International Journal of Contemporary Pediatrics
Roy SK et al. Int J Contemp Pediatr. 2021 Mar;8(3):434-439
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20210522

Original Research Article

Study of fetal hemoglobin with different gestational age and birth weight of the newborn

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Received: 13 January 2021
Accepted: 08 February 2021

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ABSTRACT

Background: In many parts of the developing country estimation of antenatal gestational age is still not possible and challenging condition of proper perinatal care. This study aimed to find out relationship between the gestational age and birth weight of the newborn with fetal hemoglobin concentration.
Methods: In this comparative study, we included 90 pregnant women who delivered their babies by normal vaginal delivery. Out of these 90 babies, 27 were preterm with gestational age 28-36 weeks, 55 were term with gestational age 37-41 weeks and remaining 8 were post term with gestational age of more than 41 weeks. All these 90 newborn infants were also divided into two groups: low birth weight (birth weight <2.5 kg) and birth weight ≥2.5 kg. Fetal hemoglobin was estimated by using alkali denaturation technique of Chernoff and Singer on appropriate spectrophotometer. Statistical analysis was performed using SPSS windows version 20.0 software.
Results: The total number of newborns were significantly ($p<0.001$) higher in term group and with normal birth weight group. Fetal hemoglobin level was significantly ($p<0.0001$) lower in term, post term and normal birth weight groups. Study showed a definite negative correlation between gestational age and the fetal hemoglobin concentration. Fetal hemoglobin level was gradually declining with increasing gestational age and birth weight.
Conclusions: It is concluded from this study that the concentration of fetal hemoglobin decreases at the rate of 2.4% per week with considerable variation of values at every week of advancing gestational age. Hence level of fetal hemoglobin estimation can be taken as an important criterion for evaluation of gestational age.

Keywords: Birth weight, Fetal hemoglobin, Gestational age, Infants

INTRODUCTION

Preterm birth influences over 15 million newborns each year and is the chief cause of neonatal mortality and morbidity globally, complications from which are the foremost cause of neonatal mortality, and contributes to 38-42% of all deaths under the age of five year. The saddle of preterm birth is particularly high in resource-poor settings where major risk factors including infection, inadequate nutrition, and poor socioeconomic circumstances are common. Knowledge of gestational age at the time of birth is critical for population level surveillance, to guide postnatal care by facilitating identification of infants with immediate high-resource needs and guiding developmental assessments. Differentiation of infants born by preterm birth versus those who are small for gestational age is important to further distinguish infant medical requirements. Unfortunately, in many low-resource environments limited access to prenatal ultrasound dating services and poor recall of self-reported menstrual histories impair accurate and timely gestational age assessment.[1] Hemoglobin has been the subject of intensive research for many years and is one of the most thoroughly understood

of all protein molecules. Hemoglobin is an iron containing protein complex, which in all vertebrates, is enclosed in a specialized cell, whose main function is transportation of oxygen from lungs to the tissues.[2] Hemoglobin syntheses start in the proerythroblasts stage of erythrocyte differentiation in the bone marrow and may continue even after the maturing erythrocyte has lost the nucleus and becomes a reticulocyte. The structure of hemoglobin consists of four polypeptide chains together with four heme groups and has a molecular weight of about 68000. The four goblin chains are held together by relatively weak forces and at an acid pH dissociation rapidly occurs. There are basically five globin chains designed by the Greek letters α, β, δ, γ and ε. The hemoglobin considered here is fetal hemoglobin (Hb-F), composed of 2α and 2γ chains.[3] Replacement of fetal hemoglobin by adult hemoglobin, in fact is essentially a maturational process not affected by the physical growth of the body but related more to length of gestation. In addition, the significance of fetal hemoglobin in evaluation of post conception age of the newborn babies is also reported in several studies.[4-7] The proportion of fetal hemoglobin in the cord blood is associated with gestational age and birth weight hence, Hb-F estimation in newborn can be recommended as an additional method for judging the degree of maturity of newborn when laboratory facility is available.[1] Considering the limitation of the methods mentioned above the present work has been undertaken to find out-(I) whether concentration of fetal hemoglobin has got any relationship with the gestational age and birth weight of the newborn. (II) Whether it could be used as a criterion for evaluation of gestational age of newborn and (III) whether it could be possible to grade the maturity status of the newborn by simple estimation of cord blood Hb-F.

