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Chapter

Thrombocytopenia in Neonates

Bernhard Resch

Abstract

Thrombocytopenia defined as platelet count below 150,000/μL is not an uncommon event at the neonatal intensive care unit (NICU). In our region we calculated a prevalence of nearly 2 of 1000 live births. Early-onset neonatal thrombocytopenia (NT) occurring within the first 72 hours of life is more common than late-onset NT. Preterm infants are affected more often than term infants and bacterial infection is the most common diagnosis associated with NT. There are a lot of maternal, perinatal, and neonatal causes associated with NT and complications include bleedings with potentially life-threatening intracranial hemorrhage. Alloimmune thrombocytopenia (NAIT) often presents with severe thrombocytopenia (<30,000/μL) in otherwise healthy newborns and needs careful evaluation regarding HPA-1a antigen status and HLA typing. Platelet transfusions are needed in severe NT and threshold platelet counts might be at ≤25,000/μL irrespective of bleeding or not. Immune mediated NT recovers within 2 weeks with a good prognosis when there happened no intracranial hemorrhage. This short review gives an overview on etiology and causes of NT and recommendations regarding platelet transfusions.

Keywords: neonatal thrombocytopenia, prematurity, platelet transfusion, alloimmune thrombocytopenia, early- and late-onset thrombocytopenia, severity, intracranial hemorrhage, bleeding, incidence, mortality

1. Introduction

Thrombocytopenia, defined as a platelet count <150,000/μL or below 150×10^9/L, occurs more often during the neonatal period than in any other populations. Thrombocytopenia implicates an increased risk of bleeding, and is associated with significant morbidity mainly due to intracranial hemorrhage. As a result, it is important to identify infants at risk, and if indicated (see below recommendations for platelet transfusion), to initiate therapy to prevent complications.

Recently our research group on neonatal infectious diseases and epidemiology at the Medical University of Graz, Austria, published retrospectively collected data on neonatal thrombocytopenia (NT) [1]. Of 371 neonates diagnosed as having NT, 312 (84.1%) had early-onset NT (EOT) and 59 (15.9%) had late-onset NT (LOT) defined as NT before or after 72 hours of age, respectively. The degree of NT was defined as mild, platelet counts of 100,000–150,000/μL; moderate, counts of 50,000–<100,000/μL; severe, counts of 30,000–<50,000/μL; and very severe, counts of <30,000/μL, according to the description of Wiedmeier et al. [2]. The majority—nearly three-fourth of the cohort—had mild (33%) to moderate (38%) NT; only 14% had severe and 15% very severe NT [1]. Seventy-six percent of the neonates were born preterm and this rate was approximately the same for

either EOT or LOT (76 and 77%, respectively). The percentage of extremely low gestational age newborns (ELGAN, below 28 weeks of gestational age) was 20% in total. The incidence of NT in preterm infants was 4% (282/6964) in our population during the years 1990–2012. Thus, we calculated the prevalence of NT as being 1.8/1000 live births in our region (Southern Styria with around 200,000 live births during the study period) [1].

A total of 40 neonates (10.8%) died; 36 (90%) had EOT, and 4 (10%) had LOT; and 30 (75%) neonates were still thrombocytopenic at the time of death. Interestingly, bleeding signs were significantly associated with mortality in our study. On the other hand, severity of NT was not associated with mortality. Only cutaneous bleedings were found to be associated with severity of NT. The mean duration of NT was significantly longer in case of LOT compared to EOT (8.9 vs. 16.8 days; $p < 0.001$); and the duration was positively correlated with severity of NT. At least we found that platelet transfusion did not shorten the duration of NT [1].

2. Etiology and causes of neonatal thrombocytopenia

Thrombocytopenia is present in 1–5% of newborns at birth, and severe thrombocytopenia defined as platelet count below 50,000/μL occurs in 0.1–0.5% [3]. But thrombocytopenia is more common in neonates needing intensive care at the neonatal intensive care unit (NICU) with rates up to 50%. Every fifth newborn is at risk at the NICU to develop thrombocytopenia, and 8% of preterm and 6% of term infants are at risk for severe thrombocytopenia [4].

Main mechanisms of thrombocytopenia include increased platelet consumption and/or sequestration, and often neonatal thrombocytopenia is of multifactorial origin. Thus, on the one hand there is rapid consumption like in case of necrotizing enterocolitis (NEC) and on the other hand slow recovery by impaired platelet production.

