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Glutathione S-transferase mutation and iron status in Kol tribals

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ABSTRACT

GST is a detoxification agent. Few study reported the GST polymorphism associated with iron status. Our aim of this study was to estimate GST gene frequency and iron status in healthy Kol tribals. Two hundred subjects were evaluated to determine the frequency of GST gene deletions. The GST null genotype was significantly present in population however their was no correlation was found with GST genotype and iron status.

KEYWORDS

GST;
Kol;
Tribal.

INTRODUCTION

The glutathione S-transferases (GSTs) are a multigene family of iso-enzymes which catalyze the conjugation of glutathione to electrophilic substrates. GST polymorphisms may be disease modifying, certain GST appear to exert a statistically significant and biologically relevant impact on disease susceptibility[1]. *GST* gene family encodes genes that are critical for certain life processes, as well as for detoxification and toxification mechanisms, via conjugation of reduced glutathione (GSH) with numerous substrates such as pharmaceuticals and environmental pollutants[2]. These enzymes catalyze the reaction of such compounds with the -SH group of glutathione, thereby neutralizing their electrophilic sites and rendering the products more water-soluble[3,4]. These enzymes are involved in the conjugation reactions between glutathione (GSH) and a variety of potentially toxic and carcinogenic electrophilic compounds. Additionally, GSTs display peroxidase activity and this can protect against oxidative damage. Deficiency in the activity of this enzyme may be due to inherited GST polymorphisms, e.g., GSTT1 (22q11.23); GSTM1 (1q13.3) and GSTP1 (11q13)[5,6]. Although the evidence is minimal for the influence of GST polymorphisms on susceptibility to various types of cancer, asthma, atherosclerosis, allergies, diabetes and other inflammatory diseases[7-9]. A recent study of GST polymorphism with SCD was found no correlation with iron overloading while HbE/beta thallasemia patient found relation with iron overloading[10,11]. There is no available literature on GST deletions in healthy population of Kol tribal. Thus the aim of this study was to estimate the prevalence of the GSTM1 and GSTT1 null genotypes in Kol tribal and their effect on iron status.

MATERIALS AND METHODS

The subjects were healthy population of Kol tribal with age group 15-40 Years. Five ml. venous blood samples were collected from subjects after consent was

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given. DNA extraction was done by the phenol-chloroform method. GSTM1 and GSTT1 null genotypes were determined by multiplex polymerase chain reaction (PCR) according to the published literature[12]. Iron profiling were done according to standard laboratory method.

RESULTS AND DISCUSSION

Total 200 healthy Kol tribal subjects were selected within the age group of 15 to 40 years (120 male and 80 female with mean age of 21.1 ± 5.36 and 19.6 ± 6.2 years respectively). The frequency of GSTM1 was 3.5%, GSTT1 was 5.5% and GSTT1/M1 was 2.5% while normal were 89%. Details of iron profile with GST mutation and frequencies of GST deletions are given in TABLE 1 and 2 respectively. There was no significant difference in iron profile with GST mutations and without GST mutant subjects. Glutathione S-transferases (GST) are a family of enzymes involved in phase-II detoxification of endogenous and xenobiotic compounds. Polymorphisms in GST genes have been associated with susceptibility to different diseases. Alterations in GSH concentration have been demonstrated in many pathological conditions including sickle cell disease (SCD).An altered glutathione (GSH) metabolism in association with increased oxidative stress has been implicated in the pathogenesis of many diseases[8,13,14].

In this study the GST genotype frequency was similar in male and female. And gender was not associated with GST deletions. The iron metabolism in SCD is different to thalassemia. SCD is an inherited disorder of hemoglobin synthesis characterized by life-long hemolytic anemia, increased erythropoiesis and a chronic inflammatory state with endothelial activation and enhanced red cell and leukocyte adhesion.[15,16] In this study, subjects iron profile was not correlated with GST mutations. GST polymorphism was significantly present in population however GST genotypes were not associated with iron levels.

TABLE 1 : Iron status with GST polymorphism

Iron profile	Mean ±SD				
	Genotype				
	GSTM1 (N= 7)	GSTT1(N= 11)	GSTM1/ GSTT1 (N=5)	Normal (N=177)	P-value
Serum Ferritin µg/L	165.2±23.8	160.3±17.3	158.3±25.3	162.3±27.2	0.073
TIBC µg/dl	325.1±245.2	328.3±32.1	325.7±28.3	331.2±26.8	0.084
% Transferrin saturation-%	29.3±4.6	25.4±7.8	24.6±5.3	27.3±4.8	0.062

TABLE 2 : Frequency of GST genotype

Genotype	Frequency %	
	Male	Female
	N= 120	N= 80
GSTM1	4 (3.34)	3 (3.75)
GSTT1	7(5.83)	4 (5)
GSTM1/ GSTT1	3(2.5)	2 (2.5)
Normal	106(88.34)	71 (88.75)

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