AGE AT MENARCHE AND FIRST CONCEPTION IN SICKLE CELL HEMOGLOBINOPATHY

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ABSTRACT

Sickle cell hemoglobinopathy has emerged as a major public health problem in the tropical countries of the world including India. This paper deals with the age at menarche and first conception of women in relation to sickle cell genotypes. The mean age at menarche was slightly higher in sickle cell affected girls compared to controls. The delay in onset of menarche affects the age at first conception of the sickle cell afflicted individuals.

Key words: *Menarche, Age at first conception, Sickle cell genotypes, Hemoglobinopathy, Western Orissa.*

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The age at onset of first menstrual cycle in adolescent girls is to a large extent genetically controlled physiological bioevent. However, the nongenetic factors like latitude and ecological setting, ethnic background, socio-economic status, food habits, moral and psychic environment, *etc.* also influence the attainment of menarche(l,2). Hemoglobinopathy seems to play a major role in influencing the age at menarche(3).

Sickle cell hemoglobinopathy has emerged as a major public health problem in India(4). There are several regions of the country which are under the ravage of this hereditary disease so much so that there exists a sickle cell belt in Western (Maharashtra, Gujarat and Rajasthan), Central (Madhya Pradesh) and Eastern (Orissa and Andhra Pradesh) parts of India. To **a** large chunk of the population of this belt, it causes high morbidity, mortality and, health hazards affecting their normal life(5). It has not even spared the human physiology, growth and development, and sexual maturation of the afflicted persons and thus has become a focal point of research in India.

The aim of the present study is to find any change in the age at menarche of the persons afflicted with sickle cell hemoglobinopathy and consequent effect on the age at first conception.

Material and Methods

This study was carried out at the Field Station of Regional Medical Research Centre (ICMR), V.S.S. Medical College-Hospital, Burla (Sambalpur) in Orissa. All the suspected cases of sickle cell hemoglobinopathy were referred to this station from Medical Out Patient Departments and wards and the female subjects attending this Field Station formed our study group for the present investigation. They were consecu-

tively selected from the general rural population of Western Orissa and were not related to each other. All the subjects had almost similar climatic conditions, socio-economic status, food habits, life-style, *etc.*

The diagnosis of the abnormal hemoglobin was established in our laboratory as per the standard procedure(6).

All the subjects were diagnosed as normal controls (HbAA), sickle cell trait (HbAS) and sickle cell disease (HbSS) and the subjects with other abnormal hemoglobins genotypes were excluded from the study. All the female subjects aged 8 years and above who were referred to us for hematological investigations were asked the age at which they had first menstruated. In the women who had atleast conceived once, the age of first conception was recorded employing the status quo as well as retrospective methods dependent upon recall based on outstanding events in that calendar year. To all these rural married women who were either cohabiting with their husbands or otherwise, use of any contraceptive measure was determined. None bf them used any contraceptives after- the marriage but only three women (HbAA) reported about the use of rhythmic method for the initial one year. Further, the age at marriage and consummation, in most of these cases, almost coincided with the age at menarche. The response to our queries was very good and almost all the cases provided accurate information.

The data so collected were subjected to statistical analysis employing the one way analysis of variance, F-ratio and Studentized range for critical difference to find out the significance of the difference, if any.

Results

The distribution of age at menarche in relation to various sickle cell genotypes is given in *Table I.* It is apparent from the Table that the majority of the girls start their first menstruation cycle at the age of 14 (28.9%), 15 (27.4%) and 13 (16.3%) years in Western Orissa. The lowest age was recorded to be 10 years and the maximum as 19 years.

The mean age of menarche with standard deviation was 14.07 ± 1.34 and 14.93 ± 1.55 years for sickle cell trait and sickle cell disease, respectively. In normal control (HbAA) girls, the mean age of menarche was 13.71 ± 1.37 years. This normal age of menarche was consistent with the range of 11.5 to 13.6 years earmarked for the Indian girls(7). There was slightly elevated or delayed mean menarcheal age of the girls affected with sickle cell gene as compared to controls *(Table I),* though the difference was not statistically significant when F-test was applied.

Table II gives the distribution of age of women at which they had conceived for the first time according to different sickle cell genotypes in comparison to controls. The range varies between 14 to 27 years of age in case of sickle cell trait and controls, whereas for homozygous sickle cell disease cases, it was between 18 to 25 years *(Table II).* It is apparent from *Table II* that the mean age at first conception of women with sickle cell disease is delayed as compared to controls as well as sickle cell traits ($p < 0.001$). The difference between controls and sickle cell traits was statistically significant ($p < 0.01$).

