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Original Article

Paediatrics Section

A Study on Incidence, Pattern of Clinical Features, Laboratory Abnormalities and Outcome of Neonatal Polycythaemia in a Tertiary Care Hospital, Odisha, India

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ABSTRACT

Introduction: Neonatal polycythaemia is a commonly encountered morbidity and mortality among neonates admitted to neonatal care units and sick newborn care units. Most affected infants have no clinical symptoms and signs, but neonates may present with lethargy, poor feeding, plethora, cyanosis and jaundice within 12-72 hrs.

Aim: To find out the incidence and clinical manifestations of neonatal polycythaemia along with detection of disease by laboratory abnormalities.

Materials and Methods: This was a hospital-based, prospective, observational study conducted in the Neonatal Care Unit of Sriram Chandra Bhanja Medical College, Eastern Odisha, India, in 1760 neonates, from October 2018 to September 2020. All neonates admitted through Outdoor and Emergency were included in this study irrespective of gestation, birth weight, maturity and mode of delivery with haematocrit >65% at 12 hours of life. These polycythaemic babies were further categorised on the basis of maturity, gestational age, birth weight, gender and the clinical features, laboratory abnormalities were noted, Partial Exchange Transfusion (PET) when required was done through central route, the umbilical venous catheter was used for withdrawing blood while same amount of normal saline was replaced through a peripheral vein, and in asymptomatic cases additional fluid of 20 mL/kg was added to the daily fluid requirements either through enteral or parenteral route and outcomes were noted. Short-term outcome at 48 hours was measured by decreasing haematocrit with improvement of signs and symptoms. Chi-square test was employed to analyse the collected data using Statistical Package for the Social Sciences (SPSS) software version 20.0. The p-value <0.05 was considered statistically significant.

Results: Out of 1760 newborns enrolled, (n=75) were polycythaemic. The incidence of polycythaemia was 4.26%, which was significantly higher among Small for Gestational Age (SGA) compared to Large for Gestational Age (LGA) neonates (p-value=0.0214). Clinical features in decreasing order were lethargy (66.6%), poor feeding (66.6%), Plethora (53.3%), cyanosis (40%) and jaundice (33.3%). Main laboratory abnormalities were hypoglycaemia (36%), hyperbilirubinaemia (28%), thrombocytopenia (22.66%) and hypocalcaemia (13.3%). Out of 75 polycythaemic neonates, n=17 (22.67%) underwent PET and rest 58 (77.33%) neonates were treated with extra fluid of 20 mL/kg/day.

Conclusion: Study showed that lethargy and poor feeding were the main presentation and hypoglycaemia as the major laboratory abnormality. The incidence of polycythaemia was high among SGA neonates and the response to partial exchange transfusion as well as extra fluid was good which was characterised by decreasing haematocrit values with improvement of signs and symptoms.

Keywords: Haematocrit, Hyperviscosity, Microcirculatory hypoperfusion, Multiorgan dysfunction, Partial exchange transfusion

INTRODUCTION

Polycythaemia otherwise known as erythrocythaemia is frequently seen in newborns and is characterised by inappropriate increase of red cell mass in circulation. Neonatal polycythaemia is a normal adaptation of foetus to hypoxaemia instead of a true defect of haematopoietic system. Rising haematocrit is detrimental leading to increased viscosity, microcirculatory hypoperfusion and multisystem organ dysfunction [1-3].

Polycythaemia is defined as haematocrit greater than 65% or haemoglobin more than 22.0 gm/dL [4,5]. Based on these values the incidence of neonatal polycythaemia has been reported to be 0.4%-5% [6]. At term haematocrit rises from cord blood levels to peak at 2 hours of life and then slowly drops over next 12-18 hours [7,8]. Polycythaemia may result from increased foetal erythropoiesis in response to intrauterine hypoxia due to placental insufficiency or secondary to foetal transfusions. Intrauterine hypoxia may be seen in maternal preeclampsia and hypertension, maternal diabetes (42% of Infants of Diabetic Mothers [IDM] have polycythaemia), genetic inheritance (trisomy 21, 13, 18), Beckweith weidemann syndrome, congenital hypothyroidism and congenital adrenal hyperplasia. Risk is 12.6 times greater in Appropriate for Gestational Age (AGA) babies born to mothers with hypertension compared to babies born to normotensive mothers [9]. Secondary foetal transfusions usually caused by delayed cord clamping, cord stripping, holding the baby below the level of introitus, twin-twin transfusions, and maternal to foetal transfusions may lead to polycythaemia [10-11].

In India, low birth weight babies represent 30% of all live births each year, more than half of these babies are born at term [12]. It is thus obvious that polycythaemia could be a real problem existing in India and babies need to be actively screened for this condition.

