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Neonatal Reticulocytes among Preterminfants of Small for Gestational Age

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Abstract: ***Aim: To assess the relationships between SGA and perinatal variables including blood counts during the early postnatal period. Method: This is a prospective cross sectional study conducted over 9 months in all preterm neonates born before 37 completed weeks of gestation. Results: The correlation between Antenatal steroids and SGA/AGA was statistically significant in our study (p=0.04). The mean APGAR 5 score in AGA score was 8.250 ±.6387 and in SGA score was 8.400 ± 0.7368. The mean RBC in AGA score was 4767.50 ± 677.76 and in SGA group was 4508.00 ± 731.36. The mean reticulocyte count in AGA was 2.81% ± 1.50 and in SGA group was 4.58% ± 2.30%. The mean WBC count in AGA was 13442.50 ± 4262.144 and in SGA group was 11504.00 ± 6123.645. The mean neutrocytes in AGA group was 57.600 ± 6.6917 and in SGA group was 53.600 ± 12.1761.1 patient (6.7%) in the SGA group had platelet count <1.5 lakhs, 20 patients in AGA group and 14 patients (93.3%) in SGA group had platelet count >1.5 lakhs. Conclusion: These results suggest that preterm infants with SGA adapted more rapidly to the postnatal environment than did non - SGA preterm infants. Moreover, a lower reticulocyte count.***

Keywords: SGA, perinatal, blood counts, preterm neonates, reticulocyte count

1. Introduction

Complete blood count is commonly indicated in the diagnosis and of blood disorders and infectious diseases even in neonatal infants.1 Reticulocytes, which make up 0.6% to 2.9% of the RBCs in adult blood and 1.7% to 5.0% of those in umbilical cord blood, are the earliest red blood cells (RBCs) seen in peripheral blood without nuclei.2 Reticulocytes are unique in a way that they only circulate in the peripheral blood for 24–48 hours and, unlike ferritin, are unaffected by presence of an infection or inflammation. Low birth weight (BW) and preterm infants' reticulocyte haemoglobin (Hb) content is also utilized as an indicator of IDA.3 However, there aren't many studies on the reticulocyte count in the postnatal period, and it's unclear what clinical importance it holds. On the other hand, higher levels of nucleated erythrocytes have been observed in cases of neonatal asphyxia and erythropoiesis is known to be influenced by hypoxemic stimulation prior to birth.[4, 5]

Even in neonatal infants, blood counts are now widely employed in the diagnosis and follow - up of blood disorders and infectious infections. If it can be demonstrated that hypoxemia and the reticulocyte count immediately after birth are connected, it may provide a more accurate diagnostic of hypoxemia. However, it is believed that the neonatal hemostatic system is both quantitatively and qualitatively different from that of adults, especially in the case of newborns that are small for gestational age (SGA).[6, 7, 8] The main cause of intrauterine growth restriction (IUGR) in SGA infants is characterized as hematological abnormalities, with polycythemia, neutropenia, or thrombocytopenia typically seen in the early postnatal period.[9] The enhanced erythropoiesis brought on by persistent fetal hypoxia is thought to be the cause of the decrease in platelet count in polycythemia, which in turn reduces the formation of megakaryocytes and neutrophils in the bone marrow.[10] Moreover, platelet consumption is thought to be linked to recurrent placental infarctions because many SGA infants are born to preeclamptic pregnant mothers.[11] It is believed that an increase in reticulocyte count may be a physiological reaction to the rapid environmental change from within outside the uterus during the early postnatal period. A similar study found that greater reticulocyte counts were detected in earlier preterm newborns.[12]

The aim of this study was to assess the reticulocyte counts among preterm neonates and in relationship between SGA and other perinatal variables during the early postnatal period. The inclusion criteria included 30 preterm neonates born before 37 completed weeks of gestation in RRMCH, Bangalore. The exclusion criteria whereas follows: admission after 1 postnatal day, birth in another hospital, major congenital malformations, presence of chromosomal abnormalities, monochorionic diamniotic infants experiencing twin - to - twin transfusion syndrome and term infants.

