European Journal of Molecular & Clinical Medicine
ISSN 2515-8260 Volume 07, Issue 02, 2020

ANEMIA OF THE NEW BORN BABIES: A REVIEW

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ABSTRACT:

Background: Anemia of newborns is a worldwide health concern. Since neonatal anemia is associated with late neurological deficits, and is a leading cause of the risk of perinatal mortality and requires urgent attention. Standard hemoglobin level for a term newborn is 19.3±2.2 g/dL. Anemia of the newborns can be physiological,owing to excessive blood loss, increased destruction of RBCor decreased production of RBC. Newborn babies with anemia are pale, and may have tachypnea, tachycardia, poor feeding, and hypotension with acute blood loss and jaundice when there is hemolysis of RBC. Hemoglobin concentration is the best tool, for the diagnosis of anemia in Newborns. The treatment depends on the underlying cause; Newborns, who have rapidly lost large amounts of blood are treated with I/V fluids followed by blood transfusion,reducing the blood loss due to repeated phlebotomy and blood extraction for investigations may reduce the need of blood transfusion. Other treatments are Autologous Placental Blood Transfusion, Erythropoietin therapy, and Nutritional Supplementation.

Key words: Physiological anemia, Hemoglobin, neonatal

Introduction:

Neonatal anemia is associated with late neurological deficits, and is a leading cause of the risk of perinatal mortality. The normal hemoglobin concentration for a term newborn is from 15-20g/dl(J. A. Widness, 2008).Low hemoglobin levels at birth are often associated with subsequent worse outcomes such as brain hemorrhage, Necrotizing enterocolitis, defective neurological development, retinopathy of prematurity, and often death(Simonsen, Anderson-Berry, Delair, & Davies, 2014). Anemia of newborns is a serious health concern. Since neonatal anemia is associated

with subsequent neurological deficits and is a leading cause of the 4-8% risk of perinatal mortality, it requires in depth knowledge and urgent attention, so as to improve the outcome of newborns(Strauss, 2010).

The incidence of early anemia in newborn is 17.5- 21 %(F & S, 2015). The study results on US newborns reported that, at birth, 21% of the neonates were anemic(MacQueen et al., 2017) and the incidence of newborn anemia to be 17.5%(Li, Liang, Liang, Shi, & Han, 2019).There is a significant scarcity of studies on the subject of anemia of newborn, although it is a frequent and often life threatening situation among newborn babies requiring attention. The current review is prepared in order to improve the quality of care provided to newborn babies with anemia. Anemia in the newborn babies is either physiological or pathological. Pathological anemia in turn may be due to excessive blood loss, increased destruction of blood in the body or decreased production of blood, which all leads to anemia of newborn babies.

Physiological Anemia in Newborn Babies:

The commonest anemia in newborn babies is the physiological anemia. Just after birth baby's own lungs start functioning this leads to decline incirculating red blood cell, and blood hemoglobin concentration, within first week of life(Andersen, Keir, Kirpalani, & Stark, 2015). Among full-term infants, due to physiological processes there is nearly drop in the level of hemoglobin, thatresult is development of physiologic anemia(J. A. Widness, 2008).This preterm infants experience much more fall in the hemoglobin concentration than in full-term infants. This is principally due to a number of problems like suboptimal erythropoietin reaction in preterm babies, shorter lifespan of red blood corpuscles and sluggish response of fetal liver to produce erythropoietin owing to hypoxia(Ohlsson & Aher, 2017).

Fetus takes its oxygen from maternal blood and own lungs are not functioning while after birth. The newborn lungs start functioning and helping in oxygenating the blood and there is an increase in the oxygen tension (PaO2) due to enough oxygen supply by functioning lungs thus it leads to rapid hematological change in newborns(Suzanne Reuter, Chuanpit Moser, & Michelle Baack, 2014). There is decline in erythropoietin level and erythropoiesis leading to decline in RBC count and anemia. There is a fall of RBC and hemoglobin in newborn babies from146 - 225 g/L at birth and this drop is much more if the baby is prematurely born and there is a more rapid and severe decrease in Hb 70 to 80 g/L(J. A. Widness, 2008).

