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H63D and C282Y HFE gene frequency in healthy population of Kol tribal in Madhya Pradesh, India

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ABSTRACT

HFE gene involve in iron metabolism while altered iron metabolism due to HFE gene mutation have been reported. Thus with the aim of the frequency of HFE gene mutation and iron status in Kol tribal had been explored. Study subject were 250 healthy Kol tribal. Frequency of H63Dmutation was present significantly while C282Y was also reported in heterozygous condition. Iron status was significantly high with HFE mutant condition than without presence of HFE mutation.

KEYWORDS

HFE;
Iron;
Kol;
Tribal.

INTRODUCTION

Kol is the second largest tribe of Madhya Pradesh after Gond. Kol tribe also found in Bihar,Orissa,Uttar Pradesh and Maharastra. Rewa, Sidhi, Satna, Shahadol, Jabalpur and Mandla district are the prime areas of this tribe. Their most dense population is in Rewa, Sidhi and Satna district of Madhya Pradesh. This tribe consider themselves as native of Farenda and Kurali village of Rewa district. On the basis of the census of 1991 the total population of the Kols was 1, 23,811 in Madhya Pradesh. As many as 22 sub-branches of the Kol tribe are accepted. Kol is one of the most ancient tribes of India. Tribal communities in India constitute the largest tribal population in the world[1].

In 1996, the HFE gene was identified on candidate for the gene bearing the primary defect responsible for hemochromatosis[2-4]. Genetic factors and acquired conditions are likely to modulate the expression of HFE hemochromatosis. Two missense mutations (C282Y, H63D) have been described on the HFE gene in patients suffering from hereditary hemochromatosis on the basis of phenotypic data. H63D is a C-G transition at nucleotide 187 of the HFE gene which results in a histidine to aspartic acid substitution. It has been found to be present with a frequency of 3.3%-15.2% in the general population across the world[5-7]. The H63D mutation has been found to be highly prevalent among Brazilians (carrier frequency: 27.5%), with a frequency similar to what is observed among white Europeans, particularly among Italians[8,9]. There are only a few studies from India on the frequency of the known HFE gene mutations[10-13].

Variations in prevalence of the HFE gene mutations

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(C282Y, H63D, S65C) have been established in many European populations and descent (United States, Canada, Australia, South Africa). Few studies are available from India on the prevalence of these mutations in the general population[13]. H63D is prevalent and C282Y is rare in north Indians and the presence of 63D mutation does not increase body iron as measured by serum ferritin in beta thalassemia traits[11]. Thus the aim of this study was to determine the prevalence of the HFE mutations in Kol tribal.. he present study is the first to report on the HFE gene frequency in the healthy Kol tribal population of Madhya Pradesh..

MATERIAL AND METHOD

A total of 250 healthy subjects of Kol tribal with age group of 15-40 year were selected for the study. About 5 ml venous blood was collected from the subjects after obtaining consents. Complete blood count and red cell indices were measured by automated cell analyzer. DNA was extracted from the peripheral blood leucocytes by phenol-chloroform method. HFE gene mutations H63D was determined by specific polymerase chain reaction restriction fragment length polymorphism (PCR-RFLP) according to Aysen Gunel-Ozcan[14] (2006) et. al. Serum iron, total iron binding capacity (TIBC) and % transferring saturation estimation was done by standard laboratory method. P-value <0.05 was considered statistically significant.

