IOSR Journal of Pharmacy and Biological Sciences (IOSRJPBS)
ISSN: 2278-3008 Volume 2, Issue 4 (July-August 2012), PP 06-08
www.iosrjournals.org

Prevalence of Hemoglobinopathies among the Konda Kammaras of Visakhapatnam District, Andhra Pradesh

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Abstract: *Hemoglobinopathies including the Sickle cell disease and the thalassemias, which are inherited recessively cause a serious problem across the world in general. In India the prevalence of sickle cell trait varies from 5-40% among many tribal populations from different states however the overall prevalence of beta thalassemia varies from 3-4% but varies from 1-17% in different ethinic groups. As these disorders are inherited prevention of this disease is therefore theoretically possible through population screening and counseling. The present study among the Konda Kammaras is done based on this concept. The present study aims to assess the prevalence of hemoglobinopathies among the Konda Kammaras of Visakhapatnam district. 103 unrelated individuals (50 male and 53 female) aged between 22-58 years were considered in this study. All the individual samples were screened by using NESTROFT, Complete blood count and Cellulose-acetate membrane electrophoresis. The suspected cases have been confirmed of the presence or absence of mutation status by sequence analysis. The overall prevalence of hemoglobinopathies among this population is 14.56% with 13.59% of Sickle cell trait and 0.97% Beta thalassemia trait.*

Keywords: *Beta thalassemia, Konda Kammara, Prevalence, Sickle cell, Visakhapatnam.*

I. Introduction

Hemoglobinopathies are the most common single gene disorders worldwide which are inherited autosomal recessively. These include the thalassemias which result due to disruption of co-ordinated synthesis of globin chains (Quantitative) and abnormal hemoglobin variants which result as a substitution of a single amino acid in either chains (Qualitative). Clinical manifestations include chronic hemolytic anaemia, jaundice, an increased propensity to infections, growth retardation, hepata-splenomegaly a number of complications due to chronic vascular occlusion like acute chest syndrome, liver disease, priapism, skin ulcers, proliferative retinopathy, renal insufficiency and acute exacerbations or crisis. Earlier, these are limited only to the Mediterranean regions, but recent migrations of people have spread the genes throughout the world. These are the commonest genetic defects worldwide with an estimated 269 million carriers [1] which include 90 million carriers from South East Asia, 85 million carriers from sub-Saharan Africa and 48 million from west Pacific region [2]. It is estimated that every year 60000 thalassemic babies are born all over the world [3].

The frequency of total hemoglobinopathies in India was reported to be 4.2%. A high frequency of HbS is predominantly found in tribal populations of Central and Southern part of India while HbE is widely distributed in North Eastern states and HbD is seen mostly in North India. The frequency of Beta thalassemia trait was reported to be varying from 1-17% which is detectable in almost every Indian population. In India, 30 million carriers and 15,000 infants with major hemoglobinopathies have been reported [4].

India has the world's second largest concentration of tribal population, next to Africa. With a population of 677.58 lakhs (1991 census), the 461 tribal groups of the country account for about one fourth of the world tribal population. Tribal populations have high risk for the beta globin gene defects [5]. In Andhra Pradesh 35 different tribal communities are distributed in 15 districts. Several studies on distribution of sickle cell hemoglobin among the tribal communities are available, at the same time there is no comprehensive data available on the interaction of thalassemias and abnormal hemoglobins. Hence this study aims to bring a base line data on the incidence of hemoglobinopathies and also to create awareness regarding the disease among the Konda Kammara, a tribal community from Visakhapatnam district.

II. Materials & Methods

The study includes 103 individuals of Konda Kammara tribe from Paderu, Peda bayalu, Munchinguput, G.Madugula mandals of Visakhapatnam district. They belonged to the age group 22-58 years. Prior consent was taken from every individual before conducting the study.

Konda Kammaras are a Scheduled Tribe inhabiting the scheduled areas and adjoining areas in Srikakulam, Vizianagaram, Visakhapatnam, East Godavari and West Godavari districts. They are also called Kammara or Metta Kamsali or Metti Kamsali or Ojas. Their population as per 1991 census is 44,613. Konda

Kammara tribe is divided into a number of totemic clans, which regulate marital relations among them. Some of the popular clans are Korra (Sun), Killo (Tiger), Bhallu (bear), Samardi (flower), Pangi (Kite) etc., and their surnames are identical with surnames of other tribal groups in Visakhapatnam district. Though the traditional occupation of Konda Kammaras of scheduled areas is black smithy and carpentry, most of them gave up their traditional occupation and resorted to shifting cultivation and settled cultivation. The total literacy rate among these Kammaras is 18.08%. They have traditional tribal council of their own, which regulates the social life of Kammaras and to settle the disputes.

