Neonatal Polycythemia, Presentations and Associations: A Case Control Study

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Abstract

Background and objectives: Neonatal polycythemia is characterized by a venous hematocrit more than 65%. Incidence of neonatal polycythemia ranges from 0.4-5%, most affected infants have no clinical signs. Neonates may present by acrocyanosis, plethoric، cyanosis, respiratory distress, poor feeding or apnea. The aim of the study was to find out the prevalence of neonatal polycythemia, identify the risks and recognize most important clinical presentations. **Methods:** A case-control study conducted at the maternity hospital in Erbil city from 1st February 2013 to 1st May 2013. The study enrolled 500 neonates, among those neonates fifty-three of them revealed central polycythemia. The newborns were considered to be polycythemic if the venous hematocrit was greater than 65%. **Results:** In this study, 53(11.85%) cases were polycythemic, 30 cases were male 36 (67.9%) with male: female ratio was 2.1:1. Polycythemic of less than 2 hours of age were 25 (47.2%) cases, 10 cases (18.9%) were premature. APGAR score in the first minute was less than three in 15 cases (28.3%) and this was statistically significant. Plethora was seen in seven cases, 5 (62.5%) cases in group one and 2 (15.6%) cases in group two. Severity of polycythemia was significantly related to maternal hematocrit. **Conclusions:** Males were affected more than females. Jaundice was the main presentation followed by plethora, irritability, respiratory distress and poor feeding.

Keywords: olycythemia; Hematocrit; Neonates.

Introduction

Neonatal polycythemia is characterized by a venous hematocrit that greatly exceeds normal values for gestational and postnatal age[1]. The most widely accepted definition is a venous hematocrit of more than 65%[2]. A newborn is also regarded as polycythemic if capillary hematocrit is 70% or greater. Hematocrit at term will rise from cord blood levels to a peak at 2 hours of age and then drop slowly over the next 12 to 18 hours[3].

The incidence of neonatal polycythemia ranges from 0.4-5% of total newborn populations[4-6]. Polycythemia of the newborns may be the consequence of compensatory mechanism for intrauterine hypoxia, as well as it may occur secondary to fetal transfusions or have fetal origin. Polycythemia secondary to fetal transfusions may occur due to delayed cord clamping after birth, acute fetal distress, twin-to-twin transfusion syndrome, maternal- fetal transfusion, perinatal asphyxia, holding the baby below the level of introitus[7- 9].

Most affected infants have no clinical signs of the condition[10]. Symptoms, when present, often begin by two hours after birth, after fluid shifts have occurred and the hematocrit is highest, onset may be delayed to the second or third day[11].

Cardiorespiratory signs such as acrocyanosis and sluggish peripheral perfusion are common; affecting 67 percent of patients in one study, infants with polycythemia may appear plethoric. Cyanosis occurs in as many as 17 percent [12, 13]. Respiratory symptoms, including tachypnea and distress, develop in 10 to 15 percent of patients [12]. Infants with polycythemia may develop heart murmurs, heart failure, and increased pulmonary vascular resistance, which may lead to persistent pulmonary hypertension of the newborn[2,4]. Neurologic symptoms (e.g., irritability, abnormal cry, jitteriness, poor feeding, lethargy, hypotonia, and apnea) occur in approximately 60 percent of affected patients [10-12]. The cause of these symptoms is uncertain but may be related to metabolic disorders associated with polycythemia or to reduced cerebral blood flow. Gastrointestinal symptoms, which occur in as many as 20 percent of affected patients, include abdominal distention and poor feeding, although the latter is sometimes due to central nervous system abnormalities[12]. Necrotizing enterocolitis is sometimes associated. Hypoglycemia is a common metabolic problem in affected patients. It occurs in 14 to 40 percent of cases[12, 14]. At least one-third of infants with polycythemia develop hyperbilirubinemia[3]. Thrombocytopenia occurs in some infants with polycythemia[15]. The aim of the study was to find out the prevalence of neonatal polycythemia, identify the risk and to recognize the most important clinical presentations

Patients and Methods

This is a case-control study, conducted at Erbil in maternity hospital, capital city of Kurdistan region.. The samples have been taken from the newborns babies regardless of the mode of delivery from 1st February 2013 to 1st May 2013.

