

The Prevalence and Risk Factors for Neonatal Thrombocytopenia among Newborns Admitted to Intensive Care Unit of Aliasghar Children's Hospital

Khalessi N ¹, Khosravi N ¹, Sanii S ^{2*}, Zareh Mehrjerdi F ²

1. Associate Professor of Neonatology, Intensive Care Unit, Hazrat-e Aliasghar Children's Hospital, Tehran University of Medical Sciences, Tehran, Iran.

2. Resident of Pediatrics, Neonatal Intensive Care Unit, Hazrat-e Aliasghar Children's Hospital, Tehran University of Medical Sciences, Tehran, Iran.

*Corresponding Author: Sanii S, Email: sanii_sara@yahoo.com

Submitted: 16-07-2012, Accepted: 10-10-2012

Abstract

Background: Determining the prevalence and risk factors of thrombocytopenia among neonates enables us to prevent the inevitable and sometimes irreversible complications. In this study we aimed to survey the frequency of thrombocytopenia and its demographic features and risk factors.

Materials and methods: In this cross sectional study the platelet counts of 364 neonates admitted to neonatal intensive care unit of Aliasghar children's hospital, Tehran, Iran, were assessed. Maternal and neonatal medical conditions, risk factors and drug history were also recorded. Patients were divided into 4 groups according to the severity of thrombocytopenia: mild ($100-149 \times 10^9/L$), moderate ($50-99 \times 10^9/L$), severe ($30-49 \times 10^9/L$) and very severe ($< 30 \times 10^9/L$). They were also grouped as presenting early (less than 72 hours after birth) and late (more than 72 hours after birth) thrombocytopenia. Demographic data and hemorrhagic manifestations were also recorded.

Results: Sixty two (17.9%) of neonates were thrombocytopenic. The average gestational age at birth for the thrombocytopenic neonates was significantly lower than the non thrombocytopenic neonates (32.2 ± 2.5 weeks versus 34.9 ± 2.5 , $P=0.0001$), and also the average birth weight was significantly lower among the thrombocytopenic neonates (1979 ± 517 gr versus 2371 ± 480 gr, $P=0.0001$). Neonatal sepsis was significantly associated with thrombocytopenia (24.1% versus 5.9%, $P=0.0001$).

Conclusion: Our study indicated a high prevalence of thrombocytopenia among neonates admitted to NICU and its association with low birth weight, prematurity, and neonatal sepsis. Regarding the importance of life threatening events among the thrombocytopenic newborns, it is best to keep the risk factors in mind to prevent the future complications.

Key words: Thrombocytopenia, risk factor, neonate, preterm

Introduction

The term thrombocytopenia is referred to neonates with less than 150000 platelets count per micro liter which might be caused by less production or higher destruction of platelets or a combination of both mechanisms ^{1,2}. The prevalence of thrombocytopenia in the general population of neonates is about 1 to 4 percent but the prevalence is much higher among sick neonates especially those with low birth weight or immature neonates ². The prevalence of thrombocytopenia among neonates hospitalized in the intensive care units have been reported to be between 22 to 35 percent ^{3,4}. Although there have been studies on the

cause of this high prevalence of thrombocytopenia among these neonates still the cause is unknown in many circumstances. The known etiologies are immune responses, congenital and acquired infections, genetic abnormalities, drug induced thrombocytopenia, necrotizing enterocolitis, pregnancy induced hypertension, intrauterine growth retardation, asphyxia, and idiopathic cases ^{5,6}. Neonatal thrombocytopenia has been categorized to early onset (less than 72 hours after birth) and late onset (more than 72 hours after birth) ¹.

Thrombocytopenia has many potential

dangers for the neonate including intracranial hemorrhage, fatal gastrointestinal and respiratory tract hemorrhages, umbilical cord hemorrhage, and circumcision hemorrhage⁶. The identification of neonates susceptible to thrombocytopenia, constant monitoring of clinical findings and routine platelets count among neonates hospitalized in NICU is necessary steps in identifying and timely treatment of these neonates. Due to the scarcity of studies considering the thrombocytopenia and its risk factors among neonates in Iran we decided to perform this study among neonates hospitalized in NICU of Aliasghar Children's Hospital.

