IJN
Iranian Journal of Neonatology
http://ijn.mums.ac.ir

Open Access
Review Article

Thrombocytopenia during the First Week of Life among Neonates with Down Syndrome: Data from Multihospital Healthcare Systems

Shahin Mafinezhad[1*], Hasan Boskabadi[2], Ghasem Bayani[1], Hojatollah Ehteshammanesh[1]

1. Department of Pediatrics, North Khorasan University of Medical Sciences, Bojnurd, Iran
2. Department of Pediatrics, Mashhad University of Medical Sciences (MUMS), Iran

ABSTRACT

Background: Abnormal number of chromosomes in a cell while cell division occurs can lead to aneuploidy, which is associated with thrombocytopenia. Various hematological abnormalities have been reported among neonates with Down syndrome (DS). Neutrophilia, thrombocytopenia, and polycythemia were the most common hematological abnormalities observed among neonates with DS. In particular, thrombocytopenia below 150×109/L was found approximately in two-thirds (66%) of DS and 6% of counts <50,000/microl was detected during the first week of life. Although the exact mechanism remains unknown, the reason for this deficiency can be due to decreased platelet production from chronic fetal hypoxia. Fetal hypoxia also leads to intrauterine growth retardation and suboptimal response of the thrombopoietin system to thrombocytopenia in DS during the neonatal period. The results were indicative of a few cases of alloimmune thrombocytopenia with DS due to anti-HPA antibody.

Methods: The obtained data from multihospital healthcare systems indicated two large case series of infants with cytogenetically diagnosed DS and a reference group of infants without birth defects during 2009-2015. During this period, a total number of 145, 522 live births were recorded at 18 hospitals and DS was recognized in 226 cases (1 in 644). Data were analyzed using multivariate logistic regression analysis expressed as adjusted odds ratio (aORs) with 95% confidence intervals (95% CIs).

Results: Infants with DS had a significantly higher risk for thrombocytopenia (aOR=32.4, 95% CI: 15.2-68.9). The average platelet counts in DS patients were 104600 per microliter. The mean platelet volume did not correlate with the platelet counts; however, it was slightly large (9.2±1.3 fl). The persistence of thrombocytopenia for more than 8-12 postnatal weeks warrants a hematology consultation. Thrombocytopenia can be associated with some types of congenital heart defects. Karyotype testing should be performed for all obviously dysmorphic infants with thrombocytopenia. It seems reasonable to recommend complete blood counts for all neonates with DS.

Conclusion: Pediatricians involved in the care of patients with DS need to be aware of the associated bleeding tendency and other hematologic problems since these patients will often require surgical procedures. It seems recommend to obtain one or more CBCs on all neonates with DS.

Keywords: CBC, Down syndrome, Neonate, Thrombocytopenia

Introduction

Multiple chromosomal disorders can lead to neonatal thrombocytopenia; however, it follows various mechanisms among individuals with different chromosomal diseases. The most common encountered chromosomal anomalies are Trisomies of 13, 18, and 21 (1). Down syndrome (DS: Trisomy 21) is the first described chromosome disorder with maximum viability among autosomal trisomies, occurring in approximately 1 out of 700-800 live births. The incidence of thrombocytopenia in neonates with DS is higher in comparison with the general population (2). Up to 80, 66, and 34% of DS neonates have neutrophilia, thrombocytopenia, and polycythemia, respectively (3-5). Neutrophilia, thrombocytopenia, and polycythemia were the most common hematological abnormalities observed among newborns with DS. In particular, thrombocytopenia below 150×109/L was approximately two-thirds (66%) of DS and 6% of counts <50,000/microl was

* *Corresponding author*: Shahin Mafinezhad, Department of Pediatrics, North Khorasan University of Medical Sciences, Bojnurd, Iran. Tel: 09153101504; Email: shahinmaf@yahoo.com

