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ORIGINAL RESEARCH

Assessment of platelet indices as a biomarker for diagnosis neonatal sepsis

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Abstract

Aim and objectives: The aim of this research was to compare conventional procedures of diagnosis & treatment of newborn sepsis with an evaluation of platelet indicators.

Materials and method: The study was done in NICU division of Department of Paediatrics in TMMC & RC, Moradabad. All neonates admitted in the neonatal intensive care unit with clinical diagnosis of neonatal sepsis were included for entire study duration. The cases were all neonates with culture positive sepsis or clinical sepsis symptomatic babies with positive septic screen. The controls were all neonates suspected of having sepsis but had negative blood culture, negative sepsis screen & whose antibiotics was then stopped.

Results: Neonatal sepsis was found more among subjects with late onset sepsis (55.26%) as compared to early onset sepsis (44.74%).Neonatal sepsis was found more among subjects delivered vaginally (81.03 %) as compared to subjects delivered LSCS (11.29%). The average platelet count was inferior in cases (sepsis screen positive & blood culture positive) group than in the control cluster. The average MPV was significantly high in the case cluster than in the control cluster.

Conclusion: Thus, it may be concluded that platelet indices are readily available, inexpensive and sensitive markers to diagnose septic babies and when integrated with traditional sepsis screen help to specifically make the diagnosis of neonatal sepsis.

Keywords: Platelet indices, Biomarker, Neonatal sepsis

Introduction

Neonatal sepsis is a life-threatening infection that occurs when microorganisms enter the circulation of a newborn & generate toxins, triggering a systemic inflammatory response.[1]There were 2.4 million infant fatalities in 2020, accounting for almost 47% of all deaths in children under the age of five.[2]More than a third of the 4 million newborn deaths that occur annually are attributable to illnesses, with neonatal sepsis/pneumonia accounting for almost a million of those deaths.[2]

Neonatal sepsis is classified as either early-onset sepsis (occurring within the first 3 days of life) or late-onset sepsis (After 3 days). In most cases, microbes picked up during labor & delivery cause early-onset sepsis, whereas environmental factors are more often to blame for late-onset sepsis.[3]

Most infants can be saved if they are diagnosed & treated for sepsis as soon as possible. However, identifying sepsis can be difficult because of the overlap of symptoms.[4] For sepsis to be diagnosed quickly, a high index of suspicion must be present & confirmed. Various tests have been used historically.[5] A blood culture is usually the best way to tell what's wrong, although it has its drawbacks.

Several studies have inspected the belongings of newborn sepsis on platelet counts & platelet indices inclusive of Mean Platelet Volume (MPV) & Platelet Distribution Width (PDW).[6,7] Activated platelets release several cytokines & inflammatory mediators that contribute significantly to the body's inflammatory & immunological responses.[8,9]

In newborns, thrombocytopenia is utilized as a preliminary, nonspecific sign of sepsis.[10] Platelet size is quantified by mean platelet volume (MPV), with larger platelets having greater metabolic activity & thrombotic potential. Increased mean platelet volume (MPV) implies a large number of immature platelets are circulating.[11] The median MPV in the newborn phase is 10–12fl.[11,12] In destructive thrombocytopenia, the MPV level is high, while in hypoproliferative thrombocytopenia, the MPV level is low.[13,14] The width of the platelet distribution (PDW) reveals the extent to which platelet sizes vary. PDW levels typically range from 10%-17.5%.[15]

Studies have shown that newborn sepsis patients exhibit considerable alterations in platelet indices. More research is needed because there is currently no agreement on this issue.

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Materials and method

It was an observational cross- sectional study conducted over the period of one year after final approval from the university. The study was done in NICU division of Department of Paediatrics in TMMC & RC, Moradabad. All neonates admitted in the neonatal intensive care unit with clinical diagnosis of neonatal sepsis were included for entire study duration.It was a time bound study, after the approval from ethical committee on 16/08/2021 till June 2022 and all cases confirming inclusion criteria were enrolled in the study.