METHODS

The present comparative study was performed in department of obstetrics and gynecology, at C.U. Shah medical college, Surendranagar, Gujarat, India for duration of two years from July 2014 to June 2016. Total 90 pregnant women were randomly selected from attending to the labor room, department of obstetrics and gynecology for the present study. After normal vaginal delivery all the newborns were grouped according to their gestational age. Out of 90 newborns, 27 were preterm with gestational age 28-36 weeks (group-I), 55 were term with gestational age 37-41 weeks (group-II) and remaining 8 were post term with gestational age of more than 41 weeks (group-III). Only those pregnant women were included for present study who were healthy and without any sign of any kind of illness, who had normal duration of menstrual cycle, normal labor with no sign of fetal distress and who had no history of bleeding during 1st two months after last menstrual period. Those pregnant women who had history of any systemic disease, malignancy, liver disease and any kind of blood disorders were excluded from study.

A comprehensive reproductive (period of gestation, present and past illness, obstetric history) and menstrual (LMP and EDD) history of all the women was taken and their general, physical and systemic examination was performed to exclude any disease which was known to affect the present study. Abdominal examination was also performed in references to contour & girth of abdomen, height of fundus, size of uterus, fetal presentation and position and auscultation of fetal heart sound. Furthermore, using a structured questionnaire, all pregnant women were interviewed to obtain information regarding their socio-demographic characteristics, physical activity, dietary characteristics, personal and family history of diseases and hospitalization record. Informed consent was obtained from all the women or their relatives prior to start of the study. The study protocol was approved by institutional ethics committee.

After normal delivery, all 90 newborn infants were divided into low-birth-weight infants <2.5 kg (group-I) and infants of birth weight ≥2.5 kg (group-II). It was assured that these newborns were free from any disease and they were not having any congenital malformations.

Anthropometric measurement was done after recording one-minute APGAR score and complete general, systemic, and external characteristics examination of each newborn.[8] The birth weight of newborns babies was recorded in kilogram by standard digital weighing scale. Blood samples were taken into double oxalate vials from the umbilical cords of all delivered newborn infants under aseptic conditions. Fetal hemoglobin was estimated by using alkali denaturation technique of Chernoff and Singer on appropriate spectrophotometer. [9]

Statistical analysis

Statistical analysis was done on IBM statistical package for social science (SPSS) version 20.0 and expressed as mean ± SD. Chi-square test and Fischer's exact chi square test were used for the comparison of qualitative data. Statistical analysis of the variance (fetal hemoglobin) between different gestational age and birth weight of newborn were compared by using unpaired independent student's-t test. The p values<0.05 were considered statistically significant.

RESULTS

The present comparative study was done in the department of obstetrics and gynecology, at C.U. Shah medical college, Surendranagar, Gujarat, India, total 90 cases were randomly selected from attending to the labor room, department of obstetrics and gynecology for the present study.

The distributions of male and female newborns in different gestational age groups are shown in Table 1. It has been observed that out of 90 cases, 27 were in preterm group (i.e., <37 weeks of gestation), 55 (61.11%)

were in term group (37-41 weeks) and 8 (8.89%) were in post term group (>41 weeks). In preterm group, 14(51.99%) were male and 13 (48.01%) were female newborns. Similarly, 26 (47.27%) were male and 29 (52.73%) were female newborns in term group while equal numbers of newborns were seen in post term group. The total newborns babies were statistically significantly higher in term group as compared to pre term ($p<0.001$) and post term ($p<0.001$) group as per chi square test while there was no statistically significant difference ($p>0.05$) observed in sex preponderance in either individual gestational age groups.

Table 1: Distributions of male and female newborns in different gestational age groups.

Gestational age groups (weeks)	Total no. of cases	Percentage (%)	Male	Percentage (%)	Female	Percentage (%)
Preterm (<37)	27	30	14	51.99	13	48.01
Term (37-41)	55	61.11	26	47.27	29	52.73
Post term (>41)	8	8.89	4	50	4	50
Total	90	100	44	48.89	46	51.11

The distributions of total newborns babies according to different birth weight groups are shown in Table 2. It has been observed that out of 90 newborns 55 (61.11%) were of equal to or more than 2.5 kg birth weight whereas 35 (38.89%) were of less than 2.5 kg birth weight. As per chi square test, newborns babies with normal birth weight were significantly higher ($p<0.01$) as compared to low-birth-weight group.

