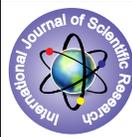


A Predictor of Neonatal Outcome – Umbilical Cord Blood Nucleated RBCs.



Medical Science

NRBC

Pendurthi Venkata Krishna

Associate Professor, Department Of Pediatrics, Shadan Institute of Medical Sciences, Teaching Hospital and Research Centre, Himayathsagar Road, Hyderabad-08, Telangana State, INDIA

Abhishek Mahankali V

Assistant Professor, Department Of Pediatrics, Shadan Institute of Medical Sciences, Teaching Hospital and Research Centre, Himayathsagar Road, Hyderabad-08, Telangana State, INDIA.

ABSTRACT

BACKGROUND AND OBJECTIVES

1. To compare nucleated red blood cells (NRBC) count in the umbilical cord blood of normal term newborns, of mothers with pregnancy induced hypertension and preterm newborns who were delivered spontaneously without any risk factors.
2. NRBC count and its relation to immediate neonatal outcome.

METHODOLOGY

Peripheral smear was prepared from the umbilical cord blood of 150 newborns born in Shadan Hospital, Hyderabad. The study included 50 term babies, 50 spontaneously delivered preterm babies, and 50 babies of mothers having pregnancy induced hypertension.

Basic data of mothers like age, parity, haemoglobin level, diabetes, pregnancy induced hypertension and foetal presentation were collected. Also natal risk factors like prolonged second stage, mode of delivery and presence of meconium stained amniotic fluid were documented. Babies were examined soon after birth and preliminary data regarding the babies were also noted. Immediately after delivery umbilical cord is double clamped and cord blood was obtained. Peripheral smear was prepared soon after, stained with Leishmans stain. The number of NRBC was studied in prepared slides. These babies were followed up till discharge and data regarding morbidity and mortality were also documented.

RESULTS

Normal values of NRBC in normal term babies were found to be 3.54 ± 1.05 in the present study. It was also found that NRBC are significantly increased in preterm babies (6.54 ± 4.74) followed by newborns of mothers with PIH (6.42 ± 3.08).

Significant association was found between Apgar at 1 minute ($P=0.016$), respiratory distress ($P=0.002$) and elevated NRBC in preterm babies. No significant association was found between age of mother, parity, blood group of mother, Apgar at 5 minutes, intrauterine growth retardation, maternal anaemia and elevated NRBC.

CONCLUSION

NRBC can be used as a marker of intrauterine hypoxia and it is significantly associated with bad outcome in terms of morbidity and mortality. This test is quick, reliable, cost effective and easy to do. So it can be used as a bedside test to predict early neonatal outcome.

1. INTRODUCTION

Perinatal asphyxia is a major cause of acute mortality and chronic neurologic disability amongst survivors, and is a complication that occurs between 3-10% of deliveries. Parameters that have been used to predict or define perinatal asphyxia include intrapartum electronic foetal monitoring, foetal or umbilical cord pH measurement, meconium-stained amniotic fluid, Apgar score, hypoxic ischemic encephalopathy (HIE) and major organ disorder. However, no single marker of perinatal asphyxia has shown good predictive efficiency and only a combination of various indices can help in the early diagnosis of perinatal asphyxia. NRBC count is one such marker of foetal hypoxia.[1-12]

Nucleated red blood cells (NRBC) represent the stages of a red blood cell before it matures. Under normal condition NRBC is found only in the blood of the foetus and neonate. Under all other condition NRBC is an indicator of pathology, either increase in erythroid activity or damage to the bone marrow architecture.[1]

It has been suggested that the presence of elevated nucleated red blood cells in umbilical cord blood is a sign of foetal hypoxia.[1-12] Studies have established that in infants, this index may be affected by factors such as prematurity, preeclampsia, foetal growth restriction, isoimmunization, maternal tobacco use, maternal diabetes mellitus and chorioamnionitis.[1]

In term babies elevated NRBC is found to be related to perinatal brain damage[13], neonatal seizures[14] and severity of encephalopathy.[15,16] Preterm babies with high-

er counts of NRBC are found to be correlating with higher incidence of intraventricular enterocolitis[17], cerebral white matter injury[18], retinopathy of prematurity[19] and necrotizing enterocolitis[20]. It is also proved to be an early marker of brain damage[21] in newborns of mothers with preeclampsia elevated NRBC is a sign of foetal hypoxia even with well controlled hypertension.[22,23,24] Since the increased level of NRBC is found in different high risk conditions, it can be used as a marker to predict neonatal outcome.[25,26,27]

The purpose of this study was to determine the umbilical cord blood NRBC levels in normal newborns, newborns of mothers with pregnancy induced hypertension and clean preterm, and correlate the levels with immediate neonatal outcome and try to evaluate its usefulness as an indicator of the same.