Five ml of venous blood was collected in centrifuge tubes containing anti-coagulant and transported to the DNA laboratory of Human Genetics Department, Andhra University. Preliminary screening tests were conducted prior to molecular sequencing for the suspected samples. Naked eye single tube red cell osmotic fragility test (NESTROFT) was done for all the samples in the field itself. This technique is base on the limit of hypotonicity which the red blood cells can withstand [6]. A full blood count was performed on all samples by using an electronic red cell counter (Sysmex K 100 Japan). Cellulose acetate membrane electrophoresis at pH 8.6 in TEB buffer was performed to characterize the hemoglobin variants [7]. Fetal hemoglobin was estimated by alkali denaturation method [8]. Hemoglobin A_2 was estimated by elution [9]. DNA was isolated using phenol chloroform method. The suspected samples were sequenced for the β-globin gene defects using AB 3730 DNA Analyser in the DNA laboratory of Anthropological Survey of India ; Kolkata.

III. Results

From the preliminary screening tests done, out of 103 samples a total number of 30 cases (after excluding the overlapping cases) were suspected to have mutant allele for either thalassemia or hemoglobin variant. TABLE 1 shows the number of cases picked up using different screening procedures.

TABLE 1: Number of suspected cases picked up in each test

S.No	Test Conducted	Number of Cases	
		Male	Female
1.	NESTROFT	7	10
2.	Complete Blood Count (MCV<73 fl; MCH<23 pg)	13	16
3.	HbF > 1 %	2	3
4.	Hb A_2 > 3.5%	3	5

These samples were sequence analyzed for the detection of mutation.

The distribution of hemoglobin variants among the Konda Kammaras is summarized in TABLE 2. Among the 103 individuals screened, 88 were normal, while 14 individuals were HbS carriers and one individual was detected as beta thalassemia carrier. None were found to be homogygous for sickle cell disease. Sickle-thalassemia cases were also absent. Allelic frequencies were calculated using Gene Count Method.

TABLE 2: Distribution of Hemoglobin Variants among the Konda Kammara Population

Total No. of samples screened	Normal		HbAS		HbS		BTT	
	No	%	No	%	No	%	No	%
Male 50	44	88%	6	12%	0	0	0	0
Female 53	44	83.01%	8	15.09%	0	0	1	1.886%

BTT: Beta thalassemia trait

IV. Discussion

The geographical distribution of sickle cell disorder, beta thalassemia and other hemoglobinopathics in central eastern parts of India shows the differential migration pattern of the population. Earlier work done by Naidu et al [10], Banerjee et al [11], Rao et al [12], Blake et al [13], Goud et al [14], Sudhakar Babu et al [15] reported the presence of Sickle cell gene among the tribal populations from 0 - 31.79% . The prevalence of sickle cell trait is 13.59% in the present study with 0.067 HbS allelic gene frequency.

Out of the total thalassemias reported in India, β-thalassemia accounts for 80-90%. Beta thalassemia is a common hemoglobinopathy in India as per WHO records. The highest frequency of beta-thalassemia trait is reported in Gujarat, followed by Sindh, Punjab, Tamil Nadu, South India and Maharastra. There are several reports on the spectrum of mutations in different States of India [16,17]. Among the 200 thalassemia mutations across the world, 28 different β- thalassemia mutations have been identified among the Indians [18]. Due to the peculiar Indian population structure, the frequencies of these mutations vary considerably in different States [19]. The IVS 1 nt 5 (G→C) mutation is the commonest mutation found in Indian population and its prevalence

varies from 22.8 to 81.4% in different regions of India, the highest being Tamil Nadu [20]. In any population, there are few common mutations and some rare ones also. IVS 1 nt 5 (G→C), CD 8/9 (+G), CD 41/42 (-CTTT), CD15 (G→A), CD 30 (G→C) and 619 bp deletion can be accounted for majority of molecular defects seen in Indians along with HbS and HbE [17,21]. No study was done among the Konda Kammara population for the presence of beta thalassemia trait earlier. An attempt was made to screen for the mutations of beta thalassemia and 0.97% prevalence is found among this community.

V. Conclusions

Very few studies have been done for characterization of thalassemia mutations from the Andhra Pradesh State. These studies were hospital based. This study therefore provides for the first time, the type of β-thalassemia mutation prevalent among the Konda Kammara tribe of Andhra Pradesh. Among the hospital studies that were carried out in Andhra Pradesh, Bashyam et al, 2004 [22] reported IVS 1-5 (G□C), Codon 15 (G□A), CD 41/42 mutations while Anjana et al, 2009 [23] reported IVS 1-5 (G□C) and 6I9 bp deletion mutations. IVS 1-5(G□C) mutation is present in the single beta thalassemia carrier observed among the Konda Kammaras screened.

An extended study among these tribal populations would be of immense value for future reference and monitoring of these genetic disorders where ignorance, lack of awareness and publicity, low income status and high cost of treatment make these populations particularly vulnerable.

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