Study population

The cases were all neonates with culture positive sepsis or clinical sepsis symptomatic babies with positive septic screen. The controls were all neonates suspected of having sepsis but had negative blood culture, negative sepsis screen & whose antibiotics was then stopped.[as per Centre For Disease Control (CDC) definition].[3]

The cases excluded neonates with Congenital and acquired cause of thrombocytopenia and platelet indices other than sepsis, i.e. Autoimmune disorders of platelets alloimmune disorder of platelets, Congenital hematological disorders e.g. malignancies, Congenital TORCH group of infections and Mothers on antiplatelet medications.

Methodology

Neonates at high risk were submitted to battery of tests collectively called the “sepsis screen”. The sepsis screen looked for aberrant values of several parameters, including a total leukocyte count (TLC) below 5000/mm3, an absolute neutrophil count (ANC) below 1800/cumm, an immature neutrophil to total neutrophil ratio (INR) above 0.2, & CRP level above 1 mg/dl. Sepsis screen was judged positive when 2 or more parameters was positive.

The NICU's blood collection process was conducted in a sterile environment. Soon after admission 2 ml blood sample was obtained in EDTA vacutainer & was processed for TLC, PBS, DLC& ANC. One millilitre of blood was drawn for the purpose of estimating CRP levels. Investigation which was sent for all cases & controls which included blood culture, (platelet count, MPV,PDW).

Blood sample was tested, with an automated haematology analyser- The TLC count<5000/cumm was considered abnormal. Leishman's stain was used to determine ANC in PBS, & a value of less than 1500/cumm indicated an abnormality. Before administering antibiotics, a blood culture was taken from newborns suspected of having the disease. They took one millilitre of blood & put it into five millilitres of blood culture broth.

Urine culture was acquired by supra-pubic puncture or bladder catheterization & was suggested in suspicious patients. To diagnose a UTI, one of the following must be present: Having more than ten white blood cells per millimeter in a centrifuged sample of 10 millilitres or more than ten organisms per millilitre of catheterized urine are two examples of how to determine infection.

Abdominal X-rays were taken to diagnose necrotizing enterocolitis, while chest X-rays were taken when there was respiratory distress or apnea. For this study, we used the normative values for infant haematological measures established by Monroe et al.[4] All cases & controls had their clinical information & laboratory test results recorded in the case record.

We co-related the platelet indices with respect to birth weight & gestational age (as per WHO defined categories of both).We observed the babies enrolled in the study for 7 days for their clinical and lab interpretation.

Statistical analysis

All findings were recorded in a structured data entry form at various points in the study. Statistical Package for Social Sciences version 28 (SPSS) was used for all analysis. All the variables were present as frequency and percentage and was tested using chi square test. The ‘p’ value less than 0.05 was considered statistically significant.

Results

A total of 100 neonates 58 cases & 42 controls were recruited. The average gestation age was 36.4weeks +/- 3.2weeks & average birth weight was 2434.50grams +/- 631.44grams.

Table 1: Distribution of Patients by Age, Sex, Weight, & Gestational Age in Case(n=58) & Control(n=42) Groups

Variables	Cases(n=58)	Control(n=42)	Total	p-value
Sex				
Male	37 (63.79%)	24 (57.14%)	61	0.79
Female	21 (36.21%)	18 (42.85%)	39	
Birth Weight				
<2500 grams	16 (27.58%)	13 (30.95%)	29	0.71
>2500grams	42 (72.41%)	29 (69.04%)	71	
Gestational Age				
Preterm	17 (29.31%)	6 (14.28%)	23	0.07
Term	41 (70.69%)	36 (85.71%)	77	

In this study, in case group there were 37 male (63.79%) & 21 female (36.21%) & in control group there were 24 males (57.14%) and18 females (42.85%). In case group, 16 babies (27.58%) had birth weight of <2500 grams &

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42 babies (72.41%) had bit weight >2500grams. Preterm gestational age was reported in 29.31% & 14.28% of the subjects in case & control group respectively (table 1).

