Reveiw Article

Prevalence of Neonatal Polycythemia and an Assessment of Its Related Risk Factors

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Citation Al-Zahiri J, Kumar A, Nair A, Watts T. Prevalence of Neonatal Polycythemia and an Assessment of Its Related Risk Factors. Journal of Pediatrics Review. 2022; 10(4):297-304. http://dx.doi.org/10.32598/jpr.10.4.1053.1

http://dx.doi.org/10.32598/jpr.10.4.1053.1

Article info:
Received: 16 May 2022
First Revision: 20 Jul 2022
Accepted: 11 Sep 2022
Published: 01 Oct 2022

Keywords:
Neonatal polycythemia, incidence, Prevalence, Pathophysiology, Etiology, Twin to twin transfusion

ABSTRACT

Background: Neonatal polycythemia is a condition that is incidentally encountered in clinical practice. It is characterized by elevated hemoglobin levels (above 22 g/dL) and hematocrit ratios above 65%. It is important to understand both the prevalence as well as the related risk factors of this condition as untreated preventable risk factors can result in the development of hyperviscosity syndromes leading to potential multiple organ failure.

Prevalence and Risk Factors: Risk factors include the presence of twin-to-twin transfusion, pre-eclampsia, maternal hypertension, operator-dependent cord clamping, and the presence of co-morbid conditions in neonates. The prevalence of neonatal polycythemia varies among regions and factors that may affect this variation include elevation above sea level of the patient and the mother, management of perinatal conditions such as gestational diabetes mellitus, and the method of delivery.

Conclusions: From this study, it is evident that not only do existing neonatal and maternal risk factors such as twin-to-twin transfusion syndrome and post-term deliveries, respectively, increase the risk of neonatal polycythemia but also the geographical and socioeconomic status are major factors. It is therefore imperative to conduct more thorough large-scale cohort studies to further understand the reasons for this.

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Introduction

Neonatal polycythemia is a hematological condition that is composed of a spectrum of risk factors and outcomes [1]. More precisely, polycythemia is an abnormally elevated number of circulating erythrocyte counts within the bloodstream that can be characterized by hemoglobin levels greater than 22 g/dL and hematocrit ratios of 65% or more, which is the standardized measure to diagnose polycythemia in newborns [1, 2]. Polycythemia has been known to have various factors that determine its incidence as well as the degree to which it can affect neonates [2]. The overall prevalence of neonatal polycythemia typically ranges between 2% to 15% with a higher prevalence predominant in neonates born small for gestational age [1].

An increased hematocrit can result from three main mechanisms: Response to hypoxia, blood transfusions, and decreased plasma volume secondary to multiple causes [1]. The original source of these disturbances may be due to both maternal and neonatal factors, suggesting that this is a complex multifactorial process [3] and the prevalence is highly influenced by these factors [1]. Several studies demonstrate neonatal polycythemia is likely to prevail in areas such as Tibet and Bolivia with a percentage of up to 83% [1]. Accordingly, many reports have concluded that the causality of neonatal polycythemia in these regions is closely linked to high altitude [1]. However, other studies reject this hypothesis due to the low prevalence (of less than 7%) of neonatal polycythemia found in Latin America and the Andean zone, which are areas also known to have high altitudes [1]. Along with high altitude, other maternal risk factors can contribute to the development of neonatal polycythemia, such as mothers that give birth to babies less than 34 weeks of age, diabetes, hypertension, maternal cyanotic heart disease, and smoking [3]. Neonatal factors can also play an equal role, such as newborns of perinatal asphyxia, twin pregnancies, intrauterine growth retardation, delayed cord clamping, chromosomal anomalies, congenital adrenal hyperplasia, and thyrotoxicosis [3]. As shown in a study conducted by Alsafadi et al. in 2014, small gestational age was suggested to be the most common risk factor for neonatal polycythemia followed by pregnancy-induced hypertension and infants of diabetic mothers [4].

A controversial question that is commonly encountered in this particular subject is the determination of whether polycythemia is always physiological or pathological [3]. It can be defined as a pathological process due to the increased risk of hyperviscosity and hypoperfusion which results in organ failure. Despite that, it can also be considered a benign condition in the first two hours of life, usually resolving on its own [3]. There is no need for further screening if the hematocrit decreases after two hours of age unless symptoms begin to appear due to the fatal consequences [3]. Most infants appear asymptomatic, and if symptoms appear two hours after birth, it is usually due to the fluid shifting resulting in a significantly elevated hematocrit [3]. The most common presenting symptoms are plethora, feeding problems, and hypoglycemia [3]. Other symptoms include irritability, jitteriness, tachycardia, hypotonia, and cyanosis [3].