There are a lot of maternal, perinatal, and neonatal causes that might be associated with the occurrence of NT. **Figure 1** shows the main features and causes of NT by separating early- and late-onset thrombocytopenia [5].

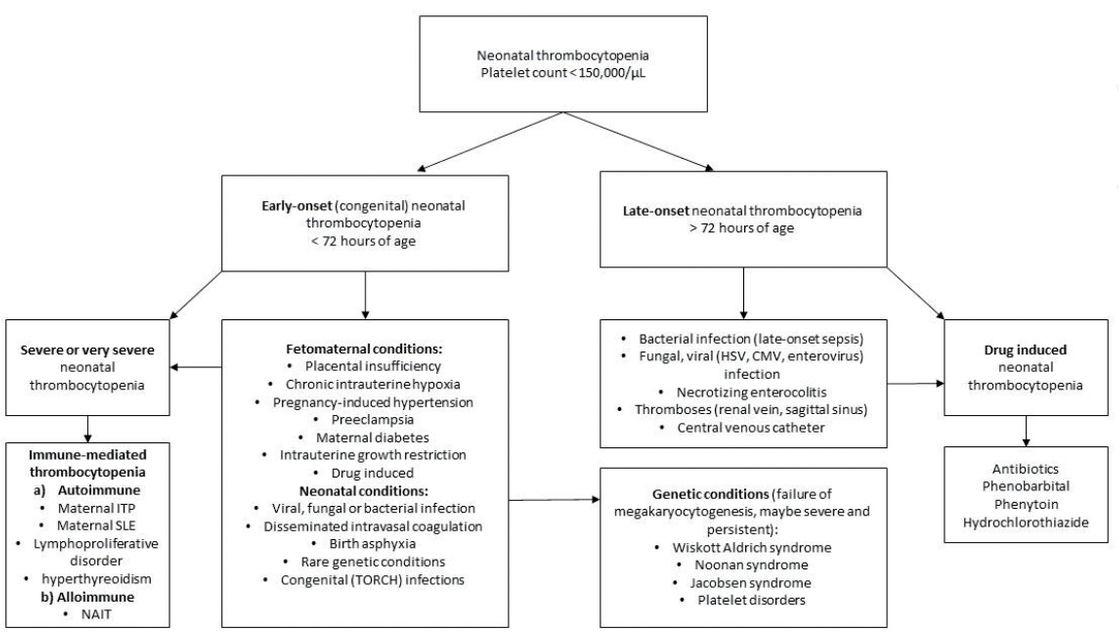

Figure 1.
Etiology and causes of early- and late-onset thrombocytopenia.

Own data on neonatal diagnoses associated with thrombocytopenia retrospectively collected over 23 years compared to data from Tunisia and Turkey—in order to give a broader view on dominant causes and diagnoses—are shown in **Table 1** [1]. Main diagnoses were early- and late-onset sepsis, and intrauterine growth restriction. Other dominant features like asphyxia and NEC differed between centers as did more sporadic causes of NT.

An association of NT with bacterial infection is well known. Rates have been reported of 30% [7], 36% [8], and 47% [1]. And severe NT and very severe NT were commonly associated with sepsis [1, 8]. Late-onset NT often is reported to result in prolonged courses of NT [1, 9, 10].

Birth asphyxia is a common diagnosis associated with NT and reported up to 25% [1, 7, 8]. NEC is a morbidity often complicated by NT. Resch et al. reported a rate of 4.1% [1] and that was twice as high as reported elsewhere [7, 8]. Other associations, including chromosomal anomalies, metabolic disorders, and thromboses,