To find the difference, if any, for the delay in age between menarche and first conception of various women with sickle cell genotypes and controls, the analysis of data is presented in *Table III.* The mean age

TABLE I-*Distribution of Age at Menarche in Different Sickle Cell Genotypes and Controls (HbAA)*

Age at menarche (years)	Hemoglobin genotypes							
	HbAA		HbAS		HbSS		Total	
	No.	%	No.	%	No.	%	No.	%
10	0	0.0	1	0.7	0	0.0	1	0.4
11	2	4.2	0	0.0	1	1.2	3	1.1
12	10	20.8	16	11.9	2	2.3	28	10.4
13	7	14.6	24	17.8	13	14.9	44	16.3
'13	14	29.2	49	36.3	15	17.3	78	28.9
15	12	25.0	30	22.2	32	36.8	74	27.4
16	2	4.2	8	5.9	12	13.8	22	8.2
17	1	2.0	5	3.7 ..	5	5.7	11	4.1
18	0	0.0	2	1.5	5	5.7	7	2.6
19	0	0;0	0	0.0	2	2.3	2	0.6
Total	48	100.0	135	100.0	87	100.0	270	100.0
Mean		13.71		14.07		14.93		
SD		1.37		1.34		1.55		-

gap was statistically highly significant ($p<0.001$) for the women with various sickle" cell genotypes and controls. The mean gap in age for sickle cell heterozygote and sickle cell homozygote ($p<0.001$) and heterozygote and control women ($p<0.01$) was highly significant, the lowest being represented by the sickle cell trait women.

Discussion

The age at menarche is the most important physiological bioevent in the life of a girl at adolescence. The onset of menarche is dependent upon many factors including the affliction of disease. Abnormal hemoglobin genotype seems to influence the onset of menarche(3). In this context, the present study has revealed that the onset of menarche of girls afflicted with homozygous sickle cell disease and sickle cell trait was slightly, delayed as compared to the normal control girls (*Table I).* These findings get further support from Jamaican girls studied by Serjeant(8).

In Washington DC area of United States of America, a mean age of 13.9 years for menarche was noted as compared to 12.2 years among the normal Black controls(9). In Jamaica, the age of menarche in different studies of sickle cell disease patients with standard deviation has been 15.4 ± 1.7 years(10) and 15.7 ± 2.0 years(11) compared to a recent estimate of 13.1 ± 1.7 years among normal control girls(l0). In our series from India, the mean menarcheal age was 14.93 ± 1.55 years for the homozygous sickle cell disease cases as compared to 13.71 ± 1.37 years for the normal control girls. For the sickle cell trait cases, it

TABLE II - *Distribution of Age at First Conception in Different Sickle Cell Genotypes and Controls (HbAA)*

Age at 1st conception (years)	Hemoglobin genotypes							
	HbAA		HbAS		HbSS		Total	
	No.	%	No.	%	No.	%	No.	%
14	1	3.0	1	0.9	0	0.0	2	1.3
15	1	3.0	0	0.0	0	0.0	1	0.6
16	3	9.1	5	4.5	0	0.0	8	5.1
17	3	9.1	12	10.8	0	0.0	15	9.6
18	4	12.1	19	17.1	4	33.3	27	17.3
19	4	12.1	25	22.5	1	8.3	30	19.2
20	3	9.1	11	9.9	1	8.3	15	9.6
21	3	9.1	15	13.5	1	8.3	19	12.2
22	1	3.0	9	8.1	2	16.7	12	7.7
23	5	15.2	3	2.7	0	0.0	8	5.1
24	3	9.1	6	5.4	1	8.3	10	6.4
25	0	0.0	0	0.0	2	16.7	2	1.3
26	1	3.0	2	1.8	0	0.0	3	1.9
27	1	3.0	3	2.7	0	0.0	4	2.6
Total	33	100.0	111	100.0	12	100.0	156	100.0
Mean		20.0		19.8		20.8		-
SD		3.2		2.5		2.6		-

F-ratio = 9.385, $p<0.001$; HbAA *vs* HbAS, $p<0.01$; HbAA *vs* HbSS, P = NS; HbAS *vs* HbSS, $p<0.00l$; NS = Not significant; SD = Standard Deviation.

was slightly elevated (14.07 ± 1.34 years) compared to controls. Comparatively, the mean age at menarche was lower (14.93 ± 1.55 years) in the Indian girls afflicted with the sickle cell disease. The reasons for this lower mean menarcheal age from those of Jamaican girls (15.4 ± 1.7 - 16.1 ± 1.9 years) may be the genetic diversity of the background of the subjects, low fetal hemoglobin level, and other nongenetic factors.

