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Prevalence of Male Sex among Families with Sickle Cell Anemia

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Summary. **In the present study the frequency of hemoglobin'S' was determined based on 10 tribal families and 31 non-tribal families of Andhra Pradesh, South India. The incidence of sickle cell anemia was found to be high in males as compared to females in both populations. Sickle cell trait remained more or less equal in both sexes. The gene frequency (q) of HbS was also predominantly high in males (0.231, 0.387 and 0.347) as compared with females (0.072, 0.297 and 0.241) in native, non-native, and pooled sample' respectively. Sex ratio in HbSS individuals in both groups was found to be 2: 1, which showed a statistical significance, whereas no such deviation was observed in heterozygotes (SS). There was no significant relationship between parental genotypes or sex ratio among offspring. It is known that in acute anemic conditions, the chain synthesis is switched on to combat anoxic conditions due to a lowered hemoglobin level. We have estimated HbF levels in different genotypes, i. e. AA, AS & SS. The mean HbF levels were significantly elevated in SS genotype. This indicates that the γ chain synthesis is an alternative in acute hemolytic episodes due to the sickling.**

Key words—sex ratio, sickle cell anemia, fetal hemoglobin, acute hemolytic episodes.

INTRODUCTION

Hemoglobin is a tetrameric protein carrying out the function of oxygen transport. Most of the hemoglobin variants cause alterations in rheology and erythrocyte morphology. Because of their prevalence and world wide distribution, the disorders resulting from hemoglobin variants S, C, D & E are of enormous clinical importance. Sickle cell anemia is the most common heritable hematological disease affecting humans.

Sickle cell anemia is a widely distributed, autosomal recessive disease caused by alterations in the 6th aminoacid of β globin chain, viz., valine is replaced by glutamic acid[13]. The most common clinical symptoms include hemolytic anemia, recurrent vasoocclusive episodes, widespread organ involvement and susceptibility to infections. Under such acute anemic conditions HbF having more oxygen affinity is resynthesized to compensate for lowered hemoglobin level due to red cell loss[5].

The highest prevalence of the HbS gene is seen in tropical Africa (45%)[17], US Blacks[12,19], Latin America and Caribbeans (8%)[14,20]. In India the HbS gene is mostly prevalent in native populations with frequencies ranging from 5 to 40% in Central India and South India[2,4]. A remarkable incidence of the HbS gene is also seen in caste populations of Andhra Pradesh, such as Rellis[16], and Malas[21].

The present study aims to assess the frequency of the HbS gene in males and females in families (native and non-native) with incidences of sickle cell anemia and also to estimate the levels of fetal hemoglobin, to analyse whether any compensatory mechanism operates in these affected individuals.

MATERIALS AND METHODS

Routine hemoglobin typing of patients with anemia referred to King George Hospital during the period from 1992-1994 revealed 10 tribal families and 31 non-tribal families of populations with HbS inci-

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Table 1. Frequency distribution of hemoglobin genotypes in males and females

Hemoglobin type	Male	Percentage	Female	Percentage
HbAA	17	15.3%	22	25.8%
HbAS	51	45.9%	46	54.1%
HbSS	43*	38.7%	17	20 %

*Deviation from 1, 1 ratio; $P<0.05$.

Table 2. HbS gene frequencies in males and females

	Male	Female
Tribal	0.231	0.072
Non-tribal	0.381	0.297
Pooled	0.347	0.241

Table 3. Distribution of HbS phenotypes with respective genotypes

Matings			no.	Affected individuals among offsprings	
Father	X	Mother		Males*	Females
AS	X	AS	27	21	10
SS	X	AA	2	1	1
AA	X	SS	3	0	1
SS	X	AS	1	1	0
AS	X	AA	5	2	1
AA	X	AS	3	7	1

*Significance deviation from a 1: 1 ratio.
N. B. The analysis was not done for other matings due to the small sampling size.

Table 4. HbF levels in different hemoglobin types

Hemoglobin type	Mean HbF
Hb AA	4.31±1.01
Hb AS	3.53±0.58
Hb SS	12.58±0.51

dence. After identification of the families, all available family members were tested for hemoglobin patterns by Cellulose acetate membrane electrophoresis at pH 8.9 using Tris, EDTA, Boric acid (TEB) buffer[7]. Fetal hemoglobin estimations of these individuals was done using a one-minute alkali denaturation test[18]. The data were presented as mean ±SD, comparisons between males and females were made with respect to frequency of hemoglobin genotype and sickle cell gene frequency (q) using appropriate statistical methods. Apart from this, the distribution ok male and female affected offsprings of among different parental combinations was also analysed.

RESULTS

Table 1 shows the distribution by sex of hemoglobin genotypes in both native and non-native populations. It can be observed that there is a high frequency of males with HbSS genotype and females with HbAS and HbAA genotype. Sex ratio deviates from the expected ratio of 1:1 ($2=8.85$, $p<0.05$). Further, HbS gene frequency (q) is predominantly higher in males (0.231, 0.381 & 0.347) as compared with females (0.072, 0.297 & 0.240) among native, non-native and the pooled sample, respectively (Table 2). The distribution of parental mating types and sex ratio among affected children is presented in Table 3. An interesting observation is the prevalence of affected males in heterozygote matings (AS×AS). The observed sex ratio in AS×AS matings is 2:1, significantly deviating from the expected sex ratio. Estimated levels of fetal hemoglobin in different hemoglobin genotypes (HbAA, HbAS and HbSS) are presented in Table 4. Elevated mean fetal hemoglobin (12.58±0.51) was observed in HbSS genotype individuals when compared with HbAA (4.3±1.01) and HbAS (3.5±0.5).

DISCUSSION

The incidence of sickle cell anemia was found to be high in males as compared with females in native as well as in non-native . In an earlier study, Kar et al[10] has also reported a high prevalence of males with sickle cell anemia as compared with females in the Orissa state population, whereas the sickle cell trait (AS) remains more or less equal in both sexes. Sex ratio in HbSS individuals in both native and non-native population was found to be a statistically significant 2:1. This may indicate prenatal selection operating against female homozygotes for the HbS gene. Further, there is a prevalence of affected males

among AS×AS parental mating.

The mean HbF levels are elevated significantly in SS genotype as compared to AS, AA genotypes (Table 4). High levels of HbF are said to be associated with a lower hemolytic rate of erythrocytes[10]. Sickle cell anemia with elevated fetal hemoglobin levels tend to have less severe clinical manifestations and a greater probability of survival[11,15]. Concentrations of HbF in erythrocytes affect the extent of S polymerisation and the sickling of red cells[3,6,8]. It is known that in acute anemia, the gamma chain synthesis is switched on to combat anoxic conditions, as HbF^{22} has more Oxygen affinity. Adekile and Huisman[1] noted that the mean HbF levels are some what higher in females than males among sickle cell anemia patients. In our study, however, males[12,6] and females[12,2] with the HbSS genotype did not differ significantly with respect to HbF level. These results are in accordence with the findings of Gupta et al[9].

The widely held opinion that HbF ameliorates the clinical severity in sickle cell anemia patients has still not been completely proven in different populations of the world.

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