This paper aims to identify variations, if any, in the prevalence of neonatal polycythemia in regions around the world and potentially deduce the basis of these variations. By identifying risk factors for the development of polycythemia, this literature review also further aims to ascertain if any of the identified risk factors would be preventable.

Materials and Methods

A literature review style was adopted to assess and consolidate the pre-existing literature. The search strategy utilized was aimed at retrieving articles related to the incidence, pathophysiology, presentation, etiology, risk factors, and treatments of neonatal polycythemia. A combination of controlled keywords was used, including, “Incidence,” “Pathophysiology,” “Treatment,” “Etiology,” “Polycythemia,” and “Neonates.” Articles were initially found using Google Scholar and Pub Med. The reference list of relevant articles was then screened for additional literature. Subsequent full-text screening and application of the inclusion and exclusion criteria finalized the articles reviewed in this study.

Articles that were included, had to focus on a factor of polycythemia incidence, pathophysiology, presentation, etiology, risk factors, and or treatments. The population had to be neonates defined as babies within the first 28 days of life. Only free, full-text articles were utilized. Articles could not be written in any other language other than English or could not have been written before the year 2014. After the application of the inclusion and exclusion criteria, a total of 21 articles were reviewed in this study.

Articles were compiled on a data sheet and reviewed by all investigators. Meetings over Zoom were utilized to plan, discuss, analyze, and review relevant data.

Table 1. Description of the global prevalence of neonatal polycythemia with an overview of risk factors from each country

Country	Overall Incidence	Additional Findings or Risk Factors
Iraq	21.47% [5]	Prevalence of polycythemia overall was 21.47% in 149 patients Most patients are polycythemic on days 1 and 2 of life 12% of polycythemic neonates had a birth weight of less than 2500 grams
	11.85% [6]	Overall prevalence of polycythemia was 11.85% among 500 neonates (53 neonates) 67.9% of polycythemic neonates were male but this association is not statistically significant 52.8% of polycythemia were identified at age more than 2 hours 18.9% of polycythemic neonates were premature (statistically significant) 13.2% of polycythemic neonates were under the tenth percentile for weight (statistically significant) 28.3% of polycythemic infants had an APGAR score of less than 3 in the first minute (statistically significant) 56.6% of polycythemic neonates were born via normal vaginal delivery 9.4% of polycythemic neonates were born to mothers who smoked tobacco during pregnancy Statistically significant symptoms associated with neonatal polycythemia included plethoric appearance, irritability, jaundice, jitteriness, and respiratory distress
	10.33% [3]	Prevalence of polycythemia overall was 10.33% Statistically significant differences existed between normal vaginal delivery (NVD) and Caesarean-Section 12.4% of NVD neonates were polycythemic 4.8% of Caesarean-Section neonates were polycythemic Statistically significant prevalence in premature neonates 9.5% of premature neonates were polycythemic Statistically significant prevalence in low-birth-weight neonates 22.5% of neonates weighing less than 2.5kg were polycythemic
	2.2% [7]	Prevalence of polycythemia overall was 2.2% among 2256 patients (50 patients identified) Most common presentation in polycythemic neonates was jaundice (29 out of 50 patients connoting 58%) Risk of jaundice and lethargy as presenting symptoms was statistically significant Risk factors for polycythemia identified included preterm, neonate of a diabetic mother, small for gestational age, and twin pregnancy Delivery via Caesarean Section was found to reduce the risk of development of polycythemia 28 out of 50 (56%) of patients required partial exchange transfusion
Saudi Arabia	0.4% [8]	Prevalence of polycythemia overall was 0.4% in 239 infants Prevalence of polycythemia in neonates with indirect hyperbilirubinemia was 2.6%
	14.5% [4]	Overall prevalence was 14.5% 21.7% of polycythemic neonates were preterm 2.9% of polycythemic neonates were post-term 57% of polycythemic neonates were male 57% of polycythemic neonates were born via Caesarean Section 34% of polycythemic neonates were small for gestational age 18% of polycythemic neonates were infants of diabetic mothers 18% of polycythemic neonates were born to mothers who had pregnancy-induced hypertension 46% of polycythemic neonates had jaundice, 24% had tachypnea, 14% had poor feeding, and 13% had lethargy 40% of polycythemic jaundiced infants had ABO or Rh incompatibility 28% of polycythemic neonates had hypoglycemia, 24% had hypocalcemia, 21% had thrombocytopenia 39% were asymptomatic and 17% were discovered incidentally 61% of interventions including increased total fluid intake were successful whereas 55% responded to conservative treatment
Iran	1.7% in jaundiced patients [9]	Prevalence of polycythemia in jaundiced neonates was 1.7%
	30.2% in neonates with confirmed sepsis [10]	13 out of 43 (30.2%) neonates with confirmed sepsis were found to be polycythemic 145 out of 299 (48.5%) neonates with no evidence of blood infections were found to be polycythemic
Pakistan	7.1% [11]	Overall prevalence of polycythemia was 7.1% Prevalence of polycythemia in the group with cord clamping done in less than 1 minute was 2.9% Prevalence of polycythemia in the group with cord clamping done after 1 minute was 11.2%
India	7% [12]	All identified polycythemic neonates were born to mothers with gestational diabetes mellitus