Please cite this paper as:
Mafinezhad S, Boskabadi H, Bayani G, Ehteshammanesh H. Thrombocytopenia during the First Week of Life among Neonates with Down Syndrome: Data from Multihospital Healthcare Systems. Iranian Journal of Neonatology. 2019 Jun: 10(2). DOI: 10.22038/ijn.2019.31995.1444

detected within the first week of life (6). The causes of neonatal thrombocytopenia can be classified based on platelet size (large, normal, and small), mode of acquisition (congenital or acquired), early (<72 h of age) or late (≥72 h of age) onset, gestational age (preterm versus term), or underlying pathologic mechanisms (7). In a report of 247 cases of fetal blood sampling, a chromosomal abnormality was detected in 43 (17%) cases among platelet counts less than 150,000/microL (8). Although the exact mechanism is still unknown, it is believed that neonatal thrombocytopenia occurs due to decreased platelet production from chronic fetal hypoxia leading to intrauterine growth retardation and suboptimal response of the thrombopoietin (TPO) system to thrombocytopenia in DS during the neonatal period. Alloimmune thrombocytopenia with DS was reported infrequently due to anti-HPA antibody (9). The incidence rates of hematological abnormalities among these patients were reported high; therefore, it seems reasonable to recommend complete blood counts (CBCS) for all neonates with DS (10). The present study aimed to evaluate the obtained data of hematological abnormalities within the first week of neonates with DS from multihospital healthcare systems. Differential diagnosis of thrombocytopenia in neonates with DS is very important for prognosis (11). Pediatricians, including neonatologists, are involved in the care of patients with DS need to be aware of the associated bleeding tendency and other hematologic problems since these patients will often require surgical procedures.

Methods

Data from multihospital healthcare systems shows a large case series of babies with documented DS and a reference group of infants without congenital anomalies all born during 2001-2015. Data were analyzed using multivariate logistic regression analysis expressed as adjusted odds ratio (aORs) with 95% confidence intervals (95% CIs). To acquire hematological data from a larger case series, the CBCs of all neonates with DS were obtained during the first postnatal week from an Intermountain Healthcare (IHC) Hospital, Utah, United States of America (10).

Results and Discussion

A total number of 145,522 live births were recorded at 18 hospitals from January 1, 2001 to December 31, 2005. The obtained results were indicative of DS in 226 cases (1 in 644) out of whom 158 (70%) cases had one or more CBCs obtained before the seventh day (144 hr). Neutrophilia was reported as the most common hematological abnormality, with 80% of absolute neutrophil counts above the upper limit of normal for age. Blasts identification was reported in the blood smear of 6% (9/158) of cases out of whom 3 cases were referred to the pediatric hematology services for further evaluation. The second common abnormality was thrombocytopenia, with 66% of platelet counts below 150,000/microl, and with 6% of counts <50,000/microl. Polycythemia (hematocrit values above 65%) was detected in one- third (33%) of cases as the next most common hematological abnormality. In addition, six patients needed partial exchange transfusion. As a result, neutrophilia, thrombocytopenia, and polycythemia were the most common hematological abnormalities observed among neonates with DS. Anemia, thrombocytosis, and neutropenia were not more common in neonates with DS, compared to babies with no DS (10). In one series, 60% of all infants with trisomy-aberrations were found to have thrombocytopenia. Platelet counts of neonates with DS averaged 104600 (SD 53000; median 90500; 10- and 90-percentile at 45000 and 175000) per microliter (12). Newborn Services Clinical Guideline Reviewed by Carl Kuschel showed that thrombocytopenia (<100) occurred in up to 28% of infants and this thrombocytopenia was usually mild (>40) and transient (2-3 weeks) (13). In contrast to previous studies, they reported higher TPO concentrations in thrombocytopenic non-DS newborns than those in non-thrombocytopenic counterparts. It indicated the suboptimal response of TPO system to thrombocytopenia in DS during the neonatal period (9).

Thrombocytopenia might be associated with some types of congenital heart disease. The reason for the thrombocytopenia remains unknown; one theory could be that there is a temporary lack of regulation of the platelet precursor cells in neonates with DS. Newborns with thrombocytopenia should be followed carefully for any other signs of transient leukemia (14). The reason is that neonates with DS have several hematological disorders, such as transient myeloproliferative disorder which occurs in 4-10% of neonates with DS. As a result, it may be associated with the complication of thrombocytopenia (15, 4, 5).