Treatment of newborns having polycythaemia is relatively simple but controversial. It is well accepted to treat symptomatic newborns with polycythaemia whereas, asymptomatic neonates requiring PET is not universally accepted because of lack of controlled date [13]. This study aimed to find out the incidence, pattern of clinical features, laboratory abnormalities and outcome of neonatal polycythaemia in a tertiary care hospital, as well as to study the management outcomes of both symptomatic and asymptomatic newborns.

MATERIALS AND METHODS

This was a hospital-based prospective observational study, carried out at Sriram Chandra Bhanja Medical College, Eastern Odisha, India, from October 2018 to September 2020. Institutional Ethical Committee clearance was taken (IEC Application. No:- 455). Samples were collected from all the newborn babies admitted through Outpatient and Emergency Department (irrespective of gestational age, birth weight and mode of delivery). A total of 1760 neonates were enrolled in the study.

Inclusion criteria: Neonates with haematocrit >65% within 12 hours of birth during the study period were included in the study.

Exclusion criteria: Newborn babies with sepsis, bleeding disorder, syndromic babies, congenital heart disease, babies who expired before collection of blood samples were excluded from the study.

Growth parameters including weight, length, occipitofrontal circumference were taken using digital weighing scale by MCP (Medicare products inc), infantometer by MCP, (Medicare products inc) and non stretchable plastic tape respectively.

Birth weight was categorised as:

- Very low birth weight (VLBW: <1500 gms),
- Low birth weight (LBW: 1500-2500 gms) and
- Normal birth weight (>2500 gms)

Small for Gestational Age (SGA) was taken as <10th percentile of gestational age and Large for Gestational age (LGA) as >90th percentile of gestational age [14].

As per International classification of diseases (ICD) by WHO, duly approved and adapted by the task force of National Neonatology Forum of India, neonates were classified as [14]:

- Preterm babies: <37 weeks of gestation,
- Term babies: 37-42 weeks and
- Post-term babies: >42 weeks.

Study Procedure

One mL of blood samples were collected from study subjects by venipuncture. Haematocrit values were obtained by Automated Haematology Analyser, which calculated haematocrit from direct measurement of Mean Corpuscular Volume (MCV) and Haemoglobin (Hb). The newborns were considered to be polycythaemic if the venous haematocrit was 65% or greater, when initial value was high a repeat haematocrit was performed at 12 hours or if symptoms appeared within 72 hours of life [15]. Polycythaemic babies were examined and categorised as symptomatic, asymptomatic based on clinical features like lethargy, poor feeding, plethora, cyanosis, convulsions, icterus, tachypnea.

The blood samples of all polycythaemic babies were sent for laboratory investigations like Total Platelet Count (TPC), haematocrit, haemoglobin by automated haematology analyser.

Definitions

Hypoglycaemia: Blood glucose ≤40 mg/dL irrespective of birth weight and gestational age were reported as hypoglycaemia [16].

Thrombocytopenia: It was defined as platelet count <1,50,000/mm^3. Hypocalcemia; Defined as serum total calcium <7.0 mg/dL [17].

Hyperbilirubinaemia: The serum bilirubin levels >12 mg/dL was defined as hyperbilirubinaemia [18].

Sepsis was excluded by negative sepsis screen (total leucocyte counts, erythrocyte sedimentation rate, C-reactive protein) and blood culture in symptomatic babies. Meningitis was ruled out by lumbar puncture, transcranial ultrasound was done to rule out structural anomalies of the brain.

Partial Exchange Transfusion (PET) was performed for babies with haematocrit ≥65% with symptoms and haematocrit >70% without symptoms. PET was done through central route, the umbilical venous catheter was used for withdrawing blood while same amount of normal saline was replaced through a peripheral vein. Babies were monitored throughout the procedure [15]. Asymptomatic babies with haematocrit 65 to 70% received fluid or feed of 20 mL per kg per day [19].

The volume for partial exchange transfusion was calculated using the formula [19]:

$$\frac{\text{(Observed haematocrit-Desired haematocrit)}}{\text{Observed haematocrit}} \times \text{Weight (kg)} \times \text{Blood volume (mL/kg)}$$

Desired haematocrit was taken as 55%, Blood volume as 80 mL/kg [19]. Outcomes were assessed by haematocrit values target packed cell volume of 55%, immediately after PET, repeated at 12, 24 and 48 hours along with improvement of signs and symptoms. The asymptomatic neonates who did not require PET were observed for development of signs or symptoms for 72 hours of life and managed accordingly.