Country	Overall Incidence	Additional Findings or Risk Factors
Ecuador	12.77% [1]	Overall prevalence of polycythemia was 12.77% Most prevalent maternal co-morbidities included pre-eclampsia, anemia, and urinary tract infections 93% of mothers lived in areas 2000 meters above sea level; 88% of polycythemic neonates were born to mothers living in these regions 55.5% of polycythemic neonates were asymptomatic Significant associations existed between polycythemia and low birth weight and maternal diabetes; however, none of the diabetic mothers had infants with polycythemia
Kenya	5.3% [13]	Overall incidence of polycythemia in this study was 5.3% (11/260 participants) Incidence of polycythemia in the delayed cord clamping group was 8.6% Incidence of polycythemia in the umbilical cord milking group was 2.3%

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Global prevalence of neonatal polycythemia

Pathophysiology

Polycythemia and hyperviscosity syndrome are non-synonymous yet interlinked conditions. The Hagen-Poiseuille equation characterizes fluid flow in vessels, such as blood in arteries, with the equation R=8hL/π r^4 where R represents resistance to blood flow, h represents viscosity, L represents the length of the vessel, and r represents the radius of the vessel [14]. Blood viscosity can be increased if any element of whole blood increases in number, including but not limited to platelets, white blood cells, clotting factors, and plasma proteins including antibodies. An increase in red blood cell (RBC) mass for example, also increases blood viscosity, thereby causing an increase in total resistance to blood flow and impacting organ perfusion [1]. Increased RBC count is a compensatory mechanism for states of hypoxia or overgrowth in cases where nutrient and oxygen demand are increased. The fetus' physiological response to the normally hypoxic nature of the uterine environment is erythropoiesis. Hence, other factors must be evaluated and confirmed in a clinical diagnosis of neonatal polycythemia (Table 1).

Additional criteria to assess and confirm neonatal polycythemia include the measure of hematocrit (HCT) and hemoglobin values. The Mean±SD HCT in healthy at-term neonates is 61±7 percent and Mean±SD hemoglobin values are 19.3±2.2 g/dL in blood samples taken from capillaries [15]. To diagnose polycythemia, measured RBC mass must be greater than two standard deviations from the mean RBC mass taking into account the neonatal age and gestational size. To differentiate neonatal polycythemia from hyperviscosity, neonates must present with 65% or above HCT in blood samples taken from peripheral veins. Until 65% of HCT, the relationship between HCT and viscosity is almost linear, after which, viscosity increases in an almost exponential manner when compared to HCT [15]. Thus, minuscule changes in viscosity after this threshold presents disproportionately concerning impacts on organ perfusion and neonate mortality. Although a high HCT value can be suggestive of polycythemia, confounding factors may play a role in the accuracy of this value in determining disease impact.

Neonates with mild forms of increased RBCs generally present without symptoms. The asymptomatic presentation of mild polycythemia is of multifactorial etiology. For example, the site from which the blood sample was taken can affect the RBC count. The rouleaux formation of blood cells results in almost a 5%-25% increase in HCT in capillary blood when compared to venous samples. Secondly, the time at which samples were taken can also affect this diagnosis. In the first few hours of life, the newborn is going through many physiological changes, one of them being HCT. Hematocrit tends to peak around the second hour of life. Measurements taken from newborns with an HCT of ≥65% demonstrated variation in HCT values when compared with different sites; umbilical veins, capillaries, and peripheral veins showed mean values of 71%, 75%, and 63%, respectively [15]. In both cases, though a clinical diagnosis of polycythemia can be made, the infant is asymptomatic. Symptomatic infants, however, present an immediate and fatal concern.