2. OBJECTIVES OF THE STUDY

1. The main purpose of this study were to determine:
2. Umbilical cord blood NRBC levels in
3. Normal term newborns
4. Newborns of mothers with pregnancy induced hypertension
5. Preterm newborns who were delivered spontaneously without any risk factors
6. The relationship between NRBC count and immediate neonatal outcome.

5. RESULTS

A comparative study with 50 preterm babies, 50 babies born to mothers having PIH and 50 normal babies is un-

dertaken to study the level of NRBC, associated risk factors and their outcome.

Group I : Preterm Babies

Group II : PIH Babies

Group III: Normal Babies

The following observations are made after the completion of the study.

1. Age distribution of mothers studies

Maternal Age in years	Group I		Group II		Group III	
	No.	%	No.	%	No.	%
18-20	18	36.0	12	24.0	16	32.0
21-25	25	48.0	25	50.0	25	50.0
26-30	8	16.0	9	18.0	8	16.0
>30	0	0.0	4	8.0	1	2.0
Total	50	100.0	50	100.0	50	100.0
Mean±SD	22.3±3.03		23.92±4.27		22.78±3.45	

Table 1 - Age distribution of mothers studied

Sample are age matched with P = 0.101

In the present study most of the mothers are also almost similar. They formed 48% in preterms, 50% in bodies of mothers with preeclampsia and 25% in normal term babies.

2. Parity distribution of mothers studies

Parity	Group I		Group II		Group III	
	No.	%	No.	%	No.	%
1	37	74.0	32	64.0	25	50.0
2	8	16.0	10	20.0	16	32.0
3	5	10.0	5	10.0	7	14.0
4 & above	0	0.0	3	6.0	2	4.0
Total	50	100.0	50	100.0	50	100.0

Table 2 - Parity distribution of mothers studied

Parity distribution is statistically similar with p = 0.179. Most of the mothers were primipara in all three groups.

3. Weight distribution of mothers studies

Group	Group I		Group II		Group III	
	No.	%	No.	%	No.	%
38-40	1	2.0	3	6.0	1	2.0
41-50	12	24.0	8	16.0	17	34.0
51-60	25	50.0	27	54.0	25	50.0
61-70	12	24.0	12	24.0	7	14.0
Total	50	100.0	50	100.0	50	100.0
Mean±SD	55.72±6.47		55.88±6.92		53.80±6.24	

Table 3 - Weight distribution of mothers studied

Samples are weight matched with p = 0.213

In the study most of the mothers are weighing between 51 - 60 kg in all the three groups.

4. Blood group distribution of mothers studies

Blood Group	Group I		Group II		Group III	
	No.	%	No.	%	No.	%
A+	10	20.0	12	24.0	11	22.0
B+	17	34.0	14	28.0	11	22.0
AB+	2	4.0	4	8.0	2	4.0
O+	21	42.0	20	40.0	26	52.0
Total	50	100.0	50	100.0	50	100.0

Table 4 - Blood group distribution of mothers studied

blood group distribution is statistically similar between

three groups with p=0.781

Most of them were O positive followed by B positive as expected in the general population.

5. Haemoglobin levels of mothers studies

Maternal Weight (kg)	Group I		Group II		Group III	
	No.	%	No.	%	No.	%
<10.0	31	62.0	31	62.0	22	44.0
>10.0	19	38.0	19	38.0	28	56.0
Total	50	100.0	50	100.0	50	100.0

Table 5 - Haemoglobin levels of mothers studied

Hb levels are statistically similar between three groups with P = 0.132

A majority has anaemia in all groups more in mothers of preterm babies and mothers with PIH

6. Apgar score at 1 minute

Apgar score at 1 minute	Group I		Group II		Group III	
	No.	%	No.	%	No.	%
<3	0	0.0	1	2.0	0	0.0
3-4	0	0.0	0	0.0	0	0.0
5-7	27	54.0	9	18.0	3	6.0
8-10	23	46.0	40	80.0	47	94.0
Total	50	100.0	50	100.0	50	100.0

Table 6 - Apgar score at 1 minute

Lower apgar score at 1 minute is significantly associated with Group I and Group II with P<0.001**

7. Apgar score at 5 minute

Apgar score at 5 minute	Group I		Group II		Group III	
	No.	%	No.	%	No.	%
<3	0	0.0	0	0.0	0	0.0
3-4	0	0.0	0	0.0	0	0.0
5-7	2	4.0	3	6.0	0	0.0
8-10	48	96.0	47	94.0	50	100.0
Total	50	100.0	50	100.0	50	100.0

Table 7 - Apgar score at 5 minute

Apgar score at 5 min is statistically similar in three groups with p = 0.206

8. NICU Admission

NICU Admission	Group I		Group II		Group III	
	No.	%	No.	%	No.	%
Mother side	4	8.0	32	64.0	49	98.0
NICU	46	92.0	18	36.0	1	2.0
Total	50	100.0	50	100.0	50	100.0

