Original Article

Early Detection of DIC in Neonates with Sepsis

Frequency of Early Detection of Disseminated Intravascular Coagulation in Neonates with Sepsis

Sumaira Haamid, Ubaidullah Khan and Mimpal Singh

ABSTRACT

Objective: The aim of this study was to identify frequency of early symptomatic DIC in neonates presenting with sepsis resulting in major neonatal morbidity and mortality.
Study Design: It was a cross-sectional study.
Place and Duration of Study: This study was conducted at the Pediatric department, Fatima Memorial Hospital, Lahore from July 2016 to January 2017.
Materials and Methods: A total of 200 patients were included in this study. Venous sample 3cc was collected to get CBC, CRP, blood culture and sensitivity, PT, APTT, FDP's, CXR, urine R/E and culture and sensitivity, LP when required. All the data was analyzed using SPSS version 20.
Results: The mean gestational age of the patients was 38.76 ± 1.19 weeks. The mean duration of symptoms was found as 13.25 ± 3.29 days. There were 111 (55.5%) males and 89 (45.5%) females in our study. DIC was found in 85 patients (42.5%) while not found in 115 patients (57.5%). DIC was also stratified according to gestational age, gender and duration of symptoms and was found significant for gestational age and duration of symptoms.
Conclusion: A high percentage of DIC (42.5%) was found in patients presenting with neonatal sepsis.

Key Words: DIC, Sepsis; Neonates; NICU.

Citation of article: Haamid S, Khan U, Singh M. Frequency of Early Detection of Disseminated Intravascular Coagulation in Neonates with Sepsis. Med Forum 2020;31(8):12-14.

INTRODUCTION

Sepsis is an uncontrolled progressive Infectious process, suspected or proven, which by the production of pro and anti-inflammatory cytokines can lead to systemic inflammatory response syndrome (SIRS)[1].
Based upon age of onset after birth, Neonatal sepsis is further classified into three types. First one is Early-onset infection are acquired before or during delivery and appear from birth to7days of life and usually within 72 hours of life. Second one is Late-onset infections which are usually acquired from the organism from hospital or community, appear during 7 days to1month of life. Third one is Very-Iate-onset infections which appears after 1 month of life and are mostly acquired from environment or community[2,3].

Department of Pediatrics Medicine Unit-II, King Edward Medical University, Mayo Hospital, Lahore.

Correspondence: Mimpal Singh, Assistant Professor of Pediatrics Medicine Unit-II, King Edward Medical University, Mayo Hospital, Lahore.
Contact No: 0333-4229251
Email: singh.ms1437@gmail.com

Received: March, 2020
Accepted: May, 2020
Printed: August, 2020

According to many studies neonatal sepsis is major cause of morbidity and mortality in developing countries. Incidence of neonatal sepsis varies from 1 to 5/1000 live births in developing countries. Data about its incidence in Pakistan is very limited; it is 1.13/1000 to 3.8/1000 live births in this country. About 20% of neonatal deaths are due to neonatal sepsis in Asia. According to a study on latest Pakistan Demographic and Health Survey (PDHS), 2012-13 neonatal mortality in Pakistan is 55/1000 live births[4].
Thrombotic micro-angiopathy is heterogeneous group of conditions including Disseminated Intravascular Coagulation (DIC) that results in consumption of clotting factors, platelets and anticoagulation proteins. During sepsis abnormally activated cytokines activates platelets and coagulation factors which cause damage to endothelial cells which results in increase vascular permeability and leakage which eventually leads to thrombosis in small vessels, DIC and eventually multi-organ failure[5]. Most commonly occurring complication associated with sepsis are coagulation abnormalities. Approximately 20-40% of all sepsis patients are complicated with DIC[6]. A study also reported that early DIC occurred in 44% cases in the neonates with sepsis[7]. As sepsis is major cause of DIC in our population that's why the current study want to confirm the hypothesis in our population by doing coagulation profile and septic screen of patients admitted with suspected or proven

sepsis to identify and treat early symptomatic DIC in neonates causing major neonatal morbidity and mortality.