STATISTICAL ANALYSIS

Appropriate tables and graphs were used to display the data, analysis was done by Statistical Package for the Social Sciences (SPSS) software version 20.0. Chi-square test was used to compare proportions, p-value of ≤0.05 was considered statistically significant.

RESULTS

Out of 1760 newborns 75 (4.26%) were polycythaemic and 1685 (95.73%) were not polycythaemic. From 75 polycythaemic neonates 40 (53.33%) were males and 35 (46.66%) were females. Male to female ratio was found to be 1.1:1 but this factor was statistically not significant (p-value=0.964).

Incidence in different birth weight categories were as follows; 1500-2500 grams in which 45 (60%), <1500 grams 5 (6.67%), >2500 grams 25 (33.33%) were polycythaemic [Table/Fig-1]. Fifty newborns out of 75 belonged to weight <2500 grams indicating that the incidence of polycythaemia was significantly high in babies of low birth weight (p-value=0.0214).

Weight (grams)	n	Incidence %	p-value
<1500	5	6.67	0.0214*
1500-2500	45	60	
>2500	25	33.33	

[Table/Fig-1]: Incidence of polycythaemia in different birth weights.
*p-value ≤0.05 was considered statistically significant (Chi-square test)

In respect to neonatal maturity, all the 75 polycythaemic babies were categorised into preterm consisting of 15 (20%), term 50 (66.67%) and

post-term 10 (13.33%) [Table/Fig-2]. However, no statistically significant difference existed among newborns of different gestational age groups.

Maturity (weeks)	n	Incidence %	p-value*
Preterm (<37)	15	20	0.0653
Term (37-42)	50	66.66	
Post-term (>42)	10	13.33	

[Table/Fig-2]: Incidence of polycythaemia in relation to neonatal maturity.
*Chi-square test

Furthermore, these babies were reclassified into Small for Gestational Age (SGA) consisting of 40 (53.33%), Appropriate for Gestational Age (AGA) including 30 (40%) neonates and large for gestational age (LGA) with 5 (6.66%) neonates [Table/Fig-3]. The incidence of polycythaemia was significantly higher in SGA babies (p-value=0.0372) when compared to large for gestational age babies.

Gestational age	n	Incidence %	p-value
Small	40	53.33	0.0372*
Appropriate	30	40	
Large	5	6.66	

[Table/Fig-3]: Incidence in different gestational age.
*p-value ≤0.05 was considered statistically significant (Chi-square test)

The 75 polycythaemic neonates were assessed for clinical features. 50 neonates were symptomatic and 25 were asymptomatic. The symptoms were arranged in decreasing order as follows- lethargy 50 (66.6%), poor feeding 50 (66.6%), plethora 40 (53.3%), cyanosis 30 (40%), icterus 25 (33.3%), convulsion 20 (26.66%) and tachypnea 15 (20%) [Table/Fig-4].

Clinical symptoms and signs	n	Percentage
Lethargy	50	66.66
Poor feeding	50	66.66
Plethora	40	53.3
Cyanosis	30	40
Icterus	25	33.3
Convulsion	20	26.66
Tachypnea	15	20

[Table/Fig-4]: Clinical features in symptomatic patients (N=75).

The results of blood investigations obtained are tabulated in decreasing order as follows: hypoglycaemia in 27 (36%), hyperbilirubinaemia in 21 (28%), thrombocytopenia in 17 (22.67%) neonates and hypocalcaemia in 10 (13.33%). The haematocrit values obtained were categorised as 65-67% which comprised of 45 (60%), followed by 68-70% constituting of 20 (26.7%) and 71-75% consisting of 10 (13.33%) neonates [Table/Fig-5].

Findings	n	Percentage
Laboratory		
Hypoglycaemia	27	36
Hyperbilirubinaemia	21	28
Thrombocytopenia	17	22.67
Hypocalcaemia	10	13.3
Haematocrit		
65-67%	45	60
68-70%	20	26.7
71-75%	10	13.3

[Table/Fig-5]: Laboratory and haematocrit findings.

All the 10 babies in 71-75% category underwent partial exchange transfusion irrespective of symptoms, whereas seven babies with symptoms in 68-70% category underwent the partial exchange transfusion. The rest of babies in 65-67% and 68-70% without symptoms were managed by adding extra fluid of 20 mL/kg/day and symptoms were observed along with repeated haematocrit evaluation [Table/Fig-6]. For babies who underwent partial exchange transfusion haematocrit values were estimated immediately after exchange and repeated at intervals of 6, 12, 24 and 48 hours. For neonates who received extra fluid, haematocrit was repeated at 24 and 48 hrs.