Table 8 - NICU admissions

9. Birth weight distributions

Birth weight (kg)	Group I		Group II		Group III	
	No.	%	No.	%	No.	%
<1.50	13	26.0	9	18.0	0	0.0
1.51 - 2.00	35	70.0	10	20.0	0	0.0
2.01 - 2.50	2	4.0	21	42.0	20	40.0
2.51 - 3.00	0	0.0	10	20.0	22	44.0
> 3.00	0	0.0	0	0.0	8	16.0

Total	50	100.0	50	100.0	50	100.0
Mean ± SD	1.75±0.19		2.15±0.49		2.73±0.37	

Table 9 - Birth weight distribution

Birth weight is significantly less in Group I when compared to Group II and Group III with P<0.001*** (Low birth weight is noticed in Group I and Group II)

10. SGA/AGA distribution

S G A /	Group I		Group II		Group III	
AGA	No.	%	No.	%	No.	%
AGA	31	62.0	27	54.0	41	82.0
SGA	19	38.0	23	46.0	9	18.0
Total	50	100.0	50	100.0	50	100.0

Table 10 - SGA/AGA distribution

incidence of SGA is significantly more in Group I and Group II when compared to Group III which is control with P = 0.008**

11. NRBC

NRBC	Group I		Group II		Group III	
	No.	%	No.	%	No.	%
< 10	41	82.0	43	86.0	50	100.0
> 10	9	18.0	7	14.0	0	0
Total	50	100.0	50	100.0	50	100.0
mean ± SD	6.54 ± 4.74		6.42 ± 3.08		3.54 ± 1.05	

Table 11 - NRBC

Incidence of elevated NRBC is significantly more in Group I (18.0%), followed by Group II (14.0%) when compared to nil in Normal group with P = 0.009**

12. Outcome

Outcome	Group I		Group II		Group III	
	No.	%	No.	%	No.	%
Normal	34	68.0	47	94.0	50	100.0
Death	16	32.0	3	6.0	0	0
Total	50	100.0	50	100.0	50	100.0

Table 11 - Outcome

Incidence of death is significantly more in Group I (32.0%) followed by only 6.0% (3 cases) with p<0.001**

3. Cause of admission

Cause of admission	Group I (n=50)		Group II (n= 50)		Group I(n=50)	
	No.	%	No.	%	No.	%
EOS	3	6.0	0	0.0	2	4.0
Hyperbilirubinemia	0	0.0	0	0.0	1	2.0
NEC	1	2.0	0	0.0	0	0.0
Observation	0	0.0	2	4.0	0	0.0
Pre term cases	8	16.0	3	6.0	0	0.0
RDS	26	52.0	10	20.0	0	0.0

Table 11 – Cause of admission

Most common cause of admission in preterms and babies of mother with preeclampsia was respiration distress. There was no cases of respiratory distress among normal term babies.

14. Comparison of study characteristics with NRBC in Preterm babies

Risk factors	NRBC		P value		
	<10 (n=41)	>10(n=9)			
	No.	%	No.	%	
Maternal age in years					
<18					
18-30	41	100.0	9	100.0	1.000
>30	-	-	-	-	
Parity					

1	30	73.2	7	77.8	1.000
2	7	17.1	1	11.1	
3	4	9.8	1	11.1	
4 & Above					
Blood Group of mother					
A+	8	19.5	2	22.2	0.758
B+	15	36.6	2	22.2	
AB+	2	4.8	0	0.0	
O+	16	39.1	5	55.6	
Apgar score at 1 min					
0-3	-	-	-	-	0.016*
4-6	1	2.4	3	33.3	
7-10	40	97.6	6	66.7	
Apgar score at 5 min					
0-3	0	0	0	0	1.000
4-6	0	0	0	0	
7-10	41	100.0	9	100.0	
N I C U admission					
MSIDE	4	9.8	0	0	1.000
NICU	37	90.2	9	100.0	
IUGR					
AGA	26	63.4	5	55.6	0.715
SGA	15	36.6	4	44.4	
Haemoglobin					
<10	24	58.5	7	77.8	0.452
≥10	17	41.5	2	22.2	
C a u s e s of NICU admission					
Pre term	8	19.5	0	0.0	0.322
RDS	17	41.5	9	100.0	0.002**
NEC	1	2.4	0	0.0	1.000

Table 14 – Comparison of study characteristics with NRBC in Preterm babies

Among 50 preterms, all mothers were in the age group 18-30 years. In that 9 babies showed increased NRBC. No significant statistical difference was found between the two groups.

Among the preterms maximum were 1st order that is 37 of them. In that 7 showed increased NRBC. No significant statistical association was found between birth order and number of NRBC.

