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Pattern of Decline of Foetal Haemoglobin in Healthy Full-term Infants

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Summary

Ogala WN. Pattern of Decline of Foetal Haemoglobin in Healthy Full-term Infants. *Nigerian Journal of Paediatrics* **1985; 13:17.** Foetal haemoglobin levels were serially determined, using the modified Betke alkaline denaturation method between the ages of 1 day and 6 months, in a cohort of 99 healthy full-term babies. The mean values (percent) were: 1 day 70.2±10.6, 1 week 63.8±10.1, 2 weeks 57.3±10.6, 6 weeks 44.2 ±12.3, 3 months 16.9±6.8, 6 months 3.4±3.5. This pattern of decline of foetal haemoglobin was identical with those reported from most parts of the world. Foetal birthweight and sex, maternal parity, method of delivery and the presence of haemoglobin S in the heterozygous form did not influence the values.

Introduction

INTEREST in the clinical significance of foetal haemoglobin (HbF) developed in the middle of this century after Singer and his colleagues[1 2] had shown that its levels were significantly raised in persons with sickle-cell anaemia (HbSS) and β-thalassaemia. Following the modifications of the original method of quantitation (one-minute alkaline denaturation of Singer, Chernoff and Singer[1]) by Betke, Marti and Schlicht[3] which ensured greater accuracy at low HbF levels, measurement of HbF has become a major haematological research and diagnostic procedure. In Nigeria, the only reported quantitative study of HbF in infants was by Hendrickse *et al*[4] in Ibadan. However, these workers[4] used the method of Singer and his colleagues[1] while their sample size towards the end of their study period was small. The present study was carried out in order to establish normal HbF levels in Nigerian children using the method of Betke, Marti and Schlicht.[3]

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Subjects and Methods

The subjects included infants born either by normal vaginal delivery or by lower segment caesarean section without labour, to Nigerian parents of various ethnic origins and socio-economic status, at the Ahmadu Bello University Teaching Hospital, Kaduna. In each case, the pregnancy and labour had been uneventful. The babies were full-term, normal, healthy singletons who had no perinatal asphyxia and were appropriate for gestational age. Clinical

assessment for the gestational age was by the method of Dubowitz, Dubowitz and Goldberg[5] which has been found applicable to African newborns[6 7] and by the maternal menstrual dates. Informed verbal consent was obtained before an infant was entered into the study.

One ml of serial blood samples was taken by venepuncture from a femoral or an antecubital vein at the following ages: 1 day, 1 week, 2 weeks, 6 weeks, 3 months and 6 months. Blood samples were collected in plastic EDTA tubes and taken for HbF estimation within 2 hours of collection. During each sampling stage, any infant was excluded from sampling if found on clinical examination, to be significantly ill or, from the history, to have had blood transfusion.

Haemoglobin F was quantitated by the modified Betke alkaline denaturation method as described by Dacie and Lewis.[8] Haemoglobin electrophoresis was performed on each infant at the ages of 1 day and 6 months by the cellulose acetate method using the buffer tris-EDTA-borate (pH 8.6) in a Shandon Southern chamber according to the method described by Dacie and Lewis.[8]

HbF values were correlated with infants' birth weights and sex, maternal parity and method of delivery on the first postnatal day and with haemoglobin genotype on day 1 and six months of age.

Statistical analysis of the data obtained was by means of the student t test.

Results

A total of 99 infants, 50 males and 49 females, was entered for the study. The mean gestational age was 38.8 weeks (range 38–40 weeks). The birthweights ranged from 2,600g to 4,600g (mean 3,300g) and the mean Apgar score at both 1 and 5 minutes was 8.9 (range 7–10).

The mean HbF values are shown in Table I. The fall in HbF was gradual from a high mean value of 70.2 ± 10.6% on day 1 to a low level of 3.4 ± 3.5% at 6 months of age.