Austria [1]	**2018**	**Tunisia [ ]**	**2016**	**Turkey [ ]**	**2013**
371 cases	23-year period	112 episodes	4-year period	134 cases	5-year period
EOS	128 (34)	LOS	29 (19)	Sepsis	45 (34)
Asphyxia	95 (25)	IUGR	26 (17)	IUGR	25 (19)
LOS	47 (13)	EOS	23 (15)	Preeclampsia	13 (9.7)
NEC	16 (4.1)	DIC	22 (14)	Maternal thr.	6 (4.5)
Chrom. aberration	15 (3.9)	PIH	18 (12)	Drug	5 (3.7)
HDN	9 (2.4)	Unexplained	15 (9.6)	Hydrops fetalis	4 (3.0)
CMV	9 (2.4)	Cong. rubella	6 (3.8)	Perinatal asphyxia	4 (3.0)
MPD	6 (1.6)	Asphyxia	5 (3.2)	Ablatio placenta	4 (3.0)
NAIT	4 (1.0)	NEC	3 (1.9)	Drug + sepsis	4 (3.0)
K-M-syndrome	2 (0.5)	Tris 21	2 (1.3)	Rh incompatibility	4 (3.0)
Metab. disorders	2 (0.5)	CMV	2 (1.3)	NEC	3 (2.2)
Thrombosis	2 (0.5)	Exchange transf.	2 (1.3)	Maternal ITP	3 (2.2)
		Toxoplasmosis	1 (0.7)	Congenital anomaly	2 (1.5)
		Neonatal lupus	1 (0.7)	Tris 21	2 (1.5)
		Maternal ITP	1 (0.7)	NAIT	2 (1.5)
				HELLP syndrome	2 (1.5)
				Metab. disorders	2 (1.5)
				Maternal GDM	2 (1.5)
				Neonatal jaundice	1 (0.8)
				Mother with SLE	1 (0.8)

Data are given as number (%).
EOS: early-onset sepsis, LOS: late-onset sepsis, NEC: necrotizing enterocolitis, HDN: hemolytic disease of the newborn, CMV: cytomegalovirus, MPD: myeloproliferative disease, NAIT: neonatal alloimmune thrombocytopenia, K-M-syndrome: Kasabach-Merritt syndrome, DIC: disseminated intravasal coagulation, IUGR: intrauterine growth restriction, GDM: gestational diabetes mellitus, SLE: systemic lupus erythematodes.

Table 1.
Neonatal diagnoses associated with thrombocytopenia from three studies (Austria [1], Tunisia [6], and Turkey [7]).

ranged between 0.5 and 3.9% in the literature [1, 6–8]. Von Lindern et al. [8] reported on a 10% rate of hemolytic disease of the newborn (HDN), which was four times higher compared to the rate of 2.4% reported by Resch et al. [1].

In preterm infants, NT is rarely diagnosed at low rates between 4 and 12% [1, 10]. Most studies report higher rates of NT ranging between 22 and 35% [2, 3, 8, 11–13], and highest rates (53–70%) have been reported from developing countries [14, 15]. Own data revealed that 75% of a cohort of thrombocytopenic neonates were preterm neonates. The association between NT and prematurity or low birth weight is well documented [3, 6–8, 11, 16, 17]. In this context small-for-gestational age (SGA) is a well-known risk factor for developing NT [11, 16, 17], and rates have been reported as high as 30–53% [1, 17, 18].

3. Pathomechanisms of neonatal thrombocytopenia

3.1 Immune-mediated thrombocytopenia

One possibility of low platelet counts is increased destruction that is observed in several neonatal conditions. Placental crossing of maternal antibodies is the cause of NT in case of immune-mediated NT, which destroys neonatal platelets. Immune-mediated processes are very common causes of neonatal thrombocytopenia, and the antibodies responsible may be autoantibodies, drug-dependent antibodies, or alloantibodies. The mechanism behind is an interaction with platelet membrane antigens or the formation of immune complexes, which can bind to reticuloendothelial cell Fc receptors. As a result platelets become cleared from blood vessels [19].

3.1.1 Neonatal alloimmune thrombocytopenia (NAIT)

In NAIT, fetal platelets contain an antigen inherited from the father that the mother lacks. The mother produces antiplatelet antibodies from the immunoglobulin G (IgG)-type against the platelet antigen during pregnancy that is recognized as being foreign. Thereafter IgG antibodies cross the placenta and destroy fetal platelets that express the paternal antigen [20].

3.1.2 Neonatal autoimmune thrombocytopenia

It is mediated by maternal autoantibodies that react with both maternal and fetal platelets. This occurs in maternal autoimmune disorders, including immune thrombocytopenia purpura (ITP) and systemic lupus erythematosus (SLE) [20].