Organ systems can be affected due to hyperviscosity, sub-ideal organ perfusion, hypoglycemia, and hypocalcemia. Increased erythropoiesis can cause microthrombi in the microvasculature, affecting the central nervous system (CNS), gastrointestinal tract, renal vasculature, and cardiopulmonary systems. Increased RBC count also increases metabolic demand on the body, decreasing levels of plasma glucose, and therefore, disturbing glucose uptake in the CNS. It has been demonstrated that in polycythemia/hyperviscosity syndrome, the major indicator of neurological damage and prognosis is

Table 2. Categorization of risk factors that have been implicated in causing neonatal polycythemia

Variables	Pescription
Passive: Transfusion	Delayed clamping of the umbilical cord Intrapartum hypoxia Acute fetal distress Holding the baby under introitus Twin-twin transfusion Maternal-fetal transfusion
Active: Erythrocyte Synthesis	Placental: Preeclampsia Hypertensive or vascular disorders Maternal: Cardiac or pulmonary disorders Drugs (beta-blockers) High altitude Smoking Post-term delivery Maternal diabetes Fetal: Large for gestational age Small for gestational age Beckwith-Wiedemann syndrome Endocrine disorders Chromosomal abnormalities

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hyperviscosity. Additionally, increased cell turnover due to the short lifespan of fetal erythrocytes can cause hyperbilirubinemia in the neonate [16].

Risk factors

In cases of a neonatal polycythemia diagnosis, several other extraneous factors must be considered before treatment is started. Common issues seen in neonates are trouble feeding, vomiting, and diarrhea which can lead to dehydration and other metabolic abnormalities. While not always pathological, they can cause a falsely elevated HCT [1] due to loss of plasma volume resulting in hypovolemic polycythemia. As mentioned previously, the timing and location of the blood samples should also be taken into consideration. After ruling out falsely elevated blood counts, there are several risk factors and mechanisms associated with the pathogenesis of neonatal polycythemia.

Discussion

Although the majority of cases of neonatal polycythemia are relatively benign, it is important to assess the severity of the condition of the neonate as well as the precipitating factors and identify how common they are and if possible, treatable and preventable (Table 2). Delayed cord clamping, for example, increases the amount of time that placental blood has to transfuse into the newborn resulting in an increased RBC mass. A delay of ≥60 seconds in cord clamping has been associated with decreased hospital mortality, a decreased incidence of low APGAR scores, and a lower proportion of blood transfusions in preterm infants. For term infants, a delay of 30-60s, though an upper limit, has not been established [17]. For those reasons, though delayed cord clamping can result in polycythemia and hyperbilirubinemia, it is still a recommended practice [17, 18]. Holding the baby under the level of the introitus applies the same mechanism of passive erythrocyte transfusion. Intrapartum hypoxia and acute fetal distress present with transcapillary leakage of plasma, which increases blood flow from the placenta into the fetus. As delayed cord clamping is operator-dependent and may cause a transient elevation in RBC mass, the benefits outweigh the risks and therefore, would not be an imminent risk factor to modify.

Twin-Twin transfusion (TTT) is also a passive mechanism that affects about 9% of monochorionic twins. TTT occurs when a paucity of artery-to-artery or arteriovenous anastomoses are present between twins sharing one placenta of which complications include twin anemia polycythemia sequence (TAPS). TAPS occurs when one twin presents with plethoric blood (polycythemia) and the other twin presents with insufficient blood (anemia). TAPS occurs spontaneously in 2%-5% of TTT cases, and 3%-16% of TTT cases treated with laser ablation [19]. TTT is still a passive mechanism of erythrocyte transfusion, however, it is pathological and seldom present asymptomatically. The incidence of mortality in expectantly man-

aged infants was 43.9% (95% CI 5.9-87.7), treatment with laser presented with a 47.3% (95% CI 21.4-70.0) mortality rate, and treatment with amino reduction presented with 28.5% incidence of death [20]. TTT is not a preventable condition; however, the risk for this condition is severely increased in multiple gestation pregnancies. Recipients of TTT were more prone to chronic polycythemia. It would therefore be advisable that in pregnancies associated with TTTs, preparation for a polycythemic neonate be made and necessary precautions should be undertaken before delivery.