Table 2: Maternal characteristics according to case & control groups

Maternal characteristics	Case		Control		Total	p-value
	N=58	%	N=42	%		
Maternal Age						
<20 years	12	20.69	4	9.52	16	0.13
≥20 years	46	79.31	38	90.48	84	
PROM ≥ 18 hours				0.00		
No	55	88.71	36	94.74	91	0.54
Yes	7	11.29	2	5.26	9	
Foul-smelling liquor				0.00		
No	56	90.32	37	97.37	93	0.68
Yes	6	9.68	1	2.63	7	
Maternal fever				0.00		
No	58	93.55	37	97.37	95	0.77
Yes	4	6.45	1	2.63	5	
Chorioamnionitis				0.00		
No	61	98.39	38	100.00	39	0.89
Yes	1	1.61	0	0.00	1	
Maternal UTI				0.00		
No	58	93.55	38	100.00	97	0.94
Yes	3	4.84	0	0.00	3	
Multiple PV examination				0.00		
≥5 times	21	33.87	11	28.95	32	0.13
<5 times	41	66.13	27	71.05	68	
Intrapartum IV antibiotics				0.00		
No	37	59.68	21	55.26	58	0.048*
Yes	25	40.32	17	44.74	42	

*: statistically significant

Table 2 shows the maternal characteristics in cases & controls. Maternal factors i.e. intrapartum IV antibiotics was significantly related to neonatal sepsis. Rest all variables maternal age, PROM, LPV, maternal fever, chorioamionitis, maternal UTI, & multiple PV examination were equally distributed in both groups

Table 3 showing the onset of sepsis in case & control group

		Case		Control		p-value
		N=58	%	N=42	%	
Onset of sepsis	EONS	33	56.9%	26	61.9%	0.620
	LONS	25	43.1%	16	38.1%	
Ventilation	Not needed	45	77.6%	37	88.1%	0.180
	Needed	13	22.4%	5	11.9%	
Platelet count	<1.5 lakhs/mm3	35	60.3%	9	21.4%	< 0.001*
	≥1.5 lakhs/mm3	23	39.7%	33	78.6%	
MPV	>10.8fl	34	58.6%	14	33.3%	0.012*
	<10.8fl	24	41.4%	28	66.7%	
PDW	>19.1 fl	33	56.9%	13	31.0%	< 0.001*
	≤19.1 fl	25	43.1%	29	69.0%	

In this study, there were 56.89% with early onset neonatal sepsis (EONS) and 43.10% babies with late onset neonatal sepsis (LONS) in case group. 61.9% with EONS and 38.09% babies with LONS in control group, which is statistically insignificant. Mechanical ventilation was required more in cases (22.41%) as related to control cluster(11.90%), though no important change was found as p=0.18. The mean platelet count, MPV and PDW was higher in the case cluster than in control group.

Table 4: Distribution of clinical features in all study subjects

		N	%
Clinical	Icterus	84	84.0%

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Features	Poor Feeding	82	82.0%
	Tachypnea chestretractions	80	80.0%
	Abdominal distension	77	77.0%
	Lethargy	73	73.0%
	Temperature Instability	58	58.0%
	Seizures	26	26.0%
	Sclerema	2	2.0%
	Renal Failure	1	1.0%
Morbidity	Pneumonia	58	58.0%
	Shock	23	23.0%
	Metabolic Acidosis	12	12.0%
	Hypoglycemia	11	11.0%
	Congenital pneumonia	7	7.0%
	Meconium Aspiration Syndrome	5	5.0%
Sepsis	Only Blood culture positive	17	17.0%
	Only sepsis screen positive	20	20.0%
	Both sepsis screen & blood culture positive	21	21.0%
	Both sepsis screen & blood culture negative	42	42.0%
Bacterial Isolates	Staphylococcus aureus	13	34.2%
	Pseudomonas	10	26.3%
	Escherichia coli	8	21.1%
	Streptococcus sp	5	13.2%
	Candida	2	5.3%

Table 4 shows the clinical features among the study subjects. Icterus, poor feeding, tachypnea, chest retractions, abdominal distension, lethargy, temperature, instability, seizures, sclerema& renal failure was present in 84%, 82%, 80%, 77%, 73%, 58%, 26%, 2% & 1% of the subjects respectively.The most common morbidity among the study subjects was pneumonia (58%) followed by shock (23%). Meconium aspiration pneumonia & congenital pneumonia was revealed in 5% & 7% of the subjects respectively.