Table 2: Distributions of newborns according to different birth weight groups.

Birth weight groups (kg)	No. of cases	Percentage (%)
Groups-I (Birth weight <2.5)	35	38.89
Groups-II (Birth weight ≥2.5)	55	61.11
Total	90	100

The Table 3 shows the mean ± SD of the fetal hemoglobin level in different gestational age groups. The fetal hemoglobin (Hb-F) levels were significantly higher in preterm newborns ($p<0.0001$) and full-term newborns ($p<0.001$) groups as compared to newborns in post term group. Moreover, the fetal Hb-F level statistically significant ($p<0.001$) lower in newborns of full-term group when compared to newborns of preterm group while significantly ($p<0.001$) higher in newborns of term group as compared to newborns of post term group. This study shows a definite negative correlation between gestational age and the fetal hemoglobin concentration and the concentration of fetal hemoglobin decreases at the rate of 2.4 percentage per week with considerable variation of values at every week of advancing gestational age.

In the present study fetal hemoglobin concentrations were studied in relations to birth weights of the newborns. The fetal hemoglobin concentration was significantly ($p<0.0001$) higher in newborns of low-birth-weight group as compared to newborns in normal birth weight group. Fetal hemoglobin level was gradually declining with increasing birth weight. The present study reveals that fetal hemoglobin is higher in the low-birth-weight group than that weighing 2.5 kg and more.

Table 3: Fetal hemoglobin level in different gestational age groups.

Gestational age groups (weeks)	Total no. of cases	Hb-F level in %			
		Range	Mean	SD	SEM
Preterm (<37)	27	64.7-84.4	78.73	7.91	1.37
Term (37-41)	55	50.0-83.4	68.75	7.82	1
Post term (>41)	8	42.0-72.4	60.08	7.88	2.63
Comparison of all age groups and level of significant					
Preterm v/s term T value=5.41, p<0.0001		Preterm v/s post term T value=5.86 p<0.0001		Term v/s post term T value=2.92 p<0.001	

Table 4: Fetal hemoglobin level in relation to different birth weight.

Birth weight groups	No. of cases	Hb-F level in %				Level of significant
		Range	Mean	S.D.	SEM	
Groups-I (Birth weight <2.5)	35	55.70-86.0	82.36	9.88	1.58	t=9.10 p<0.0001
Groups-II (Birth weight ≥2.5)	55	42.0-83.40	66.032	7.11	0.911	

DISCUSSION

In this comparative study, we observed that the total newborns babies statistically significantly higher in term group as compared to pre term and post term group while there was no statistically significant difference observed in sex preponderance in either individual gestational age groups. The results of this study were similar to Decoste and Reis reported in comparative prospective study.[10] In addition, similar trends were also found in a Andrews and Willet they studied on 407 cases, of which 105 (25.8%) were in the preterm group, 280 (68.7%) in the term group, and 22 (5.4%) in post term group and Gupta et al studied 300 cases, of which 69 (23%) belonged to the preterm group, 224 (75%) to the term group and 7 (2%) to post term group.[11,12] The present series compares favorably with Schulman, Garbie, Andrews, Willet and Gupta et al as far as incidence of preterm babies in concerned.[5,11,12,14] Percentage of prefers cases in Deshpande et al study (42.6%) is higher than that of present series (30%) where as it is lower (8.3%) in Cotton's study, who had showed only 24 cases a rather small number for good comparison with the present one.[14,15]

In general, present study is similar but slight variations with studies of Armstrong, Ott and Olsen et al.[14,17,18] Present observations is similar to the observations of authors mentioned above with negligible variations.

The result of present study shows that out of 90 newborns, 55 (61.11%) were of equal to or more than 2.5 kg birth weight whereas 35 (38.89%) were of less than 2.5 kg birth weight as per the distributions of total newborns babies according to different birth weight.

In a series of cases studied by Decosta arid Reis, 22 (11%) belonged to the birth weight group less than 2.5 kg and 178 (89%) to be 2.5 kg and more.[10] The incidence of low birth babies is lower in the studies of Garbie, Andrews and Wilcox et al.[11,13,19]

There is significant interethnic difference observed in two studies which were done in developed countries by Mongelli et al and Robertson et al.[20,21] Birth weight standard should describe the population from which they were derived. In Deshpande's series has higher incidence of low birth weight than the present study.[14] This may be explained by decreasing incidence of low birth weight with improved socioeconomic living standard of population in last 28 years.