RESULT AND DISCUSSION

In present study, total 250 healthy Kol tribal subjects were collected from Rewa district of Madhya Pradesh. Out of them 140 were male (mean age = 25.3±2.4Yrs) and 110 were female (48 were in gestation and 62 were non gestation with mean age of 22.3±2.8 and 17.9±4.2 Yrs respectively). Hemogram and iron profile of subjects are presented in TABLE 1 and TABLE 2 respectively. Out of the 250 subjects, 21 (8.4%) were positive for the H63D mutation while 2 (0.8%) were heterozygous for C282Y mutation. Details are illustrated in TABLE 3. Subjects with presence of HFE mutation had high level of hemoglobin and ferritin level. Details are given in TABLE 4. A study report the prevalence of H63D heterozygosity was 12% in normal individuals, 14.8% in 236 patients. They did not found any individual with 282Y or 65C either in the cases or in the controls[15]. Their are limited studies on the role of HFE gene in iron overload in Asian Indians and they have identified mainly the H63D mutation. A previous study in liver disease from India also did not find C282Y mutation. A study analyzed 729 north Indian samples for C282Y and H63D mutations. Of these, no allele of the C282Y mutation was seen, while 3 homozygous and 43 heterozygous for the H63D mutation were seen in the patients of thalassemia group. However, 47 cases were found heterozygous for the H63D mutation among the normal groups (11.16%). In our study, 9.28% male population was heterozygous and 1.42% was homozygous for H63D while 2.4% females were heterozygous for H63D mutation. Neither the females were homozygous for H63D and nor male were homoozygous for C282Y mutation. However 1.42% male were heterozygous for C282Y mutation and none of the females were presenting C282Y mutation. Most of the earlier studies showed complete absence of C282Y mutation in Indian population[11,12,16-18]. However, a study observed a single case of C282Y/H63D compound heterozygote for the first time in India. The resultant allele frequency for C282Y mutation hence was 0.05[19]. In the Asian, Indian subcontinent, African/Middle Eastern, and Australasian populations, C282Y homozygotes were not found, and the frequency of C282Y heterozygosity was very low (range, 0–0.5 percent)[20]. In our cases the subject with HFE gene mutation had higher iron profile, hemoglobin and red cell indices than without presence of Hfe mutations and statistically significant. In conclusion H63D and C282Y

TABLE 1 : Complete blood count of subjects

Hematological variables	Mean ±SD (N=250)		
	Male (N=140) (25.3±2.4)	Female (N=110)	
		Gestation N= 48 (22.3±2.8 Yrs)	Non Gestation N=62 (17.9±4.2 Yrs)
WBC Ths/µl	8.15±2.1	8.25±2.3	7.95±3.5
RBCmillions/µl	4.55±0.8	4.09±0.80	4.59±0.6
HGB g/dl	12.7±2.5	10.24±2.1	11.1±1.3
HCT %	31.11±6.6	43.45±5.2	39.23±3.5
MCV fl	80.87±17.4	78.5±12.3	75.53±23.4
MCH pg	28.70±4.3	27.33±4.2	27. 2±3.5
MCHC g/dl	33.11±2.1	30.57±2.1	32.25±3.3
PLT Ths/µl	249.15±62.10	241.23±75.71	230.83±56.6

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TABLE 2 : Iron profile of subjects

Iron profile	Mean ±SD (N=250) Male (N=140) (25.3±2.4)	Female (N=110) Gestation N= 48 (22.3±2.8 Yrs)	Female (N=110) Non Gestation N=62 (17.9±4.2 Yrs)
Serum Ferritin µg/L	152.2±25.4	112.3±15.6	125.7±23.4
TIBC µg/dl	312.5±25.9	325.6±37.2	321.7±32.6
% Transferrin saturation-%	27.3±6.8	21.5±8.4	23.5±5.8

TABLE 3 : Molecular data of study

Gene mutation	Genotyping (N=250) Male (N=140) (25.3±2.4)	Female (N=110) Gestation N= 48 (22.3±2.8 Yrs)	Female (N=110) Non Gestation N=62 (17.9±4.2 Yrs)
HFE	Frequency (%)		
H63D	13(+/-) (9.28)	2(+/-) (4.16)	4 (+/-) (6.45)
	2 (+/+) (1.42)		
C282Y	2(+/-) (1.42)	-	-

TABLE 4 : Comparative iron profile with HFE and without HFE mutation

Parameters	Subject with HFE gene mutation (N=23)	Subject without HFE gene mutation (N=227)	P-Value
HGB g/dl	13.8±3.4	11.24±2.3	0.0001
Serum Ferritin µg/L	155.2±23.3	113.6±13.4	0.0001
TIBC µg/dl	314.5±27.9	328.6±35.3	0.0646
%Transferrin saturation-%	28.1±5.3	22.3±7.1	0.0002

mutation present significantly in Kol tribal population and further study needed to explore the role of HFE and iron metabolic gene in hereditary hemochromatosis as well as iron deficiency anemia.

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