Blood loss is an important cause of anemia in newborn babies. The blood loss can be due to several reasons(J. A. Widness, 2008). The Salient reasons for blood loss are repeated Phlebotomy, blood extraction from newborn babies for lab investigations,cord malformations,placental abnormalities, placenta previa,fetal-to-maternal hemorrhage,twin-to-twin blood transfusion and hemolytic anemia(Colombatti, Sainati, & Trevisanuto, 2016).

Repeated blood extraction in newborn babies for investigations is an important cause for anemia in newborns(Robin K Whyte & Jefferies;, 2014). The problem is more severe in premature babies with very low erythropoietin levels. Since repeated phlebotomy and blood extractions in newborn babies for investigations increases the

risk of anemia and subsequent blood transfusion, it should therefore be avoided(Strauss, 2010).

Acute blood loss due to hemorrhage usually leads to anemia in newborn babies. As the total blood volume is low in neonates, it is 90 to 105 mL blood /kg in full term babies and 78 to 86 mL blood /kg in premature babies(Rao & Georgieff, 2009). Therefore, even a small amount of blood loss like 20 mL of blood loss may result in anemia. It has beenobserved that the use of advanced analyzers can reduce the blood loss and incidence of anemia in newborns(John A. Widness, 2008). Placenta Previa as cause of blood loss and anemia in newborns. Severe anemia is documented in the babies born to the mothers who have placenta Previa presents with severe anemia (Adere, Mulu, & Temesgen, 2020; Dong Gyu Jang, 2011).

In the pregnancies during placental separation or in case of trauma, fetal blood cells are escaped to the maternal circulation(Dawe, Tan, & Xiao, 2007; Hall, 2009; Jauniaux, Poston, & Burton, 2006). Certain procedures and situations may lead to Fetal-to-maternal hemorrhage.Usually lost blood is small (about two mL)but often in 3/1000 pregnancies huge blood loss like > 30 mLmay also occurs. Sometime in 13 to 33% of monozygotic, monochromic twin pregnancies, blood supply to two twins is unequal"Hemorrhagic" anemia occur during twin-to-twin transfusions, or during feto-maternal transfusions(Stephen Wagner, John T. Repke, & Serdar H. Ural, 2013; Veeken et al., 2019). The hemolytic anemia are due to ABO and Rh incompatibilityA-B-0 and Rh incompatibility occurs when mother’s and fetus blood groups are different(L., 2005; Mohammad Hassanzadeh-Nazarabadi , Sahar Shekouhi, & Seif, 2012).

Hereditary spherocytosis and G-6-PD deficiency and anemia of newborn:

Glucose-6-phosphate dehydrogenase deficiency affects red blood cell to breakdown. Complications can include anemia and jaundice of newborn. SometimeG6PD deficiency represents as neonatal jaundice, and acute hemolytic anemia, which is usually started by an exogenous trigger(Gomez-Manzo et al., 2016; Shinya Tsuzuki et al., 2013). The germ-free intestine of the newborn cannot produce vitamin K. If not supplemented leads to internal hemorrhages (Ceratto & Savino, 2019; Lippi & Franchini, 2011). The cause of Vitamin K–deficiency may also occur, if the mother is using drugs, which inhibits vitamin K, like anticonvulsants, isoniazid, rifampin and warfarin(Lippi & Franchini, 2011). If the mother is using broad-spectrum antibiotics, there is suppression of bowel bacteria and vit K synthesis is impaired (Ceratto & Savino, 2019; Langdon, Crook, & Dantas, 2016).

After birth beta-chain manufacturerises until adult Hb (Hb A, alpha2beta2) becomes leading. In beta thalassemia there is reduced or absent production of the beta chains of hemoglobin that leads to severe anemia. Congenital is due to Diamond-Black fan anemia and fanconi anemia, affected infants become anemic at birth, and low birth weight occurs in about 10%(Vlachos et al., 2008).

Anemia of Newborn Due To Nutritional Deficiencies:

Iron, copper, folate (folic acid), vitamin E, and vitamin B12 are essential for the RBC production and the absence may cause anemia in the early months of life.The iron

deficiency is the most common nutritional deficiency-causing anemia of newborn. Iron deficiency is due to low iron in feeds. Iron supplementation is essential for the preterm infant. The iron supplementation improves anemia in newborn (McCarthy, Dempsey, & Kiely, 2019; Moreno-Fernandez, Ochoa, Latunde-Dada, & Diaz-Castro, 2019). Further Breastfed babies who does not receive iron-fortified foods after 4 months of age develop iron deficiency anemia (Friel, Qasem, & Cai, 2018; Society, 2007).If the oxygen supply to the tissues is not optimal, the symptomatic anemia may develop. Most Signs include sluggishness, poor feeding increased resting heart rate, acidosis, and poor growth, decreased energy to nipple feed, apnea, and increased need for respiratory support.