3.1.3 Drug-induced immune thrombocytopenia

Drug-induced immune thrombocytopenia is typically caused by platelet destruction from maternal drug-dependent antibodies and, rarely, by neonatal antibodies. Bone marrow suppression also can result in thrombocytopenia due to decreased platelet production. Neonatal drug-induced immune thrombocytopenia is usually caused by maternal drug-dependent antibodies formed after drug exposure to the mother during pregnancy [19, 20]. Maternal antibodies can cross the placenta and affect fetal and neonatal platelets. This mechanism is similar to that seen in mothers with primary immune thrombocytopenia purpura (ITP). Drugs associated with maternal drug-mediated platelet destruction include quinine, quinidine, trimethoprim-sulfamethoxazole, vancomycin, penicillin, rifampin, carbamazepine, phenytoin, valproic

acid, ceftriaxone, ibuprofen, mirtazapine, oxaliplatin, suramin, GP IIb/IIIa inhibitors (e.g., abciximab, tirofiban, eptifibatide), and heparin. Some drugs may cause thrombocytopenia at the initial exposure without prior sensitization. This commonly occurs with the glycoprotein IIb/IIIa inhibitors and has also been seen with other drugs, such as vancomycin and piperacillin [21]. Rarely, platelet destruction can be caused by neonatal drug-dependent antibodies, such as seen in heparin-induced thrombocytopenia (HIT). HIT antibodies can promote thrombosis by inducing platelet activation. Patients with suspected HIT require immediate institution of a non-heparin anticoagulant [20].

3.1.4 Non-immune drug-induced NT

Many drugs used as chemotherapy cause thrombocytopenia by bone marrow suppression (*non-immune drug induced NT*). Antibiotics, such as linezolid, daptomycin, and valacyclovir can also cause moderate thrombocytopenia in some patients by suppression of platelet production [20].

3.2 Thrombopoiesis

Platelet production—thrombopoiesis—is initiated by a thrombopoietic stimulus, and the most important stimulant is the chemokine thrombopoietin (TPO) besides several cytokines and chemokines that are also involved in the process (e.g., IL-3, IL-6, IL-11, GM-CSF, stromal cell-derived factor-1 and fibroblast growth factor 4) [22]. TPO promotes the proliferation of megakaryocyte progenitors and the maturation of megakaryocytes. These mature megakaryocytes are at least responsible for generation and release of new platelets into the blood vessels [22].

3.2.1 The homeostasis of TPO levels

The homeostasis of TPO levels is regulated by the thrombopoietin c-Mpl (myeloproliferative leukemia protein) receptor-mediated uptake and destruction of the hormone with the aim to have steady-state amounts of hepatic TPO. When bound to the platelet c-Mpl receptors, the hormone gets removed from the circulation and blood levels are reduced. In case of inflammatory processes IL-6 is released from macrophages and fibroblasts (via TNF-α) and enhances hepatic TPO production [22].

Another phenomenon adding to the steady-state model of TPO regulation is the physiological response to severe thrombocytopenia of bone marrow stromal cells, which under normal circumstances produce low amounts of TPO-mRNA but increase transcription markedly in case of thrombocytopenia [22]. IL-6, stimulated by inflammation processes, leads to increased levels of TPO resulting in reactive thrombocytosis; and TPO is now confirmed as the final mediator of inflammation-induced thrombocytosis [22].

There are similarities and differences between neonatal and adult thrombocytopenia. Plasma TPO concentrations are known to be higher in healthy neonates compared to healthy adults. But in NT TPO levels are lower even when adult thrombocytopenia has the same degree [19]. Interestingly, megakaryocyte progenitors of neonates have a higher proliferative potential than those of adults resulting in larger megakaryocytes. Neonatal megakaryocyte progenitors are more sensitive to TPO both in vitro and in vivo than adult progenitors [19]. Cells are present both in the bone marrow and the peripheral blood of neonates in contrast to adult ones that are almost exclusively present in the bone marrow [19] (**Figure 2**).