Materials and methods

In this cross sectional study all patients admitted to the NICU of Aliasghar Children's Hospital, in a one year period (March 2010 to March 2011) were included. All neonates with thrombocytopenia were identified based on 2 consecutive platelets count of less than 150000 platelets per micro liter and were divided into mild thrombocytopenia (100000 to 150000 platelets per micro liter), moderate thrombocytopenia (50000 to 100000 platelets per

micro liter), severe thrombocytopenia (30000 to 50000 platelets per microliter), and very severe thrombocytopenia (less than 30000 platelets per microliter).

The sex of neonates, their gestational age (32 weeks and less, 33 to 36 weeks, 37 weeks and higher), birth weight (less than 2500gr, more than 2500gr) were recorded. The clinical findings including petechiae, purpura, ecchymosis, hematuria, intestinal and respiratory hemorrhage, and intracranial hemorrhage were also recorded. The underlying conditions among neonates including immune responses, congenital and acquired infections, genetic findings, drugs used, necrotizing enterocolitis, pregnancy induced hypertension among mothers, intrauterine growth factor levels, asfiksia, and idiopathic cases were identified and recorded. We also considered the drugs given to mother, which may cause this condition including Heparin, Cotrimoxazol, and Chloramphenicol.

All clinical and paraclinical findings were collected using a special check list. The data was analyzed using SPSS software (version 11.0, SPSS Co,

Table 1: Demographic findings among neonates hospitalized in NICU considering those who developed and those who did not develop thrombocytopenia.

Variable		Non- thrombocytopenic patients (n=285)	Thrombocytopenic patients n=62	All patients (n=347)	P-value
Sex	Male	146 (2/51%)	29 (46.7%)	175 (50.4%)	0.52
	Female	139 (48.7%)	33 (53.2%)	172 (49.6%)	
Average age at birth (weeks)		5/2 ±9/34	5/2 ±2/32	7.2 ±4.34	0.0001
Age at birth (weeks)	Less than 32	39 (13.6%)	36 (0/58%)	75 (21.6%)	0.0001
	33 to 36	164 (57.5%)	22 (4/35%)	186 (53.6%)	
	37 and more	82 (28.7%)	4(4/6%)	86 (24.6%)	
Average birth weight (gr)		480 ±2371	517 ±1979	508 ±2301	0.0001
Weight (gr)	Less than 2500	154 (54%)	51 (82.2%)	205 (59.1%)	0.0001
	More than 2500	131 (45.9%)	11 (17.7%)	142 (40.9%)	

Chicago IL). We used t-test to analyze quantitative data with normal distribution and Chi square test for qualitative data. P values less than 0.05 were considered statistically significant.

Results

In the present study 347 neonates hospitalized in NICU were included during a 1 year period. Out of these 175 patients (50.4%) were male and 172 patients (49.6%) were female. The mean gestational age at birth was 34.4 ± 2.7 weeks (range 28 to 40 weeks). Seventy five neonates (21.6%) had a gestational age at birth of less than 32 weeks, 186 neonates (53.6%) had a gestational age at birth of 32 to 36 weeks and finally 86 neonates (24.8) had a gestational age at birth of 37 weeks or higher. The mean birth weight among neonates was 2301 ± 508 gr (range 1100gr to 3200gr). Two hundred and five neonates (59.1%) weighted less than 2500gr and 142 neonates (40.9%) weighted more than 2500gr (Table 1).

The mean platelet count among these neonates was $(188 \pm 66) \times 10^9/L$. Platelets count in 285 neonates (82.1%) was higher than 150000 per micro liter and 62 neonates (17.9%) were thrombocytopenic (platelets count less than 150000 per micro liter). Among neonates with thrombocytopenia 27 patients (43.5%) had mild

Prevalence and Risk Factors for Neonatal Thrombocytopenia

thrombocytopenia (platelets count 100000 to 150000 per micro liter), 16 patients (25.8%) had moderate thrombocytopenia (platelets count 50000 to 100000 per micro liter), 15 patients (24.1%) had severe thrombocytopenia (platelets count 30000 to 50000 per micro liter) and 4 patients (6.4%) had very severe thrombocytopenia (platelets count under 30000 per micro liter). Among thrombocytopenic patients 29 neonates (46.7%) were male and 33 neonates (53.3%) were female. No statistically significant difference regarding the sex distribution was observed between neonates with and without thrombocytopenia.