Evaluation ofthe Anemia of Newborn Babies:

After history and physical examination of newborn, blood tests are performed to diagnose anemia. They include measurement of hematocrit, serum ferritin. Basically hemoglobin level considered the best instrument for the diagnosis of anemia of newborn, but other blood indices are also evaluated like reticulocyte count(Ozdemir, 2015).Tests like Kleihauer-Betke test, A CXR may be performed for pulmonary hemorrhage.Ultrasoundand blood smear tests should be performed to check for other internal bleeding possibilities. A suddenly loss of large amount of blood during labor or delivery leads to shock and babies appear pale and have a rapid heart rate and low blood pressure, along with rapid, shallow breathing. Jaundice and increased bilirubin is noted when there is rapid breakdown of red blood cells. Babies who have anemia in the early days of life experience delayed neurological deficits, retinopathy of prematurity, encephalopathy and growth retardation (Abou-Elsaad, Abdel-Hady, Baz, & ElShabrawi, 2017; Raffaeli et al., 2020).

Treatment Of Anemia Of New Born:

Anemia of newborn infants is a serious health concern. Sudden loss of large amount of blood may lead to shock; rapid destruction of RBC may result into Jaundice and kernicterus. Anemia of newborn during first week of life is an independent risk factor for retinopathy, delayed neurological deficits, encephalopathy and growth retardation. Once diagnosed exactly, anemia is easily treatable. Limit blood drawing for laboratory tests, frequent phlebotomy and blood extractions in the newborn for the investigations makes the babies vulnerable for blood transfusion and its risks therefore it should be reduced as much as possible. The problem of getting anemia of newborn is much more in extremely low birth weight babies (ELBW babies) who need most frequent blood transfusion. Decreasing phlebotomy blood loss in the early post-delivery period can reduce the RBC transfusions in new born(Brigitte Lemyre, Megan Sample, & Lacaze-Masmonteil, 2015; Society, 2002). Advanced blood analyzers can analyze the blood from smaller blood volumes, and may reduce the problem of iatrogenic blood loss and subsequent blood transfusion in newborn babies (Patel, Meyer, & Widness, 2016; Whitehead et al., 2019).

Red Blood Cell Transfusions for Anemia of newborn:

In case of reduced tissue oxygen delivery, packed red blood cells (PRBCs) are transfused to the babies with anemia.(PRBCs) transfusion improve thesymptoms and increase the hematocrit (Hct) value. Red blood cell (RBC) transfusion is the

principalremedy. Circulatory overload can be avoided by giving PRBCs or by exchange transfusion(Liumbruno, Bennardello, Lattanzio, Piccoli, & Rossetti, 2009).In newborn babies who have acute severe blood loss, transfusion of RBC is a successful and promptmediation to treat acute anemia, reducing theillness associated with anemia, and can be lifesaving. There are no definitestandards for controllingtime of RBC transfusions in newborns. In case of severe cardiopulmonary involvement, hematocrit should be maintained at 40 to 45% (0.40 to 0.45) for moderate cardiopulmonary disease hematocrit should be maintained at 30% to 35% (0.30 to 0.35). While for inexplicable breathing disorders or unsolved tachycardia, unexplained poor growth, hematocrit should be maintained at >20% to 25% (0.20 to 0.25)(von Heymann et al., 2006).If the <120 Hbpremature neonates red cell transfusions should be contemplated (Girelli et al., 2015). Premature infants with high-risk require red cell transfusions for anemia.For hematopoietic stem cell transplantation,cord blood can be used. The cord blood (CB) has high content of immature hematopoietic progenitor cells (HPCs)(Cai et al., 2008; Kita, Lee, Finnerty, & Herndon, 2011). In neonates who are severely underweight who are going to have surgical intervention,placental blood can be used (Rao & Georgieff, 2009; Robinson, 2012).