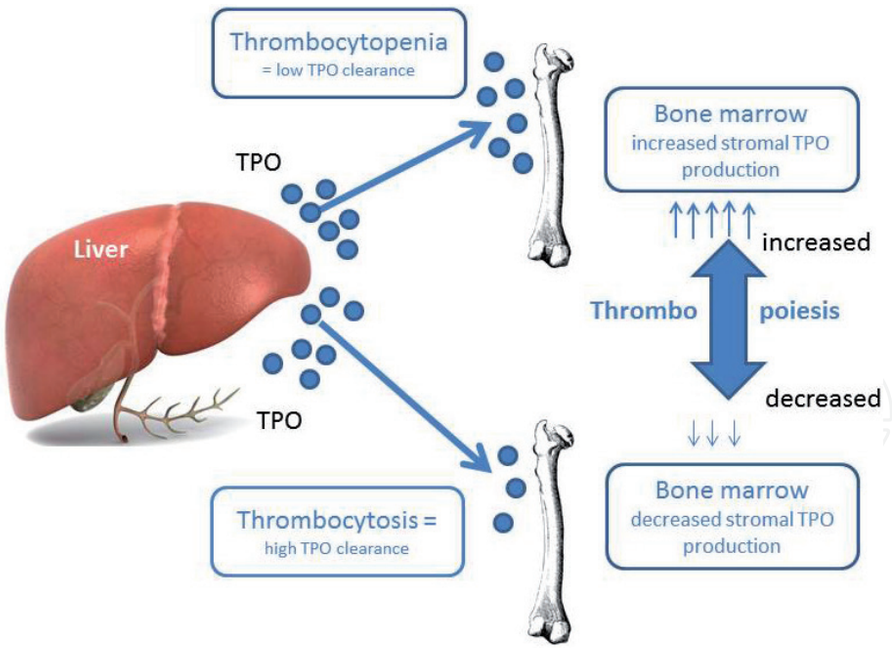

Figure 2.
A simplified model of TPO regulation.

3.2.2 Clinical conditions and their pathomechanisms

Chronic intrauterine hypoxia is commonly observed when associated with placental insufficiency due to all conditions of pregnancy-induced hypertension (hypertension alone or pre-eclampsia or hypertension-elevated liver enzymes-low platelet counts—HELLP—syndrome, and gestational or maternal diabetes) and is usually manifested by fetal intrauterine growth restriction and hematological abnormalities including NT. The pathomechanisms behind are not completely understood but lower levels of megakaryocyte progenitors have been found that increased during normalization of NT [23].

The hematopoietic microenvironment plays a significant role in chronic hypoxia-induced suppression of megakaryocytopoiesis, and, not astonishingly, preterm infants' megakaryocyte progenitors are more vulnerable to ischemic insults than progenitors from term neonates or adults [24].

Overall, observations demonstrated that thrombopoiesis is up-regulated in *neonatal sepsis and/or NEC*, but this effect can also be down-regulated resulting in "hypoproliferation" [19]. Platelet factor 4 is a potent inhibitor of megakaryocyte proliferation that is released from activated platelets during severe sepsis. This regulates neonatal megakaryocytopoiesis negatively [25].

In *HIV-associated thrombocytopenia*, evidence that splenic platelet sequestration decreased platelet production had been observed despite larger megakaryocyte mass [26]. In neonates, ineffective platelet production was described as being the main mechanism of HIV-associated thrombocytopenia [27]. The mechanisms in other *congenital infections* of the TORCH complex mostly remain to be speculative despite their common association with NT [20].

4. Neonatal alloimmune thrombocytopenia (NAIT)

Harrington et al. first described in 1953 two infants born with severe thrombocytopenia to mothers with normal platelet counts [28]. Both newborns recovered despite severe bleeding and other complications after 2 and 8 weeks, respectively.

This immunological disease now is well described as neonatal alloimmune thrombocytopenia (NAIT).

In 1962 a maternal antibody against a platelet alloantigen was detected causing NAIT [29]. This platelet alloantigen determined as PlA1 was the cause of platelet destruction in two of the newborns reported in the study by Shulman et al. [29]. Later, PlA1 was found to be identical to an antigen called Zwa [30] and now is known as human platelet antigen 1a (HPA-1a). Over the following years several other platelet-specific antigens were detected as being able to induce maternal immunization during pregnancy with subsequent fetal platelet destruction, thus, being an important complication of pregnancy with diagnostic and therapeutic challenges [31].

The incidence of NAIT calculated from large studies on women negative for HPA-1a lies in between 1 in 1000–2000 HPA-1a positive newborns [32–34]. The incidence of HPA-1a negative phenotype is about 2.5%; and one-third is at high risk to get immunized in case of a HPA-1a positive fetus, and this association is triggered by HLA-DR antigen B3*0101 positivity [31].

The main problem of NAIT is that it can lead to serious bleedings including intracranial hemorrhage and death. In full term infants it is the leading cause of intracranial hemorrhage [35]. Other clinical findings are petechiae or purpura associated with very low platelet counts without any explanation (after exclusion of bacterial and viral infection—TORCH complex, or disseminated intravascular coagulation). A previous history of NAIT results in more severe disease. Around 10–20% of the newborns have intracranial hemorrhages, and the vast majority of 80% occurs already before birth. After birth the greatest risk of bleeding is in the time span of the first 4 days of life. Untreated, NT resolves within 2–3 weeks [35].