17% babies were only blood culture positive, 20% babies were only sepsis screen positive, 21% babies were both sepsis screen & blood culture positive & 42% babies were both sepsis screen & blood culture negative.According to culture outcome, most common bacterial isolate was Staphylococcus aureus (34.21%) followed by Pseudomonas (26.31%) & Escherichia coli (21.05%). Least common bacterial isolate was Streptococcus sp (13.15%) followed by candida (5.26%).

Table 5: Diagnostic efficacy of platelet indices for Diagnosis of Neonatal Sepsis with Blood Culture Being Gold Standard

Parameters	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Platelet count <1.5 lakhs/mm^3	85.60	28.2	80.4	30.1	65.8
MPV >10.8 fl	76.35	31.7	73.6	30.2	60.4
PDW >19.1 fl	70.80	34.9	66.7	32.8	48.7
Platelet count & MPV combined	68.7	37.5	65.4	35.4	56.8
Platelet count & PDW combined	68.5	40.4	66.3	38.9	57.1
MPV & PDW Combined	62.8	42.6	60.21	39.84	62.4
Platelet count, MPV & PDW Combined	64.50	48.2	63.1	45.8	62.3

It was seen that platelet count <1.5 lakhs/mm^3 was the most sensitive marker (85.60%) followed by MPV & PDW in detectingbabies with neonatal sepsis. However, it has a low specificity (28.2%). But when we combined MPV &PDWor combined all the three markers (MPV + PDW + PC), the specificity increases & is maximum (48.2%) in detecting babies with neonatal sepsis with decrease in sensitivity to 64.5%

Discussion

Recent research shows that patients with neonatal sepsis have large shifts in platelet indices[11,16,17] These studies reveal that in newborns with sepsis, platelet count drops while MPV & PDW increase. Neonatal sepsis was

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strongly linked to maternal variables like the need for intrapartum IV antibiotics. Findings comparable to those of JimbaJatsho et al.[18] were also reported.

In our study, significantly more participants delivered vaginally (86.71%) than LSCS (11.29%) had neonatal sepsis. Therefore, newborn sepsis was associated greater with LSCS deliveries. Similar results were also found by JimbaJatsho et al.[18] in their research.

Subjects with early onset neonatal sepsis (61.90%) were more likely to have neonatal sepsis than those with late onset neonatal sepsis (43.10%), according to this study. Using a chi-square test, we discovered no statistically significant difference between cases & controls with respect to the time at which sepsis developed. The same was true for the association between EOS & LOS between the case & control groups, as found by Mittal et al.[19]

Eighty-four percent, eighty-two percent, seventy-three percent, fifty-eight percent, twenty-seven percent, two percent, two percent, & one percent of the subjects had icterus, poor feeding, tachypnea, chest retractions, abdominal distention, lethargy, temperature, instability, seizures, sclerema, & renal failure, respectively.

Lethargy, poor eating, temperature instability, & respiratory distress were shown to be the most common clinical signs of sepsis by Chandan Kumar Shaw et al.[20]The most prevalent symptoms in the study conducted by Chaudhari et al.[21] were lethargy (67.9%) & unwillingness to feed (77.4%).JimbaJatsho et al.[18] found that these symptoms were frequently seen in neonates: respiratory distress, fever, feeding intolerance, & jaundice.

In current investigation, subjects who needed mechanical ventilation were more than twice as likely to have neonatal sepsis as those who didn't need it (17.74%). Swarnkar et al.[22] found that 51.38 percent of all EOS cases involved culture-proven sepsis. Misra et al.[23] found that of 115 total cases, 65% tested positive for a culture & 34% tested negative. Chandan Kumar Shaw et al.[20]reported that 63% infants with a positive sepsis screen had positive cultures. Worldwide records suggest that the isolation rates on blood cultures vary from 6.7% to 55.4%. Blood culture positive rate of 14% was reported by Gupta &Kashyap.[24] Antibiotic treatment, insufficient or incorrect sample, & secondary causes of sepsis, such as unusual pathogens, are common reasons for the low positive rates. Staphylococcus aureus was discovered to be present in 13 samples (34.21%), followed by pseudomonas in 10 samples (26.31%), & E. coli in 8 samples (21.05%).

