflected sound waves to make pictures of the brain and its inner fluid chambers (ventricles).

Grading of germinal matrix hemorrhage

A. grade I

Restricted to subependymal region/germinal matrix which is seen in the caudothalamic groove.

B. grade II

Extension into normal sized ventricles and typically filling less than 50% of the volume of the ventricle.

C. grade III

Extension into dilated ventricles.

D. grade IV

Grade III with parenchymal hemorrhage.

II. Neutrophil-to-lymphocyte ratio (NLR)

Complete blood picture was performed conventionally and by electronic automatic hematology analyzer (ERMA PCE-210N cell counter).

The NLR for the peripheral blood was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count.

Calculation of NLR:

$$\text{NLR} = \frac{\text{Absolute \# Neutrophils}}{\text{Absolute \# Lymphocytes}} = \frac{\text{Relative \% Neutrophils}}{\text{Relative \% Lymphocytes}}$$

For group I NLR was done at the time of development of IVH.

For group II NLR was done at the time of development of IVH then repeated on developed of seizure then repeated after 3 days of seizure.

2.3 Statistical Analysis

Data were analyzed using Statistical Program for Social Science (SPSS) version 23. Quantitative data were expressed as mean \pm standard deviation (SD). Qualitative data were expressed as frequency and percentage. We the following tests of significance: Independent-samples t-test, Mann Whitney U test, Chi-square (X²) test, Fisher Exact test and Wilcoxon Signed-Ranks Test. Receiver operating characteristic (ROC) curve analysis was used to identify optimal cut-off values. Sensitivity, specificity, PPV (positive predictive value), NPV (negative predictive value) was used to plot Receiver Operating Curve (ROC). Statistical significance was assessed at P values less than 0.05.

3. RESULTS

Our study population contains 34 (56.7%) female and 26 (43.3%) males with Mean gestational age 30.65 \pm 1.894 (weeks) with Mean body weight (gram) 1523.33 \pm 398.56 (Table 1).

Regarding Lab Data at time of IVH of the whole study population; The mean value of Neutrophils was 5.17 \pm 1.5, Lymphocytes was 3.36 \pm 1.11 and NLR was 1.66 \pm 0.56. Regarding Lab Data at time of seizures of the whole study population; The mean value of Neutrophils was 5.6 \pm 1.65, Lymphocytes was 3.32 \pm 1.09 and NLR was 1.9 \pm 0.94. Regarding Lab Data 3 days after seizures for study group; The mean value of Neutrophils was 3.43 \pm 3.92, Lymphocytes was 1.23 \pm 1.32 and NLR was 1.42 \pm 1.57 (Table 2).

Regarding Transcranial ultrasound among study populations; there was 22 (36.6%) with grade 1 IVH, 19 (31.6%) with grade 2 IVH, 16 (26.6%) with grade 3 IVH and 3 (5%) with grade 4 IVH (Table 3).

There was a statistically non-significant difference between the two groups regarding Gestational age, BW, sex and Maternal History of infection with p value > 0.05 (Table 4).

There was a statistically non-significant difference between the two groups regarding Neutrophils At time of IVH with p value 0.29 (Table 5).

While there was a statistically significant difference between the two groups regarding Neutrophils At time of seizure and Lymphocytes At time of IVH and at time of seizure with a significant p value (Table 5).

Also, there was a statistically highly significant difference between the two groups regarding NLR at time of IVH and at time of seizure with p value <0.001 (Table 5).

Table 1. demographic data and maternal risk factor among study populations

Items: (No.= 60)	
Gestational Age (weeks)	30.65±1.894
Sex	26 (43.3%)
• Male	34 (56.7%)
• Female	
BW(gram)	1523.33 ± 398.56
Maternal Risk Factors	
• Infection	7 (11.7%)

Table 2. Lab Data at different times of cases

Items: (No.=60)	
Lab Data at time of IVH	
• Neutrophiles	5.17±1.5
• Lymphocytes	3.36±1.11
• NLR	1.66±0.56
Lab Data at time of seizures	
• Neutrophiles	5.6±1.65
• Lymphocytes	3.32±1.09
• NLR	1.9±0.94
Lab Data 3 days for study group	
• Neutrophiles	3.43±3.92
• Lymphocytes	1.23±1.32
• NLR	1.42±1.57