Even in mildly affected infants serological investigation including ABO, HPA and HLA typing (further details are beyond the scope of this chapter) is indicated because results can be critical for effective management of future pregnancies. For the most informative evaluation, it is important to study blood samples from both mother and father.

A systematic review on incidence and consequences of NAIT reported on 6 of 21 studies (full text analysis) from initial 768 studies [36]. Nearly 60,000 newborns were screened, with severe thrombocytopenia in 89 cases (0.15%); and NAIT was diagnosed in 24 of these 89 newborns (27%) resulting in an incidence of 1:2500. Six newborns (25%) had diagnosis of intracranial hemorrhage and most likely of antenatal origin. Hence, intracranial hemorrhage due to NAIT occurred in 1:10–11,000 newborns [36, 37]. This is the most severe complication having a 1–7% risk of death. Survivors are known to have sequelae including mental retardation, cerebral palsy, cortical blindness and seizures in 7–26% of pregnancies [38]. In contrast to ABO- or Rh-incompatibility, immunization occurs often during the first pregnancy.

Severity of NAIT is associated with parity (second pregnancy often more severe), HPA-a1 antibodies level, outcome of a former pregnancy, and the type of alloimmunization (HPA-1a more severe than HPA-5b) and the HLA type: homozygote HPA-1b and negative for HLA DRB3*0101 leads to no NAIT with negative predictive value of 99.6%, but homozygote HPA-1b plus HLA DRB3*0101 positivity leads to NAIT with a positive predictive value of 35% [39] Interestingly, antenatal IVIG is again more effective depending on HLA status [31]. Also of importance is the risk of recurrent intracranial hemorrhage of being 80–90%.

4.1 How to proceed in case of suspected NAIT?

At first the medical history should be looked for a previous neonate with thrombocytopenia of unknown origin and/or having platelet count below 50×10^9/L and/or previous history of intracranial hemorrhage of uncertain origin [40]. Is the mother

thrombocytopenic, one should evaluate for maternal anti-platelet auto-antibodies or a history of immune thrombocytopenia. Is the mother not thrombocytopenic, maternal and paternal platelet antigen typing and maternal platelet HPA antibody testing should be done. In case of incompatibility at HPA loci (1–6, 9, 15) and presence of specific maternal HPA-antibody, diagnosis of NAIT is given. Are there no incompatibilities and no anti-platelet antibodies or only nonspecific antibodies of the mother present, then no further evaluation is necessary besides maternal antibodies against paternal platelets are positive (preferred at 30 weeks' gestation). A third variant is a positive incompatibility without maternal anti-HPA antibodies (provided no reaction with paternal platelets), then there is no further evaluation necessary [40].

During pregnancy, strategies using IVIG and corticosteroids have been successful. The success rate with IVIG alone was reported to be as high as 98.7% and is in line with a Cochrane analysis reporting 97.3% [37, 41]

5. Complications of neonatal thrombocytopenia

5.1 Bleedings

The prevalence of hemorrhages in thrombocytopenic neonates is approximately 20–30% according to the literature [16, 42]. The risk of hemorrhage is associated with lower gestational age, definite causes of thrombocytopenia, and the severity of concomitant morbidities [8, 9, 43].

An observational study including 169 neonates with severe NT identified severe sepsis and NEC as the most common diagnoses associated with bleeding neonates [35]. In those neonates with mild or no hemorrhage, the most common cause of severe NT has been documented as being intrauterine growth restriction and maternal pregnancy-induced hypertension [44].

A causal link between thrombocytopenia and intracranial hemorrhage is not known. Interestingly, platelet transfusions could not reduce the risk of intracranial bleedings [1, 45]. The majority of preterm neonates with severe intraventricular hemorrhage (IVH) becomes thrombocytopenic during the course of bleeding, thus, thrombocytopenia might not be the cause of IVH [46, 47]. Additionally, considering IVH as a multifactorial event, it seems highly unlikely that an isolated low platelet count leads to bleeding [44].