Most of them have O positive blood group that is 21 of them as seen in the general population. No significant statistical association was found between blood group and number of NRBC.

Apgar score at 1 minute is <7 in 4 babies. Three of them had elevated NRBC.

Statistical there was significant association between the Apgar score at 1 minute and increased NRBC.

Apgar scores at 5 minutes were above 7 in all babies. There was no statistically significant association between Apgar score at 5 minute and increased NRBC.

Among the 50 preterms 46 were admitted in NICU. Nine of them had increased NRBC. But there was no statistically significant correlation.

Twenty six babies were admitted with RDS. All of those babies with increased NRBC had RDS. It was found that this is significant statistically.

Thirty one mothers has anaemia, but there was no statistically significant correlation between maternal anaemia

mia and NRBC.

There was no correlation between NRBC count and IUGR.

Risk factors	NRBC		P value		
	<10 (n=43)	>10(n=7)			
	No.	%	No.	%	
Maternal age in years					
<18	0	0	0	0	1.000
18-30	39	90.7	7	100.0	
>30	4	9.3	0	0.0	
Parity					
1	27	62.8	5	71.4	0.637
2	9	20.9	1	14.3	
3	5	11.6	0	0.0	
4 & Above	2	4.6	1	14.3	
Blood Group of mother					
A+	10	23.3	2	28.6	0.272
B+	10	23.3	4	57.1	
AB+	4	9.3	0	0.0	
O+	19	44.2	1	14.3	
Apgar score at 1 min					
0-3	0	0	0	0	0.017*
4-6	0	0	0	0	
7-10	43	100.0	5	71.4	
Apgar score at 5 min					
0-3	0	0	0	0	140
4-6	0	0	0	0	
7-10	43	100.0	7	100.0	
NICU admission					
MSIDE	32	74.4	0	0.0	<0.001**
NICU	11	25.6	7	100.0	
IUGR					
AGA	22	51.2	5	71.4	0.430
SGA	21	48.8	2	28.6	
Haemoglobin					
<10	26	60.5	5	71.4	0.695
>10	17	39.5	2	28.6	
Causes of NICU admission					
Pre term	2	4.7	1	14.3	0.370
RDS	6	13.9	4	57.1	0.23*
NEC	-	-	-	-	

Table 15- Comparison of study characteristics with NRBC in babies of mothers with PIH

Among 50 babies of mothers with PIH, 46 mothers were in the age group 18-30 years. In that 7 babies showed increased NRBC. No significant statistical difference was found between the two groups.

Among the babies of mothers with PIH maximum were 1st order that is 32 of them. In that 5 showed increased NRBC. No significant statistically association was found between birth order and number of NRBC.

Most of them have O positive blood group that is 20 of them. No significant statistical association was found between blood group and number of NRBC.

Apgar score at 1 minute is <7 in 2 babies. Both of them had elevated NRBC. Statistically there was significant association between the Apgar score at 1 minute and increased NRBC.

Apgar score at 5 minute was above 7 in all. There was no statistically significant association between Apgar score at 5 minute and increased NRBC.

Among the 50 babies 18 were admitted in NICU. Seven

of them had increased NRBC. This was found to be statistically significant.

The babies were admitted with RDS, Four among them had increased NRBC. It was found that this is significant statistically.

There was no correlation between NRBC count and IUGR.

Thirty one mothers had anaemia, but again there was no statistically significant correlation between maternal anaemia and NRBC.

6. DISCUSSION

Nucleated red blood cells (NRBCs) are seen in the blood of newborns, but in small number. They are primarily produced in the foetal bone marrow in response to erythropoietin. Many acute and chronic stimuli cause increase in the number of circulating NRBCs. Studies have shown decreasing NRBCs as the gestational age increases, except that post-term infants have higher counts than term infants. Up to 10 NRBC/100 WBCs are normal and values above 10 NRBC/WBC are considered to be elevated.

Common causes of increased nucleated red blood cells include prematurity, increased erythropoiesis from chronic hypoxia, anaemia, and maternal diabetes, from acute stress mediated release from the marrow stores, and from postnatal hypoxia. Elevated number of NRBC has been found to be associated with intrauterine hypoxia and subsequent neurological damage. Clinical and biochemical evidence of asphyxia are found in only about 10-20% of cerebral palsy. Therefore assessment of additional markers of intrauterine hypoxemia is a relevant task and has important medico legal aspect.

In addition to this it was found that umbilical artery pH at delivery is susceptible to acute changes during labour and is a poor predictor of neonatal morbidity or long term handicap. In contrast plasma erythropoietin is a good measure of tissue oxygenation and increase only when physiological compensatory mechanism does not prevent tissue hypoxia. The increase in plasma erythropoietin is better correlated with erythroblast count than pH. In this respect the degree of erythroblastosis may be a better index of hypoxic damage than blood pH. This study has tried to find out the normal levels of NRBC in preterm newborns, term newborns and newborns born to mothers with preeclampsia. We also tried to relate this to neonatal outcome in terms of morbidity and mortality.