Table 3. Transcranial ultrasound among study populations

Items: (No.=60)	
TC/US	
• Grade 1	22 (36.6%)
• Grade 2	19 (31.6%)
• Grade 3	16 (26.6%)
• Grade 4	3 (5%)

Table 4. Demographic data and maternal risk factor among seizure and No seizure groups

Variables	No seizures	seizures	Test of significance	Significance P value
Gestational age				
Mean ± SD	31.00 ± 1.965	30.30 ± 1.784	t=1.445	0.154
BW				
Mean ± SD	1540 ± 384.7	1506.67 ± 417.86	t=0.32	0.749
Sex				
• Male	14 (46.7%)	12 (40%)	$\chi^2=0.271$	0.397
• Female	16 (53.3%)	18 (60%)		
Maternal History				
• Infection	3 (10%)	4 (13.3%)	$\chi^2=0.162$	0.6

t: independent t- test, χ^2 : Chi square test; *Significant p≤0.05

Table 5. Lab data among seizure and No seizure groups

Variables	No seizures	seizures	Test of significance	Significance P value
Neutrophils				
• At time of IVH	4.23±1.851	4.70±2.020	t=1.058	0.294
• At time of seizure	4.973±1.492	6.233±1.595	t=3.519	0.003*
Lymphocytes				
• At time of IVH	4.10±1.213	2.67±1.241	t=3.588	0.001*
• At time of seizure	3.833±0.957	2.810±0.98	t=4.084	<0.001*
NLR				
• At time of IVH	1.058±0.422	2.157 ±1.123	t=5.241	<0.001*
• At time of seizure	1.345±0.409	2.456±0.998	t=5.636	<0.001*

t: independent t- test; *significant p≤0.05

Table 6. Transcranial ultrasound among seizure and No seizure groups

Variables	No seizures	seizures	Test of significance	Significance P value
TC/US				
• Grade 1	20 (66.7%)	2 (6.7%)	$\chi^2=12.749$	0.005*
• Grade 2	9 (30%)	10 (33.3%)		
• Grade 3	1 (3.33%)	15 (50%)		
• Grade 4	0 (0%)	3 (10%)		

χ^2 : Chi square test, *significant p≤0.05

Table 7. Diagnostic accuracy of NLR in prediction of seizure in preterm infants with IVH

Variables	Cut-off	Sensitivity	Specificity	Accuracy	AUC	95% Confidence Interval of the Difference	
						Lower	Upper
NLR	2.3	96 %	93 %	84.9 %	0.849	0.734	0.929
Neutrophils	6250	76.7 %	63.3 %	57.8 %	0.578	0.443	0.704
Lymphocytes	4850	80 %	93 %	76.8 %	0.768	0.641	0.867

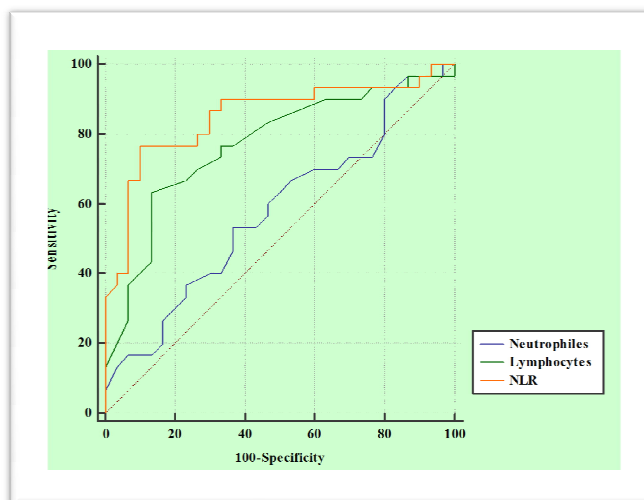


Fig. 1. ROC of NLR in prediction of seizure in preterm infants with IVH

Our study showed statistically significant difference regarding Transcranial ultrasound grading with P value =0.005 (Table 6).

ROC curve analysis for prediction of seizure in preterm infants with IVH by NLR

ROC curve analysis was done to pick up the best cut off value of different hematological indices for prediction of seizure in preterm infants with IVH which revealed:

- ☒ NLR ≥ 2.3 with sensitivity 96%, specificity 93%, Area under the curve 0.849 and accuracy 84.9%.
- ☒ Neutrophils ≥ 6250 with sensitivity 76.7 % specificity 63.3 %, Area under the curve 0.578 and accuracy 57.8 %.
- ☒ Lymphocytes ≥ 4850 with sensitivity 80 %, specificity 93 %, Area under the curve 0.768 and accuracy 76.8 %.