The mean gestational age at birth among thrombocytopenic neonates was (32.2 ± 2.5) weeks which was statistically significantly less than the average gestational age at birth among all neonates ($P=0.0001$). Out of neonates with thrombocytopenia 58 neonates (93.5%) had a gestational age at birth of less than 37 weeks while there was 203 neonates (58.5%) with gestational age at birth of less than 37 in total population of neonates hospitalized in NICU ($P=0.0001$). The mean weight of neonates with thrombocytopenia was (1979 ± 570) gr which was lower than the average weight for all hospitalized neonates in NICU ($P=0.0001$).

Thrombocytopenia was early onset (less than 72 hours after birth) in 42 neonates (67.7%) and

Table 2: The clinical findings of neonates with thrombocytopenia

Variable		Prevalence Number (Percent)
The timing of thrombocytopenia	Early onset (Less than 72 hours after birth)	42 (67.7%)
	Late onset (More than 72 hours after birth)	20 (32.3%)
The underlying cause of thrombocytopenia	Without an underlying cause	30 (48.4%)
	Maternal hypertension	11 (17.7%)
	Fetus distress	9 (14.5%)
	Blood mismatch	4 (6.5%)
	ITP of mother	3 (4.8%)
	Congenital infection	3 (4.8%)
	Drug usage	2 (3.2%)
Bleeding signs	Without bleeding sign	49 (79%)
	Petechiae	6 (9.7%)
	Gastrointestinal bleeding	4 (6.5%)
	Intraventricular bleeding	3 (4.8%)

late onset (more than 72 hours after birth) in 20 neonates (32.3%). We did not find any underlying cause for thrombocytopenia in 30(48.4%) of thrombocytopenic neonates. In 11(17.7%) neonates maternal hypertension, in 9(14.5%) neonates fetus distress during birth, in 4(6.5%) neonates blood group mismatch (Rh or ABO) between the mother and neonate, in 3(4.8%) neonates mother's ITP, in 3(4.8%) neonates congenital infections and in 2(3.3%) neonates drug usage (Heparin, Cotrimoxazol) was observed as the probable underlying cause of thrombocytopenia. Forty nine neonates (79%) had no sign of hemorrhage, 6(9.7%) had petechiae, 4(6.5%) had gastrointestinal bleeding and 3(4.8%) had intra ventricular hemorrhage (Table 2). Among neonates with thrombocytopenia 15(24.1%) developed sepsis while among neonates without thrombocytopenia 17(5.9%) developed sepsis ($P=0.0001$).

Discussion

The prevalence of thrombocytopenia among all births has been reported to be between 1 to 5 percent ⁴. In a study by Sainio et al. a 2% prevalence of thrombocytopenia among 4489 Finish full term neonates has been reported ⁵, but the prevalence of thrombocytopenia is much higher among preterm and low birth weight neonates ^{1,3,4,5, 8, 10}.

Thrombocytopenia develops in about one out of each four neonates hospitalized in NICU ³. In our study Thrombocytopenia developed in 17.9% of neonates in NICU which is in line with a study by Gupta et al. ⁷ who reported a prevalence of 16.7% and somehow lower than Aman et al. who have reported 24.1% prevalence ⁸.

In our study 5.4% of all neonates hospitalized in NICU showed severe or very severe thrombocytopenia while this was 2.4% in a study by Christensen et al. ⁹.

The prevalence of thrombocytopenia among neonates have been shown to have a relation with low gestational age at birth ^{3,4,5,8,10}, which was also observed in our study.

In our study 24.1% of thrombocytopenic patients developed sepsis which is in line with other studies ^{3,6,11}, but we did not found a high percentage of maternal preeclampsia or birth problems among our thrombocytopenic neonates which is in contrast with other studies ^{3,12}. This might be due to the fact that the mothers' records

might not be kept carefully in our hospital setting. The early and late thrombocytopenia was seen in 67.7% and 32.3% of our patients respectively which is again in line with other studies ¹³.