NRBC in normal term babies

Study	Sample size	NRBC/100 WBC	AGE	Gestaional Age
P r e s e n t study	50	3.54±1.05	Birth, cord blood	Term
Sinha et. Al[1]	84	2.3	Birth, cord blood	Term
Phelan et. Al[6]	83	3.4	Birth, cord blood	Term
Shivhare et. Al[24]	33	4.1	Birth, cord blood	Term
R o y F e r a j i [28]	60	3.88±3.92	Birth, cord blood	38.96±0.99 weeks
Roland Axt et. Al[29]	304	3.7	Birth, cord blood	Term

Table 16-NRBC count in term babies

In normal term babies NRBC count found to be 3.54+/-1.105/100WBC. This was correlating with previous studies by Sinha et. al., Phelan et. al., Shivhare et. al., Royal Faraji et.al. and Roland Axt et. al. In all studies it was found to

be below 10 per 100 WBC. Therefore in the present study NRBC count above 10 is taken as significant.

NRBC in preterms

Study	No.	NRBC/100 WBC	Gestaional Age	AGE	P value
Present study	50	6.54±4.74	32.12±1.64	Birth, Cord blood	0.01
Gea Y et. al.[10]	14	20.52±37.96	33.57±1.98	Birth, Cord blood	NS
An-adir[18]	176	7.4±3.54	27.4±2.7	Birth, P-riph-eral blood	0.22
Shiv-are[24]	7	7.1±1.8	32±3.5	Birth, Cord blood	<0.05
Akeran F[23]	25	20.2±8.2	32.2±2.2	Birth, Cord blood	<0.05

Table 17-NRBC in preterms

Incidence of elevated NRBC is significantly more in preterms (18.0%) when compared to nil in normal group with P = 0.009 in the present study. Similar results were reported in previous studies by Shivare and Akeran in their studies. But this relation between gestational age and NRBC was not found to be significant in sutides by Gea Y et.al. andanadir. Present study the NRBC in preterms was found to be 6.54±4.74. This was similar to study by Shivare et.al. andAnadir et.al. The higher values found in other studies by Akeran et.al. andGea Y et.al. Gea Y et. al. may be due to interference by the other factors which can affect NRBC count.

PIH and NRBC

Study	No.	NRBC	AGE	P value
Present study	50	6.42±3.78	Birth, Cord blood	0.009*

In preterms elevated NRBC count was significantly associated with lower Apgar scores (P=0.016*), but not with the 5 minute Apgar scores (P=1). Same in the babies of mothers preeclampsia (P=0.017*, P=0.014).

Apgar score at 1 minute	Present study				Hanlon-Lunderg et.al	
	Preterms		PIH		NRBC	P Value
	NRBC	P Value	NRBC	P Value		
0-3	0	0	2	0.017*	18.4±24.5	0.002*
4-6	11.75±6.55	0.016*	12	0.017*	13.2±23.3	0.065
7-10	6.07±4.41	0.016*	6.17±2.88	0.017*	8.6±17.3	NS

Table 19-Apgar At 1 Minutes and NRBC

Apgar score at 5 minute	Present study				Hanlon-Lunderg et.al	
	Preterms		PIH		NRBC	P Value
	NRBC	P Value	NRBC	P Value		
0-3	0	1	0	0.140	18.4±24.5	NS
4-6	0	1	13	0.140	13.2±23.3	NS
7-10	6.54±4.74	1	6297±2.97	0.140	8.6±17.3	NS

Table 20-Apgar At 5 Minutes and NRBC

Hanlon- Lundberg and Kirby studied 1561 cases of newborn cord blood. They found that NRBC count has an inverse rela-

S. Sivakumar.[22]	52	7.38	Birth, blood	Cord	<0.005**
A k e r a n F[23]	21	23.1±11.2	Birth, blood	Cord	<0.05*
Shivare et. Al[24]	34	7.1	Birth, blood	Cord	<0.05*

Table 18 – PIH and NRBC

Incidence of elevated NRBC is significantly more in babies of mothers with preeclampsia (14.0% when compared to nil in normal group with P = 0.009. Studies by Shivareet. al., S. Sivakumar and Akeran also found similar results.

B. Ghosh et.al. also demonstrated significant correlation between present of PIH and NRBC count (t=2.66, P=0.025).

Maternal age and NRBC count

Most mothers were in the age group of 18 to 30 years. There was no correlation between maternal age and NRBC levels. There were no similar studies for the comparison.

Parity and NRBC count

There were no correlation between parity and NRBC level. There were no similar studies for the comparison.