4. DISCUSSION

Preterm infants with IVH are at risk for developing significant complications, including post hemorrhagic hydrocephalus and seizures [13].

Neonatal seizures is the most common neurological event in neonates, indicating a variety of different pre-, peri-, or postnatal diseases of the CNS [14].

Seizures occur more often during the neonatal period compare to other periods in the life span. They affect up to 1.5–3.5/1000 in full-term infants and 10–130/1000 in preterm infants [15].

The neutrophil-to-lymphocyte ratio (NLR) measured from a peripheral blood complete blood count (CBC) provides a simple, cost-effective index of inflammation [16].

NLR has proven to be a reliable prognostic marker of morbidity, functional outcomes, and all-cause mortality in cancers, cardiovascular disease, renal disease, and cerebrovascular disease [17].

Several studies have reported an association between the peripheral blood NLR and outcomes following acute intracranial hemorrhage [18].

In the present study, we aimed to evaluate the value of Peripheral Neutrophil- lymphocyte ratio

as a predictor of seizure in preterm infants with intra-ventricular hemorrhage.

This prospective cohort study that comprised 60 Preterm infants with IVH admitted at NICU pediatric department Tanta University Hospital from November 2019 to May 2020 included 34 (56.7%) female and 26 (43.3%) males with Mean gestational age 30.65 ± 1.894 (weeks) with Mean body weight (gram) 1523.33 ± 398.56 .

Studied Preterm infants were divided into two groups according to presence of seizure group I contain 30 preterm infants with IVH without development of seizure and group II contain 30 preterm infants with IVH with development of seizure.

Our study population contains 34 (56.7%) female and 26 (43.3%) males with Mean age 30.65 ± 1.894 (weeks) with Mean body weight (gram) 1523.33 ± 398.56 .

The main difference between the groups was statistically non-significant regarding the Gestational age (P =0.154), body weight (P =0.749) and sex (P-value=0.397).

This was in agreement with Christian et al., [19] who study the characteristics of hospitalized preterm infants with intraventricular hemorrhage in the United States and found that from 2000 through 2010, 147,823 preterm neonates with IVH were admitted Fifty-six percent were male infants and 41% of preterm neonates with IVH had a birth weight between 500 and 999 g.

Our results regarding the Gestational age and body weight was against Mosayebi et al., [20] who study Markers of Intraventricular Hemorrhage in Very Premature Infants. One hundred premature infants with gestational age (GA) < 34 weeks divided into two groups, infants with IVH had lower birth weight (Mean difference: 0.48, 95%CI: 0.08 to 0.87, P = 0.018) and GA (Mean difference: 2.9, 95%CI: 1.95 to 3.92, P < 0.001), compared to infants without IVH.

This discrepancy between our results and Mosayebi et al., [20] results due to all study population included in our study have IVH while Mosayebi et al, [20] study population was infants with IVH and infants without IVH.

Regarding Maternal History, group I there were 3 (10%) with positive history of infection and group

II there were 4 (13.3%) with positive history of infection.

There was a non-statistically significant difference between the groups with (P-value=0.6).

This was in agreement with Lu et al., [21] who study Risk Factors for Intraventricular Hemorrhage in Preterm Infants Born at 34 Weeks of Gestation or Less Following Preterm and found no significant differences regarding parameters indicating every clinical sign of Maternal infection such as maternal temperature, leukocyte count, and elevated maternal CRP.

Our study showed statistically significant difference regarding Transcranial ultrasound grading with P value =0.005.

This was in agreement with Shah et al., [22] who study Electrographic Seizures in Preterm Infants (infants under 30-wk gestation) During the First Week of Life and divided Preterm Infants into two groups according to incidence of Seizures and found IVH Transcranial ultrasound grading was statistically significant difference between Seizures and no Seizures group with P value = 0.008.

Also, in agreement with Han et al., [23] who study Predictors of mortality for preterm infants with intraventricular hemorrhage (a population-based study) and found that complications as Seizures and hydrocephalus were most frequently used in grade IV IVH (118/848 or 13.9%), followed by grades III (85/955 or 8.9%), II (20/1328 or 1.5%), and I (14/4306 or 0.3%).