The study enrolled 500 neonates irrespective of the gestational age and birth weight. Among these 500 neonates ninety-nine of them had peripheral polycythemia which undergone central venus sampling from antecubital area to confirm polycythemia and to exclude local causes, fifty-three of them revealed central polycythemia. One hundred forty cases taken as control in this study, they included neonates delivered in the same place without clinical

or laboratory findings of polycythemia and were clear from any neonatal problems. Gestational age determined from mother's menstrual history and confirmed by modified Ballard's scoring. Small for gestational age (SGA) is a birth weight that is below the 10th percentile for gestational age and large for gestational age (LGA) is birth weight above 90th percentile for gestational age[16]. Preterm birth refers to a birth that occurs at or before 37 weeks of gestation, a term birth is defined as a birth occurring between 38 and 42 weeks, and a post-term birth is defined as a birth occurring after 42 week[17]. Apgar score was taken for each delivered neonate in both groups in first and fifth minutes and documented in each case sheet of delivered neonate. Growth parameters including weight, length and occipitofrontal circumference had been taken using scale for measuring weight and tape measure for measuring length and occipitofrontal circumference. Capillary hematocrit determined on blood samples obtained by pricking the neonate's pre warmed heel with med point blood lancet in the first twelve hours of life. All capillary hematocrits were determined in duplicate in 17 mm long and 1 mm wide (internal diameter) capillary tubes spun at 10,000 RPM for 5 minutes, in a micro hematocrit centrifuge (H-1200F) and the hematocrit read using a reading device (REMI reading device). Plasma separates and the packed cell volume is measured to give the hematocrit. Most of the reported data on polycythemia is on centrifuged hematocrits. In cases were the capillary hematocrit was 70% or greater, a central venous sample from antecubital area was taken to confirm polycythemia and to exclude possible local causes, if the venous hematocrit was greater than 65%. Investigations like total serum bilirubin and blood sugar have been done for all polycythemic babies. Criteria of exclusion were cord milking, Holding the baby below the level of mother's introitus and newborn of mothers who had received blood before delivery. Written and oral consent was taken from all mothers guardians. Chi square test of association was used to compare between proportions and when the expected count of > 20% of the cells of the table was <5 fishers exact test was used. Independent t test used to compare between means. A p value of Ś0.05 was considered significant.

Results

Among the 500 newborns, 53(11.85%) were polycythemic and 447 were non-polycythemic. From 53 polycythemic neonates, 30 cases were male 36 (67.9%) and 17 (32.1%) cases were female, with male: female ratio equal to 2.1:1, while in the control group, 79 (56.4%) cases were male and 61 (43.6%) cases were female, being male gender increases the risk of polycythemia by (0.6) times but this factor was statistically not significant. Age of neonates less than 2 hours that showed center polycythemia were 25 (47.2%) cases while those showed to be polycythemic after 2 hours of age were 28 (52.8%) cases, the values were not significant statistically p value 0.59 but OR was 0.82. Regarding gestational age; 10 (18.9%) cases of premature neonates showed to be polycythemic while no premature neonates in control group, and this was statistically highly significant with p value <0.001with OR 4.25. Anthropoemetric measures in both group were significant, number of cases that lies below 10th centile in weight among were 7 (13.2%) cases while in control group were 4 (2.87%) cases, p value was 0.022. Apgar score also showed significant values, Apgar score of less than three in the first minute was present in 15(28.3%) cases while in control group score was present in 4(21.1%) cases, p value was less than 0.001, as shown in Table 1.

Table (1): Comparison between neonate with central polycythemia and control group regarding certain variables of the newborn

Factors	variable	Control *(n = 140 cases)*	Central polycythemia *(n = 53 cases)*	P value	OR (CI)
Age	<2hr	60(42.9%)	25 (47.2%)	0.590	0.84(0.44-1.58)
	>2hr	80(57.1%)	28 (52.8%)		
Sex	Male	79 (56.4%)	36 (67.9%)	0.146	0.61(0.31-1.19)
	Female	61 (43.6%)	17 (32.1%)		
Gestational age	Preterm	0 (0%)	10 (18.9%)	<0.001	4.25(3.27 -5.52)
	Term	140 (100%)	43 (81.1%)		
Weight in centile	<10th	4 (2.87%)	7 (13.2%)	0.022	
	normal	125(89.3%)	42(79.2%)		
	>90t^{h}	11(7.9%)	4(7.5%)		
Length in centile	<10th	3(2.1%)	6(11.3%)	0.004	
	normal	134(95.7%)	43(81.1%)		
	>90th	3(2.1%)	4(7.5%)		
OFC in centile	<10th	1(0.7%)	6(11.3%)	0.001	
	normal	135(96.4%)	44(83.0%)		
	>90th	4(2.9%)	3(5.7%)		
Apgar score 1 min	≤3	4(2.9%)	15(28.3%)	<0.001	0.07(0.02-0.23)
	>3	136(97.1%)	38(71.7%)		
Apgar score 5 min	≤3	0(0%)	3(5.7%)	0.020	3.800 (2.99-4.82)
	>3	140(100%)	50(94.3%)		