Platelet indices were similar across various gestational age groups and birth weight groups. In the current study, the cases group had a significantly lower mean platelet count than the control group did. Nearly half (44%) of the people tested had abnormally low blood platelet counts. Significantly increased MPV+PDW were seen in case group contrast to control group($p<0.0001$). Abdulla et al.[25] found that 42.8% of infants with sepsis experienced thrombocytopenia. Ahmad et al.,[26] the prevalence of thrombocytopenia in newborn sepsis was 24.7% & its association with increased mortality was observed. This variance may be attributable to the fact that in this study we considered a cut-off of platelet counts of less than 1.5 lakhs/mm3 while other current studies regarded a cut-off of 1 lakhs/mm3. Research by Mittal et al.[19] found that septic infants had lower platelet counts & higher PDW & MPV. Our results are consistent with this.

For the diagnosis of newborn sepsis, a rise in MPV was found to have a sensitivity of 54% & specificity of 46% in a research by Arad et al.[27]Mittal et al.[19] reported that late-onset sepsis newborns have thrombocytopenia and increased MPV. When all platelet indices (MPV + PDW + PC) or (MPV + PDW) were combined, thrombocytopenia was a highly specific indication of sepsis. Platelet indices outperformed sepsis screens. Sepsis screen and platelet indices improved specificity. Our results agree.MPV & PDW were also found to be meaningfullychanged between sepsis patients & the control cluter, as demonstrated by Guclu et al.[28]

Neonates with MPV >10.8 fL&/or PDW >19.1% have been linked by Patrick & Lazarchick.[21] to an increased risk of bacteremia. It correlatedwith the study by Arijit Majumdar et al.,[29] thrombocytopenia (platelet count 1.5 x 109/l) had the highest sensitivity to detect sepsis (87.91%), followed by MPV & PDW with a sensitivity of 84.9% & 79.12%, respectively, in the culture proved group; however, our study included both blood culture positive & sepsis screen positive infants.

The most sensitive measure (85.60%) for identifying infants with neonatal sepsis was a platelet count 1.5 lakhs/mm3, followed by MPV & PDW. However, its specificity is quite low (only 28.2%). Specificity for identifying infants with neonatal sepsis was improved, however, when MPV & PDW were used together, or when all three markers were used (MPV + PDW + PC). In this research, the sensitivity of the sepsis screen was 58% (less than the sensitivity of platelet indices), while the specificity was 32.62%. Diagnostic specificity for neonatal sepsis is improved, however, when the sepsis screen is combined with platelet indices. Similar findings were also reported in a study done by Mittal et al.[19]

In the present study, platelet count had highest AUC in ROC curve analysis (.782), among all platelet indices. It differed from a study done by Mittal et al.[19] which showed MPV was the most sensitive marker. This observed difference may be due to difference in sample size of the studies.

Conclusion

Thus, it may be concluded that platelet indices are readily available, inexpensive and sensitive markers to diagnose septic babies and when integrated with traditional sepsis screen help to specifically make the diagnosis of neonatal sepsis.