2. Materials and Method

Hematological investigations were routinely performed among NICU preterm SGA infants. All blood samples from enrolled infants were collected into EDTA (ethylenediaminetetra acetic acid dipotassium salt dehydrate) laboratory tubes within 3 hours after admission to the NICU. The sample volume was 1 to 2 ml, complete blood counts and reticulocyte counts were analyzed using a

Sysmex XN - 1000 system (Sysmex Ltd. Kobe, Japan). The normal reticulocyte count at birth is unknown. However, as Paterakisreported that reticulocytes comprise 17% - 50% of normal umbilical cord blood, it is presumed to be about the same level.2 In this study, the median reticulocyte count during the early postnatal period was 60.1% (range: 21.9 to 148.6). For this reason, 60% was set as a cut - off value, with reticulocyte counts less than 60% classified as low, and with those 60% or more classified as high in this study.

The following perinatal variables were examined: sex of the child, multiple birth (singleton or twin), birth weight (BW), Apgar determined at 5 min, gestational age, use of tracheal intubation, umbilical artery pH, nucleated erythrocyte counts, red blood cell, reticulocyte counts, WBC, neutrocyte, platelet count, mean platelet volume (MPV), maternal age, height, experience of infertility treatment, smoking history, consumption of alcohol, experience of GDM, HDP, chorioamnionitis, receipt of antenatal corticoid therapy, and type of delivery. **SPSS (Statistical Package For Social Sciences)** version 21. (IBM SPASS statistics [IBM corporation: NY, USA]) was used to perform the statistical analysis.

3. Results

Out of 22 multigravida patients (62.9%), 13 (65%) were AGA and 9 (60%) were SGA and out of 13 primigravida patients (37.1%), 7 (35%) were AGA and 6 (40%) were SGA. (p=0.76) 5 patients (14.3%) had chorioamnionitis, of which, 4 (20%) were AGA and 1 (6.7%) were SGA.15 patients (75%) in AGA group had received one dose of AN steroids and 8 patients (53.3%) were in SGA group.4 patients (11.4%) in SGA group had received two doses of AN steroids. (p=0.04) The mode of delivery was E - LSCS in 16 patients (80%) in AGA group and 10 patients (66.7%) in SGA group. LSCS in 1 patient of AGA and SGA group, each.3 patients (15%) were NVD in AGA group and 4 patients (26.7%) were NVD in SGA group. (p=0.66)
The correlation between AN steroids and SGA/AGA was statistically significant in our study. (p=0.04) (Table 1)

Table 1: Distribution of the Subjects based on Gravida, Chorioamnionitis, An Steroids and Mode of Delivery

			AGA/SGA		Total	Chi - square value	p value
			AGA	SGA			
Gravida	Multi	Count	13	9	22	0.092	0.762
		%	65.0%	60.0%	62.9%		
	Primi	Count	7	6	13		
		%	35.0%	40.0%	37.1%		
Chorioamnionitis	No	Count	16	14	30	1.24	0.26
		%	80.0%	93.3%	85.7%		
	Yes	Count	4	1	5		
		%	20.0%	6.7%	14.3%		
AN Steroids	1 dose	Count	15	8	23	6.03	0.049*
		%	75.0%	53.3%	65.7%		
	2 dose	Count	0	4	4		
		%	0.0%	26.7%	11.4%		
	No	Count	5	3	8		
		%	25.0%	20.0%	22.9%		
Mode of Delivery	E - LSCS	Count	16	10	26	0.83	0.66
		%	80.0%	66.7%	74.3%		
	LSCS	Count	1	1	2		
		%	5.0%	6.7%	5.7%		
	NVD	Count	3	4	7		
		%	15.0%	26.7%	20.0%		

*significant

The mean APGAR 5 score in AGA score was 8.250 ±.6387 and in SGA score was 8.400 ± 0.7368. (p=0.52) The mean RBC in AGA score was 4767.50 ± 677.76 and in SGA group was 4508.00 ± 731.36. (p=0.28) The mean reticulocyte count in AGA was 2.81% ± 1.50 and in SGA group was 4.58% ± 2.30%. (p=0.01) The mean WBC count in AGA was 13442.50 ± 4262.144 and in SGA group was 11504.00 ± 6123.645. (p=0.27) The mean neutrocytes in AGA group was 57.600 ± 6.6917 and in SGA group was 53.600 ± 12.1761. (p=0.22)

Table 2: Comparison of the Quantitative Parameters between the groups using Independent Sample T Test