Blood group and NRBC count

There was no significant association between blood group and NRBC count in preterms or babies of mothers with preeclampsia. There were no comparison studies.

Maternal anemia and NRBC count

There was no significant association between maternal anaemia and NRBC in the present study (P=0.452).

Similar studies by Hanlon- Lundberg et. al. also could not establish any significant relation between maternal anaemia and NRBC count.

Apgar at 1 minute, 5 minutes and NRBC count

tionship with Apgar scores at 1 minute and 5 minutes. This was significant only for lowest Apgar scores at 1 minute and not at 5 minute which was same in the present study as well.

Gea Y et. al. studied 25 premature babies umbilical venous blood. They found that NRBC count shows correlation to Apgar scores at 1 minute and 5 minute (P =0.029 at 1 minute and P = 0.002 at 5 minutes).

Similar studies by Dasari Papa et. al. found that NRBC count is higher in neonate with low Apgar scores of ≤ 6 at 5 minutes.

Boskabadi H, Maamouri G and Sadeghianet. al. studies 91 infants, 42 asphyxiated and 49 normal tinfants. They found that NRBC/100 WBC count increased with progressive decrease in first minute Apgar scores (P<0.001).

Burocoreet. al. Studies 337 newborn infants 47 extremely preterm, 185 preterm and 105 normal term babies as control. NRBC count in the umbilical vein blood was studied. Significant correlation was observed between the NRBC count at birth and Apgar score at 1 minute (r=-0.29; P=0.001; n=337).

B Ghosh at. al. in his study found that NRBC per 100 WBC count correlated with Apgar score. The correlation coefficient was – 0.05 (P>0.001).

Hanlon-Lundberg et. al. studies 1,112 cases umbilical cord blood NRBC count. One minute Apgar score 0-3 were significantly associated with higher NRBC counts.

Royal Faraji in his study analysed NRBC levels in cord blood of 50 newborns with meconium stained amniotic fluid and 60 newborns with clear amniotic fluid. The mean Apgar scores of in normal group was 8.50+0.54 with a range of 7 to 9 where the other group had significantly lower scores. Their results showed that NRBC count had a tendency towards an inverse relationship with Apgar scores at both 1 minute (P=0.001) and 5 minutes (P=0.005).

Axt-Fliedneret. al studied 134 newborn cord blood NRBC and tried to relate it to abnormal fetoplacental circulation detected by Doppler study. In his study he detected a weak correlation between 1 minute, 5 minute and 10 minute Apgar scores and NRBC count (P=0.05).

End Leikinet. al. in his study of 359 preterm babies with chorioamnionitis. He found a significant elevation of NRBC associated with 5 minute Apgar Scores (P=0.023).

Association between the NRBC count and Apgar Scores at 5 minute found in other studies is may be due to the fact that they included birth asphyxia also which is an important risk factor for elevated NRBC count.

NRBC count and NICU admissions

Study	NICU admissions	NRBC	P Value
Present study – Preterm	46/50	6.72±4.87	1
Present study – PIH	18/50	8.33±3.77	<0.001**
Hanlon-Lundberge and Kirby[6]	55/1561	26.9±59.6	0.03*
Dasari Papa et. al.[11]	30/52	29.8±10.9	0.006**
B Ghosh et. al.[15]	20/25	16.5±6.4	<0.001**

Table 21-NRBC and NICU admissions

Among the 50 preterms, 46 were admitted in NICU. Nine

of them had increased NRBC. But there was no statistically significant correlation. Among the 50 babies of mothers with preeclampsia 18 were admitted in NICU. Seven of them had increased NRBC. This was found to be statistically significant.

Similar observations were made by Hanlon-Lundberg et. al., Dasari Papa et. al. and B Ghosh et. al. also.

Causes of NICU admissions and NRBC count

RDS and NRBC

Study	No.	NRBC	P Value
Present study – preterms	26	8.77±5.42	0.002**
Present study – PIH	10	8.4±3.72	0.023*
Leikin et. Al[30]	246	3.11±1.09	0.001**

Table 22- RDS and NRBC

Among the 46 preterms who were admitted to NICU, 9 had NRBC above 10. All of them had RDS. This relation was found to be statistically significant in preterms (0.002**). Similarly among the babies born to preeclamptic mothers 10 had RDS. Among the 10, 4 (57.1%) had NRBC above 10. This was found to be statistically significant. Leikinet. al. has also reported correlation between NRBC count and respiratory distress in his study of 359 neonates with chorioamnionitis. He explained it as respiratory distress due to sepsis and elevated NRBC is a response to inflammatory mediators. In the present study the respiratory distress may be due to the effect of hypoxia like increased pulmonary vascular resistance, pulmonary haemorrhage, and pulmonary edema secondary to cardiac failure or secondary hyaline membrane disease (ARDS).