Maternal risk factors were pattern of delivery; in which normal vaginal delivery were more in both groups, 30 cases (56.6%) in polycythemic group while 101 (72.1%) in control group which was statistically significant (p value was 0.039). Majority of pregnancies were single, parity of mothers was also not significant between both groups (p value was 0.24) Significant important factors were clumping after three minutes of delivery on polycythemic group was 29(54.7%) cases while control was 119 (85%), more than three minutes was 24(45.3%) cases, (p value was less than 0.001 and OR was 4.69). Maternal smoking was present in 5(9.4) cases in polycythemic group while no case was reported in control group, (p value was 0.001 and OR 3.91) as shown in Table 2.

Table (2): Comparison between neonate with central polycythemia and control group regarding certain obstetrical variabls.

Factors	Variable	Control (n = 140)	Central polycythemia (n = 53)	P value	OR (CI)
Mode of delivery	CS	39 (27.9%)	23 (43.4%)	0.039	0.504 (0.26 -0.97)
	VD	101 (72.1%)	30 (56.6%)		
Type of pregnancy	single	137(97.9%	47(88.7%)	0.007	5.83 (1.40-24.23)
	multiple	3(2.1%	6(11.3%)		
Parity	<3	66(47.1%)	31(58.5%)	0.24	
	3-5	49(35.0%)	17(32.1%)		
	>5	25(17.9%)	5(9.4%)		
Time of cord clumping	<3min	119(85.0%)	29(54.7%)	<0.001	4.69 (2.3 -9.5)
	>3min	21(15.0%)	24(45.3%)		
Maternal Smoking*	Yes	0 (0%)	5(9.4%)	0.001	3.917 (3.06-5.00)
	No	140(100%)	48(90.6%)		

Mean of all anthropometric measures in cases were less than control group but all the values were close to each other and didn't showed any statistical significance. Mean oxygen saturation in polycythemic group were 95.57(± 2.8) while in control group was 94.74(± 2.01) the difference between both groups were not significant statistically. Significant values were mean maternal Hematocrit (PCV); it was 72.96(± 8.19), it was much higher in comparison to control group 68.16(± 8.05), p value was highly significant. The mean PCV of the cases were 75.25(3.14) while PCV values in control group was 57.23(5.36) the comparison between both groups was highly significant, p value was less than 0.001. All data are shown in Table 3.

Table (3): T test comparison between means of polycythemic and control group

Variable	Control *(n = 140)*	Central polycythemia *(n = 53)*	P value
Weight (kg)	3.45 (0.56)	3.16(0.99)	.011
Length (cm)	49.69(2.06)	48.64(3.48)	.011
OFC (cm)	34.96(0.85)	33.79(2.54)	<0.001
Oxygen saturation (%)	94.74(2.01)	95.57(2.80)	.024
Maternal PCV (%)	68.16(8.05)	72.96(8.19)	<0.001
PCV (%)	57.23(5.36)	75.25 (3.14)	<0.001

According to the severity of polycythemia cases were divided into two groups, maternal PCV was higher in group two 78.65(9.65) in comparison to group one 71.96(±7.59), (p value was 0.033). Mean blood sugar in group one was 68.25(mg/dl) (±29.3) while in group two was 50.51(mg / dl) (±15.64) (p value was 0.014). Other data are shown in Table 4

Table (4): Severity of polycythemia in relation to certain variables

Variable	PCV ≥ 70 group one *(n =8)* mean (SD)	PCV <70 group two *(n= 45)* mean (SD)	P value
Weight (cm)	3.07 (0.82)	3.17 (1.02)	0.795
Length (cm)	48.88 (3.31)	48.60 (3.55)	0.839
OFC (cm)	33.75 (2.05)	33.80 (2.64)	0.960
Maternal PCV (%)	78.63 (9.65)	71.96 (7.59)	0.033
blood sugar (mg /dl)	68.25 (29.30)	50.51 (15.64)	0.014
Platelet count (/mm^3)	334.75 (170.34)	406.71 (119.50)	0.148
Oxygen saturation (%)	95.88 (2.99)	95.51 (2.80)	0.739

*Values in mean (SD)