TABLE I

Foetal Haemoglobin Values in the First Six months of Life

Age	*Foetal Haemoglobin (%)*		
	Mean	*SD*	*Range*
1 day (n= 91)	70.2	10.6	36.7 - 89.3
1 week (n = 90)	63.8	10.1	35.0 - 80.4
2 weeks (n = 83)	57.3	10.6	24.6 - 76.4
6 weeks (n = 78)	44.2	12.3	10.2 - 62.5
3 months (n = 67)	16.9	6.8	5.2 - 36.2
6 months (n = 64)	3.4	3.5	0.35 - 25.7

n = Number of samples tested

SD = Standard deviation

On the first postnatal day, 10 out of 94 babies tested had sickle-cell trait (HbAS), and at 6 months, 10 out of 66 of these babies had the same abnormal genotype. One baby had the haemoglobin AC genotype while there was no case of sickle-cell anaemia (HbSS). As there was no case of HbSS, the data from all the subjects were combined for analysis.

Infant birthweight, sex, maternal parity, method of delivery and the presence of haemoglobin S in the heterozygous form had no influence on the values of HbF (Tables II and III).

Discussion

Since no further screening tests for the thalassaemias were carried out in the present study, it was not possible to include the effect of β-thalassaemia on the HbF values. However, β-thalassaemia is known to be very rare in Nigeria.[9]

The mean values of HbF showed a consistent linear fall throughout the study period with the individual values showing a wide range at each

TABLE II

Foetal Haemoglobin Levels on the First Day of Life in relation to some Variables

Variable	*No of Cases*	*Mean (%)*	*Standard Deviation*	*P*
Sex				
Male	47	69.9	9.0	>0.5
Female	44	70.4	12.1	
Birthweight (kg)				
2.6–3.4	53	70.1	11.0	>0.5
3.5–4.6	38	70.3	10.0	
Parity				
0–1	33	69.5	11.8	>0.5
2–8	58	70.8	9.8	
Mode of Delivery				
Normal vaginal	27	70.0	9.1	>0.5
Caesarian section	64	70.2	11.2	

HbF = Foetal haemoglobin

age. This pattern of postnatal decline was identical with that reported in both Nigerian and caucasian infants by previous workers.[4 10 11] However, there were differences between the mean values of the present study (70 2% at 1 day, 63.8% at 1 week, 57.3% at 2 weeks, 44.2% at 6 weeks, 16.9% at 3 months and 3.4% at 6 months) and those of the previous ones at the corresponding ages. Colombo *et al*[10] had mean values of 64.8%, 59.6%, 45.2%, 21.9% and 2.3% at ages 1 day, 1 week, 6 weeks, 3 months and 6 months respectively, while Mason *et al*[11] had mean values of 69.6%, 67.8%, 64.8%. 20.2% and 7.3% at ages 1 day, 1 week, 2 weeks, 3 months and 6 months respectively. The main reason for these differences is likely to be related to the differences in the gestational ages of the infants selected for studies, since it is well known that HbF level falls with increasing gestation.[12] Whereas the present study selected for analysis, only babies of 38 to 40 weeks gestation, Colombo *et al*[10] and Mason *et al*[11] selected for their studies, babies of 37 to 41 weeks gestation. It is also possible that these differences are due to abnor-

TABLE III

Foetal Haemoglobin Values in HbAS and HbAA Infants

	At 1 day			*P*	*At 6 months*			*P*
	No of Cases	*Mean HbF (%)*	*SD*		*No of Cases*	*Mean HbF (%)*	*SD*	
HbAA	79	70.1	10.8	>0.5	54	3.1	2.4	>0.1
HbAS	10	70.9	9.9		10	4.9	7.4	

HbAA = Haemoglobin AA
HbAS = Haemoglobin AS
HbF = Foetal haemoglobin

malities of HbF production such as occur in the various forms of the hereditary persistence of foetal haemoglobin [13 14] or in association with other haematological disorders.[15]

Two infants in the study had at six months, HbF levels which were well above the 95% confidence limit for this age—25.7% and 17.2%. The infant who had the HbF of 25.7% had haemoglobin A and S and the other had the normal haemoglobin A. It could not be concluded from the design of this study whether they were cases of abnormal persistence of HbF or normal variations as reported by Chernoff and Singer.[16] The infant with HbAA could have been HbA with hereditary persistence of foetal haemoglobin (HbA/HPFH), while the other could have been an example of HbS/$\beta^{+}\pm$ thal with persistent HbF. A longer follow-up of these subjects will be helpful in resolving this problem.

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