Parameters	Groups	N	Minimum	Maximum	Mean	S. D	Mean diff	p value
APGAR 5'	AGA	20	7.0	9.0	8.250	.6387	- 0.15	0.52
	SGA	15	7.0	9.0	8.400	.7368		
RBC	AGA	20	3820.0	6650.0	4767.50	677.76	259.5	0.28
	SGA	15	3160.0	5430.0	4508.00	731.36		
Reticulocyte Count	AGA	20	1.10%	7.10%	2.81%	1.50%	- 1.76	0.01*
	SGA	15	1.10%	10.00%	4.58%	2.30%		
WBC	AGA	20	6510	19670	13442.50	4262.144	1938.5	0.27
	SGA	15	4910	25740	11504.00	6123.645		
Neutrocytes	AGA	20	46.0	73.0	57.600	6.6917	4	0.22
	SGA	15	30.0	76.0	53.600	12.1761		

*significant

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1 patient (6.7%) in the SGA group had platelet count <1.5 lakhs, 20 patients in AGA group and 14 patients (93.3%) in SGA group had platelet count >1.5 lakhs. (P=0.24) (Table 3)

Table 3: Distribution of the subjects based on Platelet Count

Platelets		AGA/SGA		Total
		AGA	SGA	
< 1.5 L	Count	0	1	1
	%	0.0%	6.7%	2.9%
> 1.5 L	Count	20	14	34
	%	100.0%	93.3%	97.1%
Total	Count	20	15	35
	%	100.0%	100.0%	100.0%
Chi - square value - 1.37				
p value - 0.24				

4. Discussion

SGA is multifactorial and is associated with risk factors such as pre - pregnancy weight, previous history of SGA, smoking, and cardiovascular - associated diseases. Fetomaternal conditions complicated by placental insufficiency and/or fetal hypoxemia are associated with SGA or HDP.[13, 14]Thrombocytopenia is a common finding in small for gestational age (SGA) neonates and is thought to result from a unique pathophysiologic mechanism related to chronic intrauterine hypoxia.**1**[5, 16]However, in the present study, only one patient in the SGA group had thrombocytopenia.

Christensen reported that platelet counts generally increased to >150 x 10^9 /L by 2 weeks after birth, and no neonates showed pathological bleeding.[9] Similarly, in the present study, 1 patient (6.7%) in the SGA group had platelet count <1.5 lakhs, 20 patients in AGA group and 14 patients (93.3%) in SGA group had platelet count >1.5 lakhs. Thus, a perinatal confounder, such as systemic inflammation, may have influenced the results. However, chorioamnionitis was more frequently observed among non - SGA infants than among SGA infants in this study.

A systematic review and metaanalysis by Blankenship SA et al observed that ACS reduces neonatal mortality in SGA infants delivered preterm, with no apparent effect on neonatal morbidity.[17] This supports the use of ACS to reduce neonatal mortality in pregnancies with SGA infants at risk for preterm birth. The correlation between antenatal corticosteroids and SGA/AGA was statistically significant in our study. (p=0.04)

Interestingly, preterm infants with SGA had a higher Apgar at 5 min. These results suggest that although the intra - uterine environment was not particularly good in clinical terms, preterm infants with SGA adapted more rapidly to the postnatal environment than did the preterm infants who were not SGA. Furthermore, an increased in erythrocyte counts was observed among preterm infants with SGA. It is known that erythropoietin, which is the major chemical regulator of erythropoiesis, is produced by the kidneys in response to reduced renal oxygen tension.[18] As reticulocytes are the earliest red blood cells observed in the peripheral blood, in the case of increased erythropoiesis, it is expected that a large number of reticulocytes will circulate for 24 to 48 hours.[12]Similarly, we observed a higher reticulocyte count was observed among preterm infants with SGA than among those who were not SGA in this study. This suggests that an increase in reticulocyte count might be a physiological response to the rapid environmental change from inside to outside the uterus during the early postnatal period.

5. Conclusion

In conclusion, we observed significant relationships between SGA and antenatal corticosteroids, and reticulocyte counts in this study. A suggests that an increase in reticulocyte count might be a physiological response to the rapid environmental change from inside to outside the uterus during the early postnatal period. Further studies on larger populations are necessary to evaluate the clinical significance of neonatal reticulocyte count.

6. Future Scope

The strengths of this study are the data analysis of 30 patients performed prospectively. The inclusion criteria were strict, and the sample quality was standardized. Furthermore, this study was single - center in design, so that differences in management among centers can be inferred to have had little effect on the analyzed data. On the other hand, our study has some limitations. First, this study included some possible selection bias. Only NICU infants were included; therefore, our results may not be adequate in terms of physiological interpretation. Second, it was difficult to assess the cause of SGA. Exclusion criteria were set in advance; however, the cause of SGA could not be identified.

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