Presentations that seen in polycythemic neonates were classified in to two groups according to severity, group one when PCV is equal or more than 70 while group two when PCV is less than 70. Plethora was seen in seven cases out of 53, 5 (62.5%) cases in group one and 2 (15.6%) cases in group two; (p value was 0.001 and OR was 10.95). Respiratory distress also occurred in seven cases, 4 (8.89%) cases were in group two and 3 (37.5%) cases in group one, (p value was also significant.0.027, OR 3.9). Seizure occurred in one case in group two and no case reported in group one. Neonatal jaundice was present in 5 cases in group one and 8 cases in group two, (p value was 0.037 and OR was 4.6), and other presentations are shown in Table 5

Table (5): Clinical presentation seen in neonates according to severity of polycythemia

Variable that presents	≥ 70 group one *(n =8)*	<70 Group two *(n= 45)*	P value	OR (CI)
Plethoric	5 (62.5%)	2 (15.6%)	0.001	10.95 (3.33 -36.001.)
Irritability	3 (37.5%)	4 (8.89%)	0.028	3.9 (0.34- 8.78)
Jaundice	5 (62.3%)	8(20%)	0.037	4.6 (1.33-33.25)
Jitteriness	4 (50%)	7 (15.6%)	0.028	3.41 (0.51 -22.87)
Seizure	0 (0%)	1 (2.2%)	1.0	1.18 (1.05 -1.32)
Poor feeding	0 (0%)	5 (11.1%)	1.0	1.20 (1.05-1.36)
Respiratory distress	3 (37.5%)	4 (8.89%)	0.027	3.9 (1.1 -12.9)

Discussion

With regards to neonatal central polycythaemia, this study showed important risk factors including preterm delivery in 18.8%, small for gestational age 13.2%, neonates with low APGAR scores in one and five minutes (28.3 and 50.7% respectively). In a study published by Abbas[18], it is found that 36% with small for gestational age and 18% developed polycythemia. Wexner[19] showed that 36% with small for gestational age and 13.8% developed polycythemia. Other studies[6] showed incidence of polycythemia in term small for gestational age as 15% compared to 2% of term babies appropriate for gestational age. Another study showed higher risk in preterm neonates, neonates of diabetic mother (20%), and small for gestational age (28%) 20 as polycythemia may be the consequence of compensatory mechanism for intrauterine hypoxia, perinatal asphyxia which neonates in these situations are very prone to it[7,8,9,20].

Normal vaginal delivery was seen in control group 72.1% in comparison to 56.6% in cases OR was 0.5; this means that normal vaginal delivery decreases the incidence by half fold[18]. Other data showed neonatal polycythaemia can be reduced by two and half folds[14] as vaginal delivery has potent uterine contractions that prevents polycythemia if clumping not delayed[21].In multiple pregnancies there's possibility of fetal to fetal transfusion so increases the risk of polycythemia by five folds as shown this study.

Risk of polycythemia in multi pregnancies was 11%, other studies showed 12% and 15%[8,18].

Onset of clumping has a big role in developing polycythemia; as our study showed an increased the risk by 4.6 folds; this agreed with the fact that delay clumping increases the risk of polycythemia. Maternal smoking increased risk of polycythemia by 3.9 that it is due to increasing hypoxia, this finding agreed with[8,9,22] which is explained by the increase in erythropoietin level and increases RBC productions).

As this study showed that difference in mean PCV of the polycythemia neonates to control group is highly significant ($P < 0.001$) and maternal PCV was also highly significant in contrast to control group, as the PCV of the pregnant mothers highly reflects that of neonates and affects PCV of neonates proportionally[9].

Investigations done were blood sugar level, it was significantly lower in polycythemic group as glucose consumption is more in polycythemic neonates, while platelet count was higher, it reflects more blood transfusion from mother to the baby or from twin to twin or reflects more synthesis due to hypoxia[12].

Concerning clinical presentations; jaundice 13(26.4%), jitteriness 11(20.7%), plethora 7(13.2%) and respiratory distress 7(13.2%), the least recorded presentation was convulsion that occurred in one case. Published data showed occurrence of neonatal jaundice in 58%, lethargy in 30%, respiratory distress in 26%, and hypoglycemia in 26%, while feeding problems, bitterness and cyanosis were not recorded[21,22]. Al Safadi TR et al[12] in his study found jaundice in 33.5%, respiratory distress in 6.6% and hypoglycemia in 13%of cases, these all data agree on the major clinical presentation and the variation in recorded cases probably due to severity of polycythemia and associated risk factors.

Conclusions

Our study showed that male babies were affected more than females. Jaundice was the main presentation followed by plethora, irritability, respiratory distress, poor feeding and least presentation was convulsion. According to our study the risk was higher among preterm babies and when apgar score is three or less in one and 5 minutes, furthermore this study showed higher association of polycythemia with maternal smoking delaying cord clamping more than 3 minutes and multiple pregnancy,

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