Another point of interest is the fact that comparable rates of IVH have been reported independent of the severity of NT [17]. In contrast, cutaneous bleeding conditions have been associated with the severity of NT [1, 46], and the prevalence of skin bleeding in thrombocytopenic neonates has been reported as being as high as 81% [48].

5.2 Mortality

The association of increased mortality rates with increasing numbers of platelet tranfusions mainly reflects the severity of the underlying disease or condition, for example, extremely low gestational age newborn. These infants are known to be at high risk for severe IVH that again is associated with high risk of death. Additionally, the more severe NT is the higher is the rate of mortality, and some data suggest that NT contributes to mortality rather than simply being a measure of disease severity [5]. Three studies from the USA, the UK, and Mexico reported higher mortality rates in neonates who had received platelet transfusions compared with those who had not [49–51]. The direct effects of platelet transfusions are questionable, as specific effects have not been properly evaluated, and the influence of

preexisting morbidity is difficult to evaluate [44]. But as shown by Curley et al. [52] (see below), waiting until platelets have fallen below 25 × 10^9/L before indicating transfusion is of more benefit than earlier transfusion at cut-off level below 50 × 10^9/L. Again the observation of Kenton et al. [53] is of interest who did not find an improvement in NEC-associated mortality with an increasing number or volume of platelet transfusions.

6. Recommendations for treatment with platelet transfusions

Platelet transfusions are commonly used in preterm infants with NT at different threshold values. In 2018, a milestone study prospectively investigated whether platelet transfusion should be given at platelet-count thresholds of 50,000/μL (high-threshold group) or 25,000/μL (low-threshold group) [52]. In this multicenter trial, preterm infants born at less than 34 weeks of gestation in whom severe thrombocytopenia was diagnosed were included and randomly assigned to high or low platelet transfusion groups. The primary outcome was death or new major bleeding within 28 days after randomization. Of 660 infants (median birth weight, 740 g; and median gestational age, 26.6 weeks), 90% of the infants (296 of 328 infants) of the high-threshold group received at least one platelet transfusion, as compared with 53% (177 of 331 infants) in the low-threshold group. A new major bleeding episode or death happened in 26% of the infants in the high-threshold group and in 19% in the low-threshold group (odds ratio, 1.57; 95% confidence interval 1.06–2.32; p = 0.02). Most exciting, there was no significant difference between corresponding rates of serious adverse events (25 vs. 22%) [51].

An overview of recommendations at different thresholds of thrombocyte counts is given in **Table 2**.

Cut-off value thrombocyte counts	Recommendation	Authors
<20 × 10^9/L	All neonates (prophylactic)	Blanchette et al. [54, 55]; Gibson et al. [56]; Chakravorty et al. [57]; Carr et al. [58]
20–29 × 10^9/L	Non-bleeding term and preterm infant	Blanchette et al. [55]; Roberts et al. [59]; Calhoun et al. [60]; Sola-Visner et al. [61]; Murray [62]; Gibson et al. [56]; Carr et al. [58]; Sparger et al. [63]
	Bleeding neonates	Murray et al. [62]; Roberts et al. [4, 44]; Chakravorty et al. [57]
30–49 × 10^9/L	Preterm infants (unstable neonate, first week of life, surgery or invasive procedures)	Blanchette et al. [54, 55]; Roberts et al. [59]; Sola-Visner et al. [61]; Calhoun et al. [60]; Murray [62]; Roberts et al. [4]; Sparger et al. [63]
	Bleeding neonates	Blanchette et al. [54]; Roberts et al. [44, 59]; Gibson et al. [56]; Chakravorty et al. [57]
50–99 × 10^9/L	Non-bleeding sick preterm	Blanchette et al. [54, 55]; Roberts et al. [59]
	Bleeding neonates	Roberts et al. [4, 44, 59]; Murray et al. [62]; Sola-Visner et al. [61]; Sparger et al. [63]
100–150 × 10^9/L	No recommendations	—

Table 2.
Recommendations for platelet transfusions depending on different thrombocyte counts.

7. Conclusions

In conclusion, neonatal thrombocytopenia is a common problem at the neonatal intensive care unit. In most cases, it is a mild to moderate, self-limited entity. In severe cases, immune-mediated disease has to be suspected warranting prompt diagnosis and careful management. The threshold for platelet transfusions better should be at thrombocyte counts of 25–30,000/μL due to recent data reporting on a reduced mortality rate using a more restrictive transfusion regimen.

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Conflict of interest

The author declares no conflict of interest.

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