Active mechanisms of polycythemia are sequences that cause erythropoiesis, thereby increasing RBC mass. They can be further classified based on their causes: Placental, maternal, or fetal. Placental distress can result in hypoxia of the neonate, resulting in increased RBC production and the diagnosis of polycythemia. Common reasons include preeclampsia and hypertension or vascular disorders. In all cases, insufficient blood is transfused through the placenta, resulting in increased erythropoietin (EPO) production and increased RBC mass [21].

Maternal factors that increase hypoxia in the intrauterine environment also induce a compensatory increase in EPO production. Reversible factors include smoking habits, beta-blockers, and high-altitude environments, and irreversible factors include maternal cardiac or pulmonary issues, intrauterine growth restriction (IUGR), and post-term deliveries. Maternal factors such as these generally cause normovolemic polycythemia; in cases where plasma volume stays the same, but RBC mass increases [16]. A majority of polycythemia cases in newborns (22%-29%) can be attributed to maternal diabetes. Macrosomia and hypoglycemia in these babies cause an increased need for oxygen and nutrients, and so, increase EPO production [16].

Fetal conditions can also increase the risk of developing neonatal polycythemia. Conditions such as Patau syndrome (trisomy 13), Edward's syndrome (trisomy 18), Down's syndrome (trisomy 21), and Beckwith-Wiedemann syndrome have all been linked with an increased incidence of neonatal polycythemia. An increased incidence of polycythemia has also been correlated with babies suffering from congenital hypothyroidism, congenital adrenal hyperplasia, and neonatal thyrotoxicosis. An increase in fetal gestational mass also increases the fetus' need for nutrients and oxygen, thereby increasing erythropoiesis [15, 16].

Conclusion

Polycythemia in neonates is a relatively common occurrence with mild presentations and a multifactorial etiology. The development can be traced to several risk factors which impact both the incidence and the severity of presentation. From this study, it can be concluded that altitude, maternal and fetal causes of hypoxia, operator-dependent practices, and various other risk factors all affect the HCT and RBC mass in neonates. Mild presentations have not warranted much investigation into treatment; however, slight increases in HCT levels present exponentially increasing mortality rates. Additionally, TAPS is a concerning and familiar outcome of monochromatic twins. Much literature has been dedicated to the description of neonatal polycythemia; however, future curiosities should be geared toward treatment and prevention through large cohort and case-control studies.

Ethical Considerations

Compliance with ethical guidelines

All ethical principles were considered in this article. The participants were informed of the purpose of the research and its implementation stages. They were also assured about the confidentiality of their information and were free to leave the study whenever they wished, and if desired, the research results would be available to them.

Funding

This research did not receive any grant from funding agencies in the public, commercial, or non-profit sectors.

Authors' contributions

Study concept and design: Al-Zahiri and Nair; Acquisition of data: Al-Zahiri, Nair, and Kumar; Analysis and interpretation of data: Al-Zahiri, Nair, and Kumar; Drafting of the manuscript: Al-Zahiri, Nair, and Kumar; Critical revision of the manuscript for important intellectual content: Al-Zahiri and Kumar; Administrative, technical, and material support: Nair and Watts; Study Supervision: Watts.

Conflicts of interest

The authors declare no conflict of interest.

References

1. Barros TM, Gavilanes ER, Barros JM. Polycythemia in the newborn: Prevalence and associated factors. Rev Cubana Pediatr. 2021; 1:1-6. [Link]

2. Bashir BA, Othman SA. Neonatal polycythemia. Sudan J Paediatr. 2019; 19(2):81. [DOI:10.24911/SJP.106-1566075225] [PMID] [PMCID]

3. Ali AF, Hasan KH. Risk Factors and Prevalence of Neonatal Polycythemia in Duhok Maternity Hospital: A Cross-Section Study. Health Sci J. 2020; 14(6):1-14. [Link]

4. Alsafadi TR, Hashmi SM, Youssef HA, Suliman AK, Haifa'A MA, Albaloushi MH. Polycythemia in neonatal intensive care unit, risk factors, symptoms, pattern, and management controversy. J Clin Neonatol. 2014; 3(2):93. [DOI:10.4103/2249-4847.134683] [PMID] [PMCID]