In India, the minimum age at marriage is fixed as 18 and 21 years for girls (brides) and boys (bridegrooms), respectively. In our study, the mean age at first conception of women comes out to be around 20 years which is compatible with the age at marriage in India. However, in women afflicted with sickle cell disease, the age at first conception is delayed for about one year because, of sexual immaturity (delayed menarche) as compared to controls *(Table II).*

TABLE III-*Age Gap in Years Between Menarche and First Conception in Different Sickle Cell Genotypes and Controls (HbAA).*

Age at menarche (years)	Hemoglobin genotypes							
	HbAA		HbAS		HbSS		Total	
	No.	%	No.	%	No.	%	No.	%
1	3	9.1	5	4.5	0	0.0	8	.51
2	2	6.1	2	1.8	1	8.3	5	3.2
3	1	3.0	15	13.5	1	8.3	17	10.9
4	4	12.1	18	16.2	3	25.0	25	16.0
5	5	15.2	23	20.7	1	8.3	29	18.6
6	3	9.1	17	15.3	1	8.3	21	13.5
7	3	9.1	10	9.0	2	16.7	15	9.6
8	1	3.0	8	7.2	1	8.3	10	6.4
9	3	9.1	2	1.8	1	8.3	6	3.8
10	3	9.1	4	3.6	0	0.0	7	4.5
11	3	9.1	3	2.7	0	0.0	6	3.8
12	2	6.1	1	0.9	1	8.3	4	2.6
13	0	0.0	3.	2.7	0	0.0	3	1.9
Total	33	100.0	111	100.0	12	100.0	156	100.0
Mean		6.4		5.6		5.9		-
SD		3.3		2.7		2.7		-

F-ratio = 11.056, p<0.001; HbAA *vs* HbAS, p<0.0l; HbAA *vs* HbSS, p = NS; HbAS *vs* HbSS, p<0.001; NS = Not significant; SD = Standard Deviation.

The delay in menarche also affects the development of secondary sexual characteristics of the sickle cell disease individuals(8). A study of 91 Jamaican patients(10) indicated a mean delay of 3.9 years in age at first pregnancy compared to controls. In our series, this delay is about six years *(Table III)*. This delay may be accounted for partly to delay in menarche, first sexual exposure (consummation of marriage) and for socio-economic factors, among others. It has been postulated that the manifestations of the sickle cell mutation in Africa and in the Middle East are severer than the Indian counterparts(12). High levels of fetal hemoglobin are encountered among the sickle cell disease patients in India(13) which probably may affect the severity of the illness. It is likely to affect the age at menarche as well as prognosis of the sickle cell disease accordingly. Clinically, the mean age at menarche is lower among the Indian sickle cell disease patients having higher level of fetal hemoglobin as compared to

the Jamaican girls who have lower level of fetal hemoglobin and severe manifestations of the sickle cell disease.

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REFERENCES

1. Tanner JM. Growth at Adolescence. 2nd edn. Oxford, Blackwell Scientific Publications, 1962, pp 35-50.
2. Balgir RS. Age at menarche and menopause among the Sikligars of Punjab. J Indian Med Assoc 1985, 83: 195-197.
3. Balgvr RS. Menarcheal age in relation to ABO blood group phenotypes and hemoglobin E genotypes. J Assoc Phys India 1993,41:210-211.
4. Balgir RS, Sharma SK. Distribution of sickle cell hemoglobin in India. Indian J Hemat 1988, 6: 1-14.
5. Balgir RS. Sickle cell disease and its reproductive outcome in Western Orissa. A paper presented in the 80th Indian Science Congress held during 3-8 January 1993, Goa.
6. Dacie JV, Lewis SM. Practical Hematology, 6th edn. Edinburgh, Churchill Livingstone, 1984, pp 179-199.
7. Agarwal DK, Agarwal KN, Upadhyay SK, Mittal R, Prakash R, Rai S. Physical and sexual growth pattern of affluent Indian children from 5 to 18 years of age. Indian Pediatr 1992, 29: 1203-1282.
8. Serjeant GR. The sickle cell disease. Delhi, Oxford University Press, 1985, pp 269-278.
9. Jiminez CT, Scott RB, Henry WL, Sampson CC, Ferguson AD. Studies in sickle cell anemia. XXVI. The effects of homozygous sickle cell disease on the onset of menarche, pregnancy, fertility, pubescent changes, and body growth in Negro subjects. Am J Dis Child 1966, 111: 497-504.
10. Alleyne SI, D'Hereux Rauseo R, Serjeant GR. Sexual development and fertility of Jamaican female patients with homozygous sickle cell disease. Arch Intern Med 1981, 141: 1295-1297.
11. Ashcroft MT, Serjeant GR. Growth, morbidity, and mortality in a cohort of Jamaican adolescents with homozygous sickle cell disease. West Indies Med J 1981, 30: 197-201.
12. Nagel RL, Fabry ME, Pagnier J, Zohoun I.Wajcman H, Baudin V, Labie D. Hematologically and genetically distinct forms of sickle cell anemia in Africa: The Senegal type and the Benin type. N Eng J Med 1985, 312: 880-882.
13. Kulozik AE, Kar BC, Satapathy RK, Serjeant BE, Serjeant GR, Weatherall DJ. Fetal hemoglobin levels and β^s-globin haplotypes in an Indian population with sickle cell disease. Blood 1987, 69: 1742-1746.