While against Christian et al., [19] who study the characteristics of hospitalized preterm infants with intraventricular hemorrhage and found Transcranial ultrasound grading affect incidence of Seizures (incidence of Seizures in Grade 1 was 2%, in Grade 2 was 5%, in Grade 3 was 10% and in Grade 4 was 17%).

Our results showed statistically significant difference regarding NLR at time of IVH and at time of seizure with P value <0.001.

This was in agreement with Stein et al., [8] who study Peripheral blood neutrophil-to-lymphocyte ratio in preterm infants with intraventricular hemorrhage. study included premature infants with IVH and a neonatal reservoir placed between January 2013 and January 2018. For

each patient, peripheral blood and available cerebrospinal fluid laboratory results within 50 days of IVH diagnosis were averaged. NLR was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count. Differences in NLR levels for patients with seizures or shunt placement were analyzed. The mean peripheral NLR (n = 13) for the study group was 1.6 ± 1.3 , and the mean CSF NLR (n = 10) was 3.0 ± 4.6 . statistically significant difference regarding NLR between the groups.

According to study done by Goksugur et al., [24], Celikbilek et al., [25] and Yu et al., [10] The NLR represents an informative index of systemic inflammation, and peripheral NLR is being increasingly studied as a potential predictor of morbidity and outcome in cardiovascular, oncologic, renal, cerebrovascular, and autoimmune inflammatory diseases.

Stein et al., [8] confirmed utility of NLR for predicting outcomes after neurologic injury in the pediatric population, especially in preterm infants. In this study population, a greater NLR was observed in patients with an increased risk of seizures.

One-Sample Statistics for comparison between NLR among Seizures group there was statistically non-significant difference with P value =0.437 and 0.137 regarding NLR at developed seizure and NLR After 3 days of seizure irrespectively.

ROC curve analysis was done to pick up the best cut off value of different hematological indices for prediction of seizure in preterm infants with IVH which revealed $NLR \geq 2.3$ with sensitivity 96%, specificity 93%, Area under the curve 0.849 and accuracy 84.9%.

This was in agreement with Goksugur et al., [24] who study Neutrophil-to-lymphocyte ratio and red blood cell distribution width is a practical predictor for differentiation of febrile seizure types and found the mean NLR in the simple FS and complex FS groups was 2.18 ± 1.9 and 3.8 ± 4.2 respectively, and the difference was significant (p = 0.024).

Also, in agreement with Stein et al., [8] who found that peripheral NLR as a predictive marker of outcomes in the population of preterm infants with IVH. Rates of seizures in this cohort correlated with higher NLR (> 3).

5. RECOMMENDATIONS

Larger sample size studies are recommended to consolidate our findings. Longer follow up periods to determine validity of NLR in predicting long term clinical outcome. Multi-center study is needed.

6. CONCLUSION

NLR is a predictor of seizure in preterm infants with intra-ventricular hemorrhage.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