There have been several studies on the relationship between neonatal thrombocytopenia and intraventricular hemorrhage and it has been reported that 29.3% ¹⁴ of thrombocytopenic neonates show this but this was only 4.8% in our study which might be due to patients selection methods in our study compared to other studies.

In the present study 48.4% of neonates had thrombocytopenia with unknown cause but maternal hypertension and fetus distress were among the causes for thrombocytopenia which is in line with other studies ^{15,16}.

Conclusion:

Our study indicated a high prevalence of thrombocytopenia among neonates admitted to NICU and its association with low gestational weight, prematurity, and neonatal sepsis. Regarding the importance of life threatening events among the thrombocytopenic newborns, it is best to keep the risk factors in mind to prevent the future complications.

References

1. Van den Hof MC, Nicolaides KH. Platelet count in normal, small, and anemic fetuses. *Am J Obstet Gynecol.* 1990;162(3):735-9.
2. Sola-Visner M, Saxonhouse MA, Brown RE. Neonatal thrombocytopenia: what we do and don't know. *Early Hum Dev.* 2008;84(8):499-506.
3. Roberts I, Murray NA. Neonatal thrombocytopenia. *Semin Fetal Neonatal Med.* 2008;13(4):256-64.
4. Roberts I, Stanworth S, Murray NA. Thrombocytopenia in the neonate. *Blood Rev.* 2008 ;22(4):173-86.
5. Sainio S, Järvenpää AL, Renlund M, Riikonen S, Teramo K, Kekomäki R. Thrombocytopenia in term infants: a population-based study. *Obstet Gynecol.* 2000 Mar;95(3):441-6.
6. Beiner ME, Simchen MJ, Sivan E, Chetrit A, Kuint J, Schiff E. Risk factors for neonatal thrombocytopenia in preterm infants. *Am J Perinatol.* 2003;20(1):49-54.
7. Gupta AK, Kumari S, Singhal A, Bahl A. Neonatal thrombocytopenia and platelets transfusion. *Asian J Transfus Sci.* 2012;6(2):161-4.
8. Aman I, Hassan KA, Ahmad TM. The study of thrombocytopenia in sick neonates. *J Coll Physicians*

- Surg Pak. 2004;14(5):282-5.
9. Christensen RD, Henry E, Del Vecchio A. Thrombocytosis and thrombocytopenia in the NICU: incidence, mechanisms and treatments. *J Matern Fetal Neonatal Med.* 2012 Oct;25 Suppl 4:15-7.
 10. Roberts IA, Murray NA. Neonatal thrombocytopenia: new insights into pathogenesis and implications for clinical management. *Curr Opin Pediatr.* 2001;13(1):16-21.
 11. Bolat F, Kılıç SÇ, Oflaz MB, Gülhan E, Kaya A, Güven AS, et al. The prevalence and outcomes of thrombocytopenia in a neonatal intensive care unit: a three-year report. 2012;29(8):710-20.
 12. de Moerloose P, Boehlen F, Extermann P, Hohfeld P. Neonatal thrombocytopenia: incidence and characterization of maternal antiplatelet antibodies by MAIPA assay. *Br J Haematol.* 1998;100(4):735-40.
 13. Roberts I, Murray NA. Neonatal thrombocytopenia: causes and management. *Arch Dis Child Fetal Neonatal Ed.* 2003;88(5):F359-64.
 14. Lupton BA, Hill A, Whitfield MF, Carter CJ, Wadsworth LD, Roland EH. Reduced platelet count as a risk factor for intraventricular hemorrhage. *Am J Dis Child.* 1988;142(11):1222-4.
 15. Kahn DJ, Richardson DK, Billett HH. Association of thrombocytopenia and delivery method with intraventricular hemorrhage among very-low-birth-weight infants. *Am J Obstet Gynecol.* 2002;186(1):109-16.
 16. Schiff DE, Roberts WD, Willert J, Tsai HM. Thrombocytopenia and severe hyperbilirubinemia in the neonatal period secondary to congenital thrombotic thrombocytopenic purpura and ADAMTS13 deficiency. *J Pediatr Hematol Oncol.* 2004 ;26(8):535-8.