The persistence of thrombocytopenia beyond 8-12 weeks after birth should warrant a hematology consultation, especially in the absence of any immunologic factors or genetic syndromes (17).

Conclusion

Karyotype testing should be performed in all dysmorphic infants with thrombocytopenia. Pediatricians who are involved in the care of patients with DS need to be aware of the associated bleeding tendency and other hematologic problems, as these patients will often require surgical procedures. It seems reasonable to recommend that one or more CBCs be obtained on all neonates with DS.

Acknowledgments

The authors would like to thank the Vice-chancellor of Research at Bojnurd University of Medical Sciences, Bojnord, Iran, for the financial support. We also extend our gratitude to Dr. Yasaman Bozorgnia for cooperation in this article.

Conflicts of interests

There are no conflicts of interest.

References

1. Fernandes CJ, Mahoney Jr DH. Causes of neonatal thrombocytopenia. New York: UpToDate; 2017.
2. Toshihico N, Tomoaki N, Takashi K, Hidehiro T, Daisuke H, Kusakari M, et al. Down syndrome with neonatal alloimmune thrombocytopenia due to HLA-A2 antibody. Fukoshima J Med Sci. 2015; 61(2):149-54.
3. Henry E, Walker D, Wiedmeier SE, Christensen RD. Hematological abnormalities during the first week of life among neonates with down syndrome: data from a multihospital healthcare system. Am J Med Genet A. 2007; 143A(1):42-50.
4. Hord JD, Gay JC, Whitlock JA. Thrombocytopenia in neonates with trisomy 21. Arch Pediatr Adolesc Med. 1995; 149(7):824-5.
5. Miller M, Cosgriff JM. Hematological abnormalities in newborn infants with Down syndrome. Am J Med Genet. 1983; 16(2):173-7.
6. Tahani Ali Bin A. Hematological manifestation in Down syndrome. Int J Biotech Bioeng. 2017; 6(3):171-5.
7. Castle V, Andrew M, Kelton J, Giron D, Johnston M, Carter C. Frequency and mechanism of neonatal thrombocytopenia. J Pediatr. 1986; 108(5 Pt 1): 749-55.
8. Hohlfeld P, Forestier F, Kaplan C, Tissot JD, Daffos F. Fetal thrombocytopenia: a retrospective survey of 5,194 fetal blood samplings. Blood. 1994; 84(6):1851-6.
9. Matsubara K, Nigami H, Yura K, Inoue T, Isome K, Fukaya T. Serum thrombopoietin level and thrombocytopenia during the neonatal period in infants with Down's syndrome. J Perinatol. 2010; 30(2):98-102.
10. Henry E, Walker D, Wiedmeier SE, Christensen RD. Hematological abnormalities during the first week of life among neonates with Down syndrome: data from a multihospital healthcare system. Am J Med Genet A. 2007; 143A(1):42-50.
11. Webb D, Roberts I, Vyas P. Haematology of Down syndrome. Arch Dis Child Fetal Neonatal Ed. 2007; 92(6):F503-7.
12. Thüring W, Tönz O. Neonatal thrombocyte values in children with Down's syndrome and other autosome trisomies. Helv Pediatr Acta. 1979; 34(6):545-55.
13. Rosen T, D'Alton ME. Down syndrome screening in the first and second trimesters: what do the data show? Semin Perinatol. 2005; 29(6):367-75.
14. Lin AE, Basson CT, Goldmuntz E, Magoulas PL, McDermott DA, McDonald-McGinn DM, et al. Adults with genetic syndromes and cardiovascular abnormalities: clinical history and management. Genet Med. 2008; 10(7):469-94.
15. Gamis AS, Smith FO. Transient myeloproliferative disorder in children with Down syndrome: clarity to this enigmatic disorder. Brit J Haematol. 2012; 159(3):277-87.