Haematocrit %		Treatment		Outcome at 48 hours
		PET	Extra fluid @ 20 mL/kg/day	
71-75%		10	-	Good
68-70%	With symptoms	7	-	
	Without symptoms		13	
65-68% without symptoms			45	

[Table/Fig-6]: Outcome of neonatal polycythaemia.
PET: Partial exchange transfusion

Clinical improvement was assessed by improvement of lethargy and poor feeding, decrease in plethora, cyanosis, icterus and tachypnnoea, well controlled convulsion and decreasing haematocrit values <65% (target packed cell volume 55%) after treatment were considered as cured.

DISCUSSION

Neonatal polycythaemia has been known to be associated with significant morbidity. It is a physiological adaptation to advancing gestational age, however with increasing haematocrit blood viscosity increases leading to decreased microcirculation and poor tissue oxygenation. There is a linear relationship between haematocrit and viscosity till 60-65%. This relationship becomes exponential when the haematocrit rises beyond 65%. Direct measurement of viscosity is not possible hence venous haematocrit is used as indirect evidence to measure this test [20].

The present study showed the incidence of neonatal polycythaemia as 4.26% in a tertiary care hospital where study was conducted. But another study conducted by Ramamurthy RS and Berlanga M, showed an incidence of 5.17%, and the study done by Singh S et al., showed as 3.06% [21,22]. Other studies conducted by Wiswell MC et al., and Ramamurthy RS and Berlanga M, showed the incidence rates varying between 1.4-5% [23, 21]. This corroborates well with the current study.

Incidence was found to be significantly higher among SGA babies which was similar to studies conducted by Wiswell WC et al., and Singh M et al., [23,24]. Incidence was also higher among post-term babies (7.14%) similar to that shown by Ramamurthy RS and Berlanga M, [21].

Regarding clinical symptoms and signs, lethargy (66.6%), poor feeding (66.6%), plethora (53.3%), cyanosis (40%) and jaundice (33.3%) were detected, which was similar to that of Ramamurthy RS and Berlanga M, [21], which showed lethargy (56%) poor feeding (56.4%), plethora (48%), cyanosis (37%) and jaundice (28.8%). The study conducted by Abbas SS and Fayadh HF, showed jaundice (58%), lethargy (30%), and respiratory distress (26%) [25]. Whereas, in the present study lethargy and poor feeding were the major symptoms. Other uncommon manifestations like necrotising enterocolitis, intracranial haemorrhage, priapism were not encountered in this study [26,27].

Most common laboratory abnormalities detected in the present study were hypoglycaemia (36%) followed by hyperbilirubinaemia (28%), thrombocytopenia (22.66%) and hypocalcaemia (13.3%) was

whereas in a study done in United States Army Hospital in 1986 showed jaundice (33.5%), followed by hypoglycaemia (13%) [23]. Another study done in Chandigarh, India showed jaundice (26%), hypoglycaemia (10%) as common laboratory abnormalities [22].

The high rates of hypoglycaemia noted in this study could be due to the distance travelled by the newborn to get to the tertiary care centre. As most of the deliveries were conducted in peripheral hospitals and newborns are transported for better care to the tertiary hospitals so mothers do not accompany them and newborns like SGA babies have feeding difficulties.

Among the study population, 25 (33.33%) polycythaemic newborns were asymptomatic which is similar to the study conducted by Wiswell with 38.2% asymptomatic polycythaemic babies [23]. Rest 50 (66.6%) neonates were symptomatic. Of them 10 newborns (13.38%) with haematocrit more than 70% irrespective of symptoms and 7 out of 20 (35%) babies with haematocrit 68-70% having symptoms underwent partial exchange transfusion. Remaining 58 out of 75 (77.33%) newborns with haematocrit more than 65% who were asymptomatic received extra fluid or feeding of 20 mL/kg/day and were kept under observation for 72 hours for development of symptoms or improvement.

All the newborns were sent for blood haematocrit estimation at admission, immediately after partial exchange transfusion, then at 6, 12, 24 and 48 hours. Short-term outcome was good with 100% recovery whereas long-term outcomes needs to be evaluated further.

Limitation(s)

This study was done in a tertiary care hospital receiving mostly referred babies hence the number of cases within 12 hours of life was less. Since a follow-up of longer duration could not be done so long-term effects of PET couldn't be assessed. Further studies are needed to observe the long term outcomes.

CONCLUSION(S)

Overall incidence of neonatal polycythaemia was 4.26% with significantly higher incidence among SGA newborns. Lethargy and poor feeding were the chief complaints, hypoglycaemia and hyperbilirubinaemia were the main laboratory abnormalities. Short-term outcome was good, long-term outcomes need further evaluations. Asymptomatic neonates responded well to administration of extra fluids at 20 mL/kg/day. Hence physicians need to be cautious regarding this entity.

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