The study was done after approval from the Ethical Committee of Tanta University.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Blencowe H, Cousens S, Chou D, et al. Born too soon: The global epidemiology of 15 million preterm births. *Reproductive health*. 2013;10:S2.
2. Ballabh P. Intraventricular hemorrhage in premature infants: mechanism of disease. *Pediatric research*. 2010;67:1.
3. Bolisetty S, Dhawan A, Abdel-Latif M, et al. Intraventricular hemorrhage and neurodevelopmental outcomes in extreme preterm infants. *Pediatrics*. 2014;133:55-62.
4. Robinson S. Neonatal posthemorrhagic hydrocephalus from prematurity: Pathophysiology and current treatment concepts: a review. *Journal of Neurosurgery: Pediatrics*. 2012;9:242-58.
5. Mizrahi EM. Neonatal seizures. *Atlas of Epilepsies*. 2010:491-502.
6. Sefil F, Ulutas KT, Dokuyucu R, et al. Investigation of neutrophil lymphocyte ratio and blood glucose regulation in patients with type 2 diabetes mellitus. *Journal of International Medical Research*. 2014;42:581-8.
7. Abbas AK, Lichtman AH, Pillai S. Cellular and molecular immunology E-book: Elsevier Health Sciences; 2014.
8. Stein AA, Eyerly-Webb S, Solomon R, et al. Peripheral blood neutrophil-to-lymphocyte ratio in preterm infants with intraventricular hemorrhage. *Clinical neurology and neurosurgery*. 2019;180:52-6.
9. Wang F, Wang L, Jiang T-t, et al. Neutrophil-to-lymphocyte ratio is an independent predictor of 30-day mortality of intracerebral hemorrhage patients: A validation cohort study. *Neurotoxicity research*. 2018;34:347-52.
10. Yu Y, Wang H, Yan A, et al. Pretreatment neutrophil to lymphocyte ratio in determining the prognosis of head and neck cancer: a meta-analysis. *BMC cancer*. 2018;18:383.
11. Sun Y, You S, Zhong C, et al. Neutrophil to lymphocyte ratio and the hematoma volume and stroke severity in acute intracerebral hemorrhage patients. *The American journal of emergency medicine*. 2017;35:429-33.
12. Xue J, Huang W, Chen X, et al. Neutrophil-to-lymphocyte ratio is a prognostic marker in acute ischemic stroke. *Journal of Stroke and Cerebrovascular Diseases*. 2017;26:650-7.
13. Radic JA, Vincer M, McNeely PD. Outcomes of intraventricular hemorrhage and posthemorrhagic hydrocephalus in a population-based cohort of very preterm infants born to residents of Nova Scotia from 1993 to 2010. *Journal of Neurosurgery: Pediatrics*. 2015;15:580-8.
14. Korzeniewski SJ, Romero R, Cortez J, et al. A "multi-hit" model of neonatal white matter injury: cumulative contributions of chronic placental inflammation, acute fetal inflammation and postnatal inflammatory events. *Journal of perinatal medicine*. 2014;42:731-43.
15. Kang SK, Markowitz GJ, Kim ST, et al. Age-and sex-dependent susceptibility to phenobarbital-resistant neonatal seizures: Role of chloride co-transporters. *Frontiers in cellular neuroscience*. 2015;9:173.
16. Yilmaz H, Ucan B, Sayki M, et al. Usefulness of the neutrophil-to-lymphocyte ratio to prediction of type 2 diabetes mellitus in morbid obesity. *Diabetes and Metabolic Syndrome: Clinical Research & Reviews*. 2015;9:299-304.

17. Proctor MJ, McMillan DC, Horgan PG, et al. Systemic inflammation predicts all-cause mortality: A glasgow inflammation outcome study. *PLoS one*. 2015 ;10:e0116206.
18. Russell CD, Parajuli A, Gale HJ, et al. The utility of peripheral blood leucocyte ratios as biomarkers in infectious diseases: A systematic review and meta-analysis. *Journal of Infection*. 2019;78:339-48.
19. Christian EA, Jin DL, Attenello F, et al. Trends in hospitalization of preterm infants with intraventricular hemorrhage and hydrocephalus in the United States, 2000–2010. *Journal of Neurosurgery: Pediatrics*. 2016;17:260-9.
20. Mosayebi Z, Sepidarkish M, Nikseresht Z, et al. Mean platelet volume as a marker of intraventricular hemorrhage in very premature infants. *Iran J Pediatr*. 2017 ;27:8322-33.
21. Lu H, Wang Q, Lu J, et al. Risk factors for intraventricular hemorrhage in preterm infants born at 34 weeks of gestation or less following preterm premature rupture of membranes. *Journal of Stroke and Cerebrovascular Diseases*. 2016;25:807-12.
22. Shah DK, Zempel J, Barton T, et al. Electrographic seizures in preterm infants during the first week of life are associated with cerebral injury. *Pediatric research*. 2010;67:102-6.
23. Han RH, McKinnon A, CreveCoeur TS, et al. Predictors of mortality for preterm infants with intraventricular hemorrhage: A population-based study. *Child's Nervous System*. 2018;34:2203-13.
24. Goksugur S, Kabakus N, Bekdas M, et al. Neutrophil-to-lymphocyte ratio and red blood cell distribution width is a practical predictor for differentiation of febrile seizure types. *Eur Rev Med Pharmacol Sci*. 2014;18:3380-5.
25. Celikbilek M, Dogan S, Ozbakir O, et al. Neutrophil–lymphocyte ratio as a predictor of disease severity in ulcerative colitis. *Journal of clinical laboratory analysis*. 2013;27: 72-6.

© 2021 Ashraf et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:

The peer review history for this paper can be accessed here:
<http://www.sdiarticle4.com/review-history/70828>