MATERIALS AND METHODS

A cross sectional study was conducted at Pediatric department, Fatima Memorial Hospital, Lahore for a duration of 6 months after approval of synopsis i.e. 07-07-2016 to 06-01-2017. The sample size of 200 children was calculated with confidence level as 95%, margin of error as 7%, anticipated proportion of DIC as 44% among those having neonatal sepsis. Non-probability and consecutive sampling was done. Children of age less than 1 month, of either gender presenting admitted with clinical suspicion of neonatal sepsis were included. Premature babies (<37 weeks of gestation) or the patients which didn't give consent were excluded.

After taking informed consent from the ethical committee of hospital and from the parents, history was obtained by researcher. Venous sample 3cc was collected to get complete blood count (CBC), C-reactive protein (CRP), blood culture and sensitivity, prothrombin time (PT), activated partial thromboplastin time (APTT), fibrin degradation products (FDP), chest x-ray (CXR), urine routine examination (R/E) and culture and sensitivity, lumbar puncture (LP) when required. Results were analyzed by researcher and consultant physician. Cut off values for these labs parameters were defined as per operational definitions and patients with deranged results were labeled as DIC in sepsis.

The collected data were entered and analyzed accordingly using SPSS version 21 through its statistical program. Mean ± SD was calculated for gestational age and duration of symptoms. Qualitative variables like gender and early asymptomatic DIC were presented as frequency and percentages. Data was stratified for gestational age, gender and duration of symptoms to control the effect modifiers. Post-stratification chi-square test was applied. P-value ≤ 0.05 was considered as significant.

RESULTS

A total of 200 patients were included in the study. The mean gestational age of the patients was found to be 38.76 ± 1.19 weeks. Patients were further categorized according to gestational age into two groups which is summarized in Table 1. The mean duration of symptoms was found as 13.25 ± 3.29 days and is given in table 2. Gender distribution of the patients showed 111 patients (55.5%) were male while remaining 89 patients (45.5%) were female.

The final outcome of the study was detection of DIC. It was found in 85 patients (42.5%) while it was not found in 115 patients (57.5%). Also DIC was stratified according to gestational age, gender and duration of symptoms and results are summarized in table 3.

Table No. 1: Gestational Age Distribution (n=200)

	No. of patients	%
37-39 weeks	82	41
40-41 weeks	118	59
Total	200	100
Mean ± SD	38.76 ± 1.19 weeks	

Table No. 2: Duration of Symptoms

	No. of patients	%
≤7 days	14	7
≥8 days	186	93
Total	200	100
Mean ± SD	13.25 ± 3.29	

Table 3: Stratification of DIC with respect to gestational age, Gender and duration of symptoms

	DIC		Total	P-Value
	Yes	No		
Gestational Age groups				
37-38weeks	46	36	82	0.001[a]
39-41 weeks	39	79	118	
Total	85	115	200	
Gender				
Male	47	64	111	0.960
Female	38	51	89	
Total	85	115	200	
Duration of symptoms				
≤7 days	14	0	14	0.000[a]
≥8 days	71	115	186	
Total	85	115	200	

DISCUSSION

Microthrombi, containing erythrocytes, platelets, leukocytes are rare, but their presence is the very important feature of DIC as well. Platelet and leukocyte microthrombi are more often observed in children with complicated sepsis. The specific feature of DIC in children is the presence of microthrombi not only in microvasculature, but also in the small vessels of macrovasculature. At the same time in capillaries they are rare. Such microthrombi localization may be explained by anatomophysiologic peculiarities of hemocirculation in premature children. The most common site of microthrombi localization is found in pulmonary circulation, independently on etiology or course of the process. The same data are presented in other reports. To explain this phenomenon the theory of "the first filter" has been suggested: toxins, activated cells (mostly neutrophils) or cytokines enter pulmonary capillaries and damage endothelial cells inducing intravascular coagulation (localized or disseminated). The occurrence of microvasculature occlusion by microthrombi in other organs depends on etiology of

sepsis. Vessels of brain layers, spleen, brain, liver, thymus are commonly involved in bacterial sepsis[8].