Erythropoietin therapy:

Erythropoietin (EPO) therapy is a harmlesscurrent way to avoid and to handle anemia of newborn.In premature infants addition of folate to the erythropoietin orally and intravenously administered iron is much better in encouraging erythropoiesis(John A. Widness & Kenneth A. Lombard, 2005). Early administration of EPO reduces the frequency and volume of red blood cell transfusions(Von Kohorn & Ehrenkranz, 2009). EPO treatment reduced the risk of long-term neurological disability (Song et al., 2016). The erythropoietin treatment is neuro-protective in clinical studies(Rey et al., 2019).

Hematopoietic stem cell transplantation:

It is a new hope for aplastic anemia and other defects. Studies have shown that the survival rates of infants who receive HSCT are encouraging (Maury et al., 2009).In a study,seventeen children were having defects in hematopoietic cell manufacture or job;they had 19 allogeneic stem cell transplantations from HLA identical siblings. It was found that during total follow-up of 36 months the survival was 77% (Pasquini et al., 2008). Supplementation of iron, folate and Vitamin E can treat mild anemia. The hemorrhagic disease of the newborn can be avoided by injecting vitamin K(Araki & Shirahata, 2020).There can be decrease in the blood transfusion decrease in the number of phlebotomy and associated blood loss by timely administration of EPO regardless of the cause of their anemia(Posluszny & Gamelli, 2010). The outcome can be improved by close checking of metabolic position hypoglycemia, hypocalcaemia, hyperkalemia, acidosis, hypo-natremia, and renal failure.

Prevention of neonatal anemia:

Prevention of neonatal anemia may result in improved long-term outcomes in babies(John A. Widness & Kenneth A. Lombard, 2005). In the first 2 weeks of life, respiratory and other illnesses are frequent requiring laboratory blood testing.

Contributing to the anemia of the newborn requiring RBC transfusion(John A. Widness & Kenneth A. Lombard, 2005).Prevention of neonatal anemia may result in improved long-term outcomes. Strategies like, increasing the removing less blood for laboratory testing and maintaining optimal nutrition significantly declines the likelihood of anemia of newborn. Delayed Cord Clamping studies have shown encouraging results with diminished Intra-Ventricular -Hemorrhage, higher hematocrit, and less RBC transfusions(Kuiper, Tibboel, & Ince, 2016).

Conclusion:

Anemia of the newborns is a worldwide health concern. Since neonatal anemia is associated with subsequent late neurological deficits and is a foremost cause of the 4-8% risk of perinatal mortality76. Anemia may develop physiologically where babies own lungs start functioning after birth providing enough oxygen and thus a decrease in the level of erythropoietin and erythropoiesis. Some non-physiologic factors such as frequent blood extraction for the sake of diagnostic investigations, and laboratory testing can contribute to anemia, further shortened RBC survival, and decreased production from diseased hematopoietic cells in bone marrow are some other contributors for the anemia of the newborn. Close observation, early detection and prompt treatment can improve the outcome and reduces the risk of neurological defects of development and mortality in newborn. Prevention as much as possible is the best way to reduce blood transfusions to the newborns. Limiting the phlebotomy and blood extractions, along with the use of advanced analyzers, which require very little blood for monitoring, are highly desired.

Acknowledgements:

This work was supported by the College of Medicine Research Center, Deanship of Scientific Research, King Saud University, Riyadh, Saudi Arabia.

PANNEL:1 Showing Salient Signs Of Anemia In New Born Babies

Pallor
Tachycardia,
Murmur
Tachypnea
Apnea
↑O2requirements
Lethargy
Poor feeding
Hepatosplenomegaly (hemolytic disease)
Jaundice
Wide pulse pressure
Hypotension
Metabolic acidosis with severe anemia

PANNEL: 2 Showing Salient Tests to Diagnose the Anemia Of New Born

Total blood count with platelets, and reticulocyte count.
•Blood group and blood type, Direct Antiglobulin test (Coombs Test)
•Bilirubin (total and direct).
•Ultra sonogram for internal bleeding. (Head, abdomen)
•Rarely, hemoglobin electrophoresis and RBC enzymes.
•Bone marrow aspiration is almost never necessary to diagnose anemia in a newborn but can be done to exclude aplastic anemia.

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