5. Mostefa AM. A study of prevalence and risk factors of polycythemia in neonatal nursery in Duhok. Isra Med J. 2015; 10. [Link]

6. Chalabi DA, Zangana KO. Neonatal polycythemia, Presentations and associations: A case control study. JKBMS. 2018; 4(1):61-72. [Link]

7. Abbas SS, Fayadh HF. Neonatal polycythemia: Risk factors, clinical manifestation and treatment applied. Iraq Postgrad Med J. 2013; 12:390-5. [Link]

8. Alkhotani A, Eldin EE, Zaghloul A, Mujahid S. Evaluation of neonatal jaundice in the Makkah region. Sci Rep. 2014; 4(1):1-6. [DOI:10.1038/srep04802] [PMID] [PMCID]

9. Boskabadi H, Zakerihamidi M, Khodashenas E. A Study of Epidemiology and Predisposing Factors of Newborn Jaundice in 3200 Infants. Pak Paediatr J. 2020; 44(4):345-50. [Link]

10. Salahi M, Moghadam AG, Mousavizadeh A, Marashifard M, Taghavi SJ, Rezanejad M, et al. Neonatal sepsis in southwest of Iran; prevalence of microbial pathogens, risk factors, clinical manifestations and laboratory findings. [Published Online] [Link]

11. Anwar NK. Correlation of early and late cord clamping time with hematological variables: An observation study focusing on the neonatal outcomes. SOJ Surg: Open Access. 2018. [Link]

12. Dhillon HS, Kushvanth KN, Dhillon GK, Sasidharan S, Singh V. A prospective case-control study to compare the clinical outcomes and metabolic profile in neonates born to diabetic mothers in a tertiary care armed forces hospital, India. J Nepal Paediatr Soc. 2021; 41(2):127-33. [DOI:10.3126/jnps.v41i2.30731]

13. Sura M, Osoti A, Gachuno O, Musoke R, Kagema F, Gwako G, et al. Effect of umbilical cord milking versus delayed cord clamping on preterm neonates in Kenya: A randomized controlled trial. PloS One. 2021; 26(1):e0246109. [DOI:10.1371/journal.pone.0246109] [PMID] [PMCID]

14. Yadav SS, Sikarwar BS, Ranjan P, Janardhanan R. Microfluidic system for screening disease based on physical properties of blood. BioImpacts: BI. 2020; 10(3):141. [DOI:10.34172/bi.2020.18] [PMID] [PMCID]

15. Garcia-Prats JA, Weisman LE. Neonatal polycythemia. UpToDate. 2019. [Link]

16. Sarıcı U, Ozcan M, Altun D. Neonatal polycythemia: A review. CMRCR. 2016:50-8. [DOI:10.23937/2378-3656/1410142]

17. Liyanage SK, Ninan K, McDonald SD. Guidelines on deferred cord clamping and cord milking: A systematic review. Pediatrics. 2020; 146(5). [DOI:10.1542/peds.2020-1429] [PMID]

18. Fogarty M, Osborn DA, Askie L, Seidler AL, Hunter K, Lui K, et al. Delayed vs early umbilical cord clamping for preterm infants: A systematic review and meta-analysis. Am J Obstet Gynecol. 2018; 218(1):1-8. [DOI:10.1016/j.ajog.2017.10.231] [PMID]

19. Tollenaar LS, Lopriore E, Middeldorp JM, Haak MC, Klumper FJ, Oepkes D, et al. Improved prediction of twin anemia-polycythemia sequence by delta middle cerebral artery peak systolic velocity: New antenatal classification system. UOG. 2019; 53(6):788-93. [DOI:10.1002/uog.20096] [PMID] [PMCID]

20. D'Antonio F, Benlioglu C, Sileo FG, Thilaganathan B, Papageorghiou A, Bhide A, et al. Perinatal outcomes of twin pregnancies affected by early twin-twin transfusion syndrome: A systematic review and meta-analysis. Acta Obstet Gynecol Scand. 2020; 99(9):1121-34. [DOI:10.1111/aogs.13840] [PMID]

21. Kalagiri RR, Choudhury S, Carder T, Govande V, Beeram MR, Uddin MN. Neonatal thrombocytopenia as a consequence of maternal preeclampsia. Am J Perinatol. 2016; 6(01):e42-7. [DOI:10.1055/s-0035-1565923] [PMID] [PMCID]

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