NEC and NRBC

Study	No.	P Value
Present study preterm	1(2%)	1
Gea Y et. al.[10]	5(12%)	0.026*
Silva et. al.[18]	57(32%)	0.07
Mandel D et. Al[20]	23(50%)	0.02*
Baschat et. Al[25]	18(10.2%)	<0.05*

Table 23-NEC and NRBC

In the present study among the preterms only one baby had NEC and among the babies born to preeclamptic mothers none had NEC. There was no statistically significant relation between the incidence of NEC and NRBC count. This was similar to the study by Silva et. al. Mandel et. al. and Baschat et. al. in their study found a significant relation between NEC and NRBC. This may be due to fact that the gestational age of the babies studied in other studies was much lesser than the present study.

Death and NRBC

Study	Death (no/%)	NRBC	Survival	NRBC	P Value
Pre-sent study	19(19%)	9.16±5.4	81(81%)	5.85±3.31	<0.05*
Boskabadi H et. Al[12]	10(27%)	24.25	26(73%)	4.9	<0.001**

Table 24- Death and NRBC

Incidence of Death is significantly more in preterms (32.0%) followed by babies of mothers with preeclampsia

sia6.0% (3 cases) with $p < 0.001$. There was no death in normal babies. But this was not correlating with elevated NRBC in individual group.

But when two groups are combined that is preterms and babies born to mothers with preeclampsia, the death rate was 19%. The NRBC count was found to be 9.16 ± 5.4 in them compared to 5.85 ± 3.31 in those who survived. This was found to be statistically significant. Boskabadi H, Maamouri G and Sadeghianet. al. studied 91 infants, 42 asphyxiated and 49 normal infants. In those 36 babies 16 had an adverse outcome (10 died within first month of life, and 6 developed neuro developmental sequelae. They found that NRBC/100 WBC count were significantly higher in neonates with adverse outcome than in those with favourable outcome ($P > 0.001$).

7. CONCLUSION

The present study attempted to look at umbilical cord blood NRBC level in normal term newborn and found that they are present in small number in them. In the present study NRBC count in normal term newborn was found to be 3.54 ± 1.05 .

Maternal anaemia is a significant problem in pregnant women; its incidence is found to be 56% in them in the present study.

The NRBC count in preterm newborn was found to be 6.54 ± 4.74 . This was significantly high compared to the count in term babies.

The NRBC count in newborns born to preeclamptic mothers was 6.42 ± 3.08 . This was significantly high compared to the count in term babies.

Elevated NRBC count does correlate with Apgar scoring at 1 minute which is an index of intrapartum depression.

Those with elevated NRBC count are more prone to NICU admissions and they are also prone to respiratory distress.

Statistically there was significant association between higher NRBC count and death in the present study.

Since high levels NRBC correlate with neonatal morbidity and mortality, this simple bedside test can be used as screening test and we can intervene early and expect a better neonatal outcome.