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References

1. Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA 2016; 315: 801–10.
2. WHO [internet]. Switzerland: World Health Organization; 2015. Available from: www.who.int/gho/child_health /mortality/neonatal/2015.
3. Chiarot E, Spagnuolo A, Maccari S, et al. Protective effect of Group B Streptococcus type-III polysaccharide conjugates against maternal colonization, ascending infection and neonatal transmission in rodent models. Scientific Reports 2018; 8(1): 2593.
4. Baiju K, Gupta NP. Clinical assessment of hemodynamic variation in the platelet count and indices in neonatal sepsis in Bihar. International Journal of Medical and Health Research. 2019; 5: 252-7.
5. Aydemir H, Piskin N, Akduman D, Kokturk F, Aktas E. Platelet and mean platelet volume kinetics in adult patients with sepsis. Platelets 2015; 26: 331-5.
6. Weyrich AS, Zimmerman GA. Platelets: signaling cells in the immune continuum. Trends Immunol 2004; 25: 489–95.
7. Zarbock A, Polanowskagrabowska RK, Ley K. Platelet-neutrophilinteractions: linking hemostasis and inflammation. Blood Rev 2007; 21: 99–111.
8. Levi M, van der Poll T. Inflammation and coagulation. Crit Care Med 2010; 38: S26–34.
9. Vincent JL. Emerging therapies for the treatment of sepsis. Curr Opin Anaesthesiol 2015; 28: 411–6.
10. Modanlou HD, Ortiz OB. Thrombocytopenia in neonatal infection. Clin Pediatr (Phila). 1981; 20(6): 402-7.
11. Patrick RH, Lazarchick J. The effect of bacteremia on automated platelet measurements in neonates. Am J Clin Pathol. 1990; 93(3): 391-4.
12. Scheifele DW, Olsen EM, Pendray MR. Endotoxinemia and thrombocytopenia during neonatal necrotizing enterocolitis. Am J Clin Pathol. 1985; 83: 227-229.
13. Littleton N. Thrombocytopenia in HIV. CME. 2007; 25: 272-275.
14. Nugent D, McMillan R, Nichol JL, Slichter SJ. Pathogenesis of chronic immune thrombocytopenia:increased platelet destruction and/or decreased platelet production. Br J Haematol. 2009; 146: 585-96.
15. Farias MG, Schunck EG, Dal Bó S, de Castro SM. Definition of reference ranges for the platelet distribution width (PDW): a local need. Clin Chem Lab Med. 2010; 48(2): 255-7.
16. Moro ML, De Toni A, Stolfi I, Carrieri MP, Braga M, Zunin C. Risk factors for nosocomial sepsis in newborn intensive and intermediate care units. Eur J Pediatr 1996; 155: 315-32.
17. Escobar GJ. The neonatal "sepsis work-up" personal reflections on the development of an evidence-based approach toward newborn infections in a managed care organization. Pediatrics 1999; 103: 360-73.
18. Jatsho J, Nishizawa Y, Pelzom D, Sharma R. Clinical and bacteriological profile of neonatal sepsis: a prospective hospital-based study. International journal of pediatrics. 2020; 2020.
19. Mittal A, Arya S, Charan LS, Saluja S, Chellani H. Evaluation of platelet indices as additional diagnostic tool for neonatal sepsis. Astrocyte. 2018; 4(4): 205.
20. Shaw CK, Prachi SH, Malla T, Malla KK. The clinical spectrum and outcome of neonatal sepsis in a neonatal intensive care unit at a tertiary care hospital in western Nepal: January 2000 to December 2005-A retrospective study. Eastern Journal of Medicine. 2012; 17(3): 119-25.
21. Chaudhari K, Shah B, Gosai D. Study of etiology, risk factors, clinical features and outcome in blood culture proven late onset septicemia. International Journal of Scientific Research. 2016; 4(12): 119-21.
22. Swarnkar K, Swarnkar M. A study of early onset neonatal sepsis with special reference to sepsis screening parameters in a tertiary care centre of rural India. The Internet Journal of Infectious Diseases. 2012; 10(1): 36-42.
23. Misra RN, Jadhav SV, Ghosh P, Gandham N, Angadi K, Vyawahare C. Role of sepsis screen in the diagnosis of neonatal sepsis. Medical Journal of Dr. DY Patil University. 2013; 6(3): 254.
24. Gupta S, Kashyap B. Bacteriological profile and antibiogram of blood culture isolates from a tertiary care hospital of North India. Tropical Journal of Medical Research. 2016; 19(2): 94.
25. Abdulla A, Maghayreh M, Khriesat W, Swedan S. The effect of neonatal sepsis on platelet count and their indices. Jordan Med J 2008; 42: 82-6.
26. Ahmad AS, El Saeed WF, Hamdy S. Neonatal Sepsis Overview and Assessment of Mean Platelet Volume for Diagnosis. European Journal of Molecular & Clinical Medicine. 2021; 8(3): 3591-602.
27. Arad ID, Alphan G, Sznajderman SD, Eldor A. The mean platelet volume (MPV) in the neonatal period. Am J Perinatol 1986; 3: 1-3.
28. Guclu E, Durmaz Y, Karabay O. Effect of severe sepsis on platelet count and their indices. Afr Health Sci 2013; 13: 333-8.
29. Majumdar A, Biswas S, Jana A. Platelet indices as an earlier and economical marker of neonatal sepsis. Iraqi Journal of Hematology. 2021; 10(2): 108.