Our study shows a definite negative correlation between gestational age and the fetal hemoglobin concentration and the concentration of fetal hemoglobin decreases at the rate of 2.4% per week with considerable variation of values at every week of advancing gestational age. The results of present study are accordance with several studies were done by to Schulman, Walker, Cotton, Garbie, Gupta, Terrenato, Thomas, Al Mufti, and Black et al.[5,6,12,13,15,22-25] The higher level of fetal hemoglobin in percentage in different series of studies is due to different methods employed for estimation of fetal hemoglobin, method of collection of blood samples and associated maternal diseases responsible for intrauterine anoxia in fetus.

Fetal hemoglobin is produced primarily by the liver and the spleen and adult hemoglobin is produced by the bone marrow. Fetal hemoglobin is perhaps, an expression of general fetal metabolism and not dependent on specific sites of origin. If the bone marrow is capable of producing adult hemoglobin in the last trimester, we would expect fetal hemoglobin to decrease in concentration with increasing gestational age.[15]

In our study the fetal hemoglobin concentration was significantly higher in newborns of low-birth-weight group as compared to newborns in normal birth weight group. Fetal hemoglobin level was gradually declining with increasing birth weight which is comparable with another study done by Thomas and Fagan et al.[6,26] Similar inferences also has been drawn by Abrahamo et al, with demonstrating same fetal hemoglobin concentration in dizygotic twins of different birth weights.[27] The higher values of fetal hemoglobin concentration in the preterm groups as compared to the term and post term group indicate their inverse relationship with length of gestation but not to that extent with the birth weight. Conversely, the observations of Garbie and Andrews et al were higher than those of present finding.[11,13] This difference can be explained by the fact that percentage of truly premature (25%) in Garbie et at study and in Andrews and Willet series (25.8%) were very high compared to the percentage of newborns, weighing less than 2.5 kg. The difference in results among various series may be due to nutritional, racial and geographical variation as well as due to difference in the method of collection of blood and estimation of fetal hemoglobin. In contrast, the results of Deshpande study, were very low as compared to those of the present series which can be explained by the fact that there only 42.6% neonates were in preterm group and 46% in low birth group.[14]

It is well known that morbidity and mortality vary inversely with the gestational age, prematurity being one of the most important causes of prenatal mortality. Similarly, when pregnancy advances beyond term the risk of prenatal mortality again rises. Walker J ,[22] states that post maturity constitute a risk for fetal life by increasing the rate of still births, fetal distress during labour and neonatal death. These complications may appear without any obstetrical complications due to senescence of placenta with post conceptional age advancing beyond term, resulting in fetal anoxia.

Any objective indices, therefore, for the determination of maturity status of the newborn as far as gestational age is concerned will definitely be of much importance. In the

present study the results and investigations suggested that concentration or fetal hemoglobin in cord blood could provide significant information as an index of maturity which is in conjunction with results of anthropometric measurements and physical examination may also indicate true gestational age of the newborn. It is not possible and practical to do fetal hemoglobin estimation in all the cases except where accurate gestational age assessment is essential for diagnosis and management of preterm and small for date newborn.

There are few limitations of the study, first is that, this is a comparative hospital-based study, further a prospective cohort study studies are needed to investigate the interactions between fetal hemoglobin with different gestational age and their relation with birth weight of the newborn. Second point of consideration is that we did not include the physical characteristics and anthropometric measurement such as length of infants, birth weight, head circumference, chest circumference and crown rump length which might be accountable for estimation of the gestational age of newborn babies.

CONCLUSION

From the outcomes of our study, we conclude that term and normal birth weight newborns babies were more than preterm and low birth weight newborns babies, respectively. In addition, a definite negative correlation has been observed between gestational age and fetal hemoglobin concentration. The concentration of fetal hemoglobin decreases at the rate of 2.4% per week with considerable variation of values at every week of advancing gestational age. Moreover, the level of fetal hemoglobin was declining with increase in birth weight. The decline is more consistent with gestational age than birth weight. Hence level of fetal hemoglobin estimation can be taken as an important criterion for evaluation of gestational age.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Roy SK, Shrivastava AK, Choudhary PR. Study of fetal hemoglobin with different gestational age and birth weight of the newborn. Int J Contemp Pediatr 2021;8:434-9.