Microvasculature of brain, thymus, intestinal wall and adrenals is altered in sepsis caused by Candida albicans, and bacterio-fungal etiology induces intravascular coagulation of brain, pia mater and intestinal wall. The current results showed that hemocoagulation is more common in cases of bacterial and bacteriofungal sepsis than in sepsis caused by Candida. However, in *Candida sepsis*, the severity of alteration depends not only on microvasculature occlusion, but also on fungal alterative vasculitis seen in macrovasculature and microvasculature of lungs, brain and rarely of other organs. Such vasculitis is manifested by vascular wall necrosis with mild inflammatory reaction, fungal growth within the wall and lumen associated with thrombosis[9].

In a study by Naeme et al 10 on adult patients, thrombocytopenia occurred in about 75% of patients. Furthermore, it was observed that the incidence of thrombocytopenia was more common in LBW babies (67.1%) as compared to normal birth weight babies (48.1%, P<.05). The former group developed a lower platelet nadir. This was similar to observation of many authors[10.]

CONCLUSION

DIC was found in 42.5% of patients presenting with neonatal sepsis in our NICU. This is a high percentage which makes it necessary to screen all neonates presenting in NICU with sepsis, to make a prompt and timely diagnosis of this important entity so that neonate is appropriately and timely managed.

Author's Contribution:

Concept & Design of Study:	Sumaira Haamid
Drafting:	Ubaidullah Khan
Data Analysis:	Mimpal Singh
Revisiting Critically:	Sumaira Haamid, Ubaidullah Khan
Final Approval of version:	Sumaira Haamid

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Del Vecchio A, Stronati M, Franco C, Christensen RD. Bi-directional activation of inflammation and coagulation in septic neonates. Early Human Development 2014;90:S22-S25.
2. Rajagopal R, Thachil J, Monagle P. Disseminated intravascular coagulation in paediatrics. Archives of disease in childhood 2017;102:187-93.
3. Giuliani S, Tan Y-W, Zheng D, Petropoulou E, Sohail A, Bradley S, et al. Coagulation Gene Expression Profiling in Infants With Necrotizing Enterocolitis. J Pediatr Gastroenterol Nutr. 2016;63:e169-e75.
4. Ishikura H, Nishida T, Murai A, Nakamura Y, Irie Y, Tanaka J, et al. New diagnostic strategy for sepsis-induced disseminated intravascular coagulation: a prospective single-center observational study. Critical Care 2014;18:R19
5. Goksever Celik H, Celik E, Ozdemir I, Ozge Savkli A, Sanli K, Gorgen H. Is blood transfusion necessary in all patients with disseminated intravascular coagulation associated postpartum hemorrhage? J Maternal-Fetal & Neonatal Med 2017:1-5.
6. Liu Y, Kretz CA, Maeder ML, Richter CE, Tsao P, Vo AH, et al. Targeted mutagenesis of zebrafish antithrombin III triggers disseminated intravascular coagulation and thrombosis, revealing insight into function. Blood 2014;124:142-50.
7. Wang W, Xu D, Han Y, Yang Z. Risk factors for early disseminated intravascular coagulation in neonates with sepsis. Zhongguo dang dai er ke za zhi. Chinese J Contemporary Pediatr 2015;17: 341-44.
8. Pospishil YO, Tomashova SA, Gavrilyuk EM. DIC syndrome in multiorganic failure caused by neonatal sepsis. Production Editor 2003;7:25
9. Selim TE, Ghoneim HR, Khashaba MT, Rakha SA. Plasma soluble fibrin monomer complex is a useful predictor of disseminated intravascular coagulation in neonatal sepsis. Haematologica 2005;90:419-21.
10. McPherson RJ, Juul S. Patterns of thrombocytosis and thrombocytopenia in hospitalized neonates. J Perinatol 2005;25:166.