10. BIBLIOGRAPHY

- Hermansen MC. Nucleated red blood cells in the fetus and newborn. *Arch Dis Child Fetal Neonatal Ed.* 2001;84:211-215.
- D' Souza SW, Black P, MacFarlane T, Jennison RF, Richards B. Haematological values in cord blood in relation to fetal hypoxia. *BMJ* 1981; February; 88:129-132.
- Soothill PW, Nicolaiades KH, Campbell S. Prenatal Asphyxia, hyperlactacemia, hypoglycaemia, and erythroblastosis in growth retarded fetuses. *BMJ* 1987; 294:1051-3.
- Thilaganathan B, Athanasios S, Ozmen S, Creighton S, Watson NR, Nicolaiades KH, Umbilical cord blood erythroblast count as an index of intrauterine hypoxia. *Arch Dis Child Fetal Neonatal Ed* 1994; 70: 192-19.
- Naeye RL, Localio AR. Determining the time before birth when ischemia and hypoxemia initiated cerebral palsy. *ObstetGynecol* 1995; 86:713-19.
- Korst LM, Phelan JP, Ahn MO, Martin GI. Nucleated red blood cells; an update on the marker for fetal asphyxia. *Am J ObstetGynecol* 1996; 175: 843.6.
- Low JA. Intrapartum fetal asphyxia: definition, diagnosis and classification. *Am J Obstet Gynecol.* 1997; 176:956-9.
- Hanlon-Lunberg KM, Kirby RS. Nucleated red blood cells as a marker of academia in term neonates. *AM J ObstetGynecol* 1999; 181:196-201.
- Phelan JP, Korst LM, Ahn MO, Martin GI. Neonatal nucleated red blood cell and lymphocyte counts in fetal brain injury. *ObstetGynecol* 1998; 91:485-9.
- Gea Y, Araujo O, Silva LR. Clinical value of lactate measurement and nucleated red blood cells counts in the placental segment of the umbilical vein of premature newborns for diagnosis of phoxia-ischemia. *J Pediatr.* 2007; 82(2): 186-190.
- Papa D, Jyotsna GP, Ashok BB. Cord blood nucleated red blood cell count – a marker of fetal asphyxia. *J ObstetGynecol India* 2008 January/February; 58(1): 45-48
- Boskabadi H, Maamouri G, Sadeghian MH, Mobarhan MG, Heidarzade M, Shakeri MT et. al Early Diagnosis of perinatal asphyxia by nucleated red blood cell count: a case control Study. *Archives of Iranian Medicine*, 2010 July ; 13(4):275-281
- Buonodcore G, Perrone S, Gioia D. Nucleated red blood cell count at birth as an index of perinatal brain damage. *AM J ObstetGynecol* 1999; 181:1500-5.
- Blackwell SC, Refuerzo JS, Wolfe HM, Hassan SS, Berry SM, Sokoi RJ, et. al. The relationship between nucleated red blood cell counts and early onset neonatal seizures. *Am J ObstetGynecol* 2000; 182:1452-7.
- Ghosh B, Mittal S, Kumar S, Dadhwal V. Prediction of perinatal asphyxia with nucleated red blood cells in cord blood of newborns. *Int J Gynaecol Obstet.* 2003; 81:267 – 271.
- Haiju Z, Xiufang F, Lu Y, Sun R. The Combined detection of umbilical cord nucleated red blood cells and lactate: early prediction of neonatal hypoxic ischemic encephalopathy. *J Perinat Med* 1999 May 2008; 36(3):240-247.
- Green DW, Mimouni FB, Hendon B. Nucleated erythrocytes and in intraventricular hemorrhage in preterm neonates. *J Pediatr* 1995; 96(3):475-78.
- Silva AM, Smith RN, Lehman CU, Johson EA, Holcroft CJ, Graham EM. Neonatal nucleated red blood cells and the prediction of cerebral white matter injury in preterm infants. *Int J ObstetGynecol* 2006 Mar; 107(3):550-6
- Lubetzky R, Stolovitch C, Dollberg S, Miomouni FB, Salomon M, Mandel D. Nucleated red blood cells in preterm infants with retinopathy of prematurity. *Pediatrics* 2005; 116:619-622
- Mandel D, Lubetzky R, Mmouni FB, Cohen S, Littner Y, Deutsch V, Dollberg S. Nucleated red blood cells in preterm who have necrotizing enterocolitis. *J Pediatr* 2004;144:653-5.
- Fotopoulos S, Pavlou K, Skouteli H, Papassotiriou I, Lipsou N, Xanthou M. Early markers of brain damage in premature low birth weight neonate who suffered from perinatal asphyxia and/or infection. *Biol Neonate* 2001; 79:213-218.
- Sivakumar S, Bhat V, Badhe BA. Effect of pregnancy induced hypertension on mothers and their babies. *Indian J Pediatr* 2007; 74(7):623-625.
- Akercan F, Cirpan T, Saydam G. Nucleated red blood cells in infants of women with preterm labour and pre-eclampsia. *Int J ObstetGynecol* 2005; 90:138-139.
- Shivhare K, Chawla K, Khan MN, Mathur PS. Effect of maternal toxemia on total haemoglobin, foetalhaemoglobin and nucleated red blood cells in cord blood. *Indian J Pediatr* 1976; 43:349-355.
- Baschat AA, Gungor S, Kush ML, Berg C, Gembruch U, Harman CR. Nucleated red blood cell count in the first week of life: a critical appraisal of relationships with perinatal outcome in preterm growth restricted neonates. *Am J ObstetGynecol* 2007; 197:286.
- Minor VK, Bernstein PS, Divon MY. Nucleated red blood cells in growth-restricted fetuses: associations with short-term neonatal outcome. *Fetal Diagn Ther* 2000; 15:165-9.
- Baschat AA, Gembruch U, Reiss I, Gortner L, Harman CR. Neonatal nucleated red blood cell count and postpartum complications in growth restricted fetuses. *J Perinat Med* 2003;31:323-9.
- Darkhanesh R F, Asgharnia M, Yousefi TZ. Comparison of NRBC in term neonatal umbilical cord blood between neonates with meconium stained amniotic fluid and clear amniotic fluid. *J Turkish German Gynecol Assoc.* 2008;9(2):76-78.
- Axt-Flidner R, Ertan K, Hendrik H, Schmidt W. Neonatal nucleated red blood cell count relationship to abnormal fetoplacental circulation

- detected by Doppler studies. *J Ultrasound Med* 2001; 20:183-190.
30. Leikin E, Garry D, Visintainer P, Verma U, Tejani N. Correlation of nucleated red cell count in preterm infants with histologic chorioamnionitis. *Am J ObstetGynecol* 1997; 177:27-30.

