

RESEARCH ARTICLE



Glutathione S-transferase M1 and T1 null genotype frequency distribution among four tribal populations of western India

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Abstract. Glutathione S-transferase (GST) family is a key contributor in the detoxification mechanism of our body. Deletion of the genes within this family has been reported in the failure of detoxification system, to some extent leading to various types of cancers and other life threatening diseases. The existing data and reports on the association of null genotype of both *GSTM1* and *GSTT1* genes for various diseases are inconsistent. But knowledge of the polymorphic distributions of genotypes in different populations is important for investigating the risk factors in different epidemiological studies. The present study thus aims to determine the frequency of *GSTM1* and *GSTT1* null genotype frequency among four tribal groups, i.e. Mina, Garasia, Damor and Saharia of western India. A comparative analysis with different tribal as well as world population has also been undertaken to have a view of its worldwide frequency distribution. Our results reveal a frequency distribution varying from 22.6% to 66.9% with respect to *GSTM1* gene polymorphism and from 19.1% to 33.0% with respect to *GSTT1* gene in the studied populations. To the best of our knowledge this is the first report on the *GSTM1* and *GSTT1* frequency distribution among the tribal population of western India and our study shows that the Mina tribal population has the highest frequency of *GSTM1*.

Keywords. glutathione S-transferase; genetic polymorphisms; null genotype; frequency; *GSTM1* gene; *GSTT1* gene; western India.

Introduction

Glutathione S-transferase (GST) gene superfamily is involved in the metabolic detoxification of products generated by oxidative stress, electrophilic compounds, carcinogens, environmental toxins and therapeutic drugs (Da Fonseca *et al.* 2010; Kasthurinaidu *et al.* 2015; Hidaka *et al.* 2016). Among the GST classes, *GSTM1* and *GSTT1* were found to be associated to a loss of function with a structural deletion (*Null* mutation); moreover, they were

also found to modify the detoxification ability of the individuals exposed to tobacco or carcinogenic pollutants in the environment (Strange *et al.* 2001). Genotoxins such as aromatic hydrocarbon epoxides and products of oxidative stress such as DNA hydroperoxides, polycyclic aromatic hydrocarbon diol epoxide are catalysed and detoxified by *GSTM1*, while the constituents of cigarette smoke such as alkyl halide, benzo (a) pyrene diol epoxide, crocin are catalyzed and detoxified by *GSTT1* (Strange *et al.* 2001; Kim *et al.* 2002). The *GSTM1* and *GSTT1* null genotypes have been extensively studied in various human populations and their ubiquitous existence is well documented (Garte *et al.* 2001; Gaspar *et al.* 2002; Saadat 2007; Fujihara *et al.* 2009). For example, the prevalence of *GSTM1* null genotype among the Caucasians, Asian and Africans was 47–57%, 42–54% and 16–36%, respectively, while the prevalence of the *GSTT1* null genotype

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in Caucasians was rather low 13–26% but common in Asians (35–52%) (Garte *et al.* 2001). These differences in the frequencies of the *GSTMI* and *GSTTI* null genotypes among human populations may be related with population-specific disease susceptibilities. Contemporary ethnic populations of India are highly variable; both biologically and culturally (Majumder 1998) and western India, is particularly represented by several tribal populations of Indo-European origin, who have settled here during several waves of migration. But there is no report of such genetic polymorphism among the tribal population groups of Rajasthan. Therefore we evaluated the distribution of *GSTMI*, *GSTTI* genotype in Rajasthan population and compared it with GST polymorphism frequency in different states of India and with various populations worldwide.

Materials and methods

Sample collection

Normal healthy subjects, 700 from four tribal groups, namely Damor (115), Garasia (191), Mina (115) and Saharia (279) were taken from different localities of Rajasthan, western India. Number of total male and female samples was 408 and 292, respectively. A structured questionnaire was administered to collect socio-demographic information of the subjects and 5 mL peripheral blood was collected in EDTA coated BD vacutainers after obtaining informed consent. Ethical clearance was followed as per the Anthropological Survey of India guidelines.

Studied population

Damor: The Damor are an endogamous community and practice clan exogamy. They are also described as damoria, numerically being the smallest group of all the tribes in Rajasthan. They are concentrated in small pockets of the border of Gujarat, and the Simalwara, Sagwara, and Aspur tehsils of Dungurpur district (especially Simalwara) of Rajasthan. They claim to be the Rajput origin and recall their migration from Gujarat (Singh 1994). They speak the Gameti dialect of Rajasthan, most of them also speak Gujarati. Their main clans are the Parmar, Sisodia, Rathore, Chauhan, Solanki, Saradia and Karadiya. Most of these are also well-known Rajput clans. The Damor are mainly settled agriculturist, and include both landowners and sharecroppers (People of India, Gujarat Volume, 2012).

Mina: Of the 12 scheduled tribes of the state, Mina is the most populous tribe, having a population of 3,799,971 constituting 53.5% of the total scheduled tribe population as

per census 2011. Mina accounts for ~99% of all ST population in the five districts, namely Dhaulpur, Bharatpur, Sawai Madhopur, Karauli and Dausa. They share more than 90% of the total tribal population in Alwar, Jhunjhun, Sikar, Tonk and Churu districts. There are two divisions, namely the Zamindar Mina, the major division and the Chowkidar Mina. Zamindar Mina are called the old settlers and the Chowkidar Mina is termed the new settlers. Their names are derived from *Meen*, the Sanskrit word for fish, and they claim descent from the *Matsya avatar*, or fish incarnation of Lord Vishnu.

Saharia (particularly vulnerable tribal group): Saharia/Seharia is one of the particularly vulnerable tribal group (PVTG) out of 75 primitive tribes identified by Government of India on the basis of low growth rate, pre agricultural level of technology and extremely low level of literacy. In Rajasthan, they are mainly concentrated in Kishanganj, Shahbad block of Baran district. They live as nuclear families. Several studies have shown a close relationship between the tribal ecosystem and their nutritional status.

Garasia: Garasia is a scheduled tribe living in the forest areas of the Aravalli hills of the Indian states of Rajasthan, specifically Sirohi district, in and around Abu Road area in 24 villages which comprises of the 'Bhakkar Patta'. They are divided into Rajput Garasia and Bhil Garasia. Present study samples were collected from Sirohi district. Garasia derive their name from Sanskrit word *Gras* which means a morsel or subsistence. In Rajasthan, the population of Mina and Bhil together constitute 93% whereas Garasia, Damor, Dhanka and Saharia combine to form 6.6% of the total ST population. Constant contact with other communities has led to several changes in the social order of this tribe. Their language, known as Dungri Garasia, is an Indo-Aryan language belongs to the Bhil subgroup. During the 13th century, many poor Rajput fled to the Vindhya and Aravalli hills where they mixed with the Bhil settlers. In time, the Garasia defeated the Bhil chiefs and their followers, settling near the foothills and in the forests. There they were given land for cultivation as a reward for protecting the people and the area.

Polymerase chain reaction (PCR) and genotyping

DNA was extracted from the whole blood following the phenol–chloroform extraction protocol. The purity of DNA was determined by estimating the ratio of absorbance at 260/280 nm by spectrophotometer, Smart Spec Plus, Biorad. The region of interest was amplified by using three sets of primers to amplify the respective fragments through PCR using Biorad S1000 Thermal Cycler. The following primer sets were used for the study: *GSTMI* gene, forward primer: 5'-GAA CTC CCT GAA AAG CTA AAG C-3' and reverse primer: 5'-GTT GGG CTC AAA TAT ACG GTG G-3' with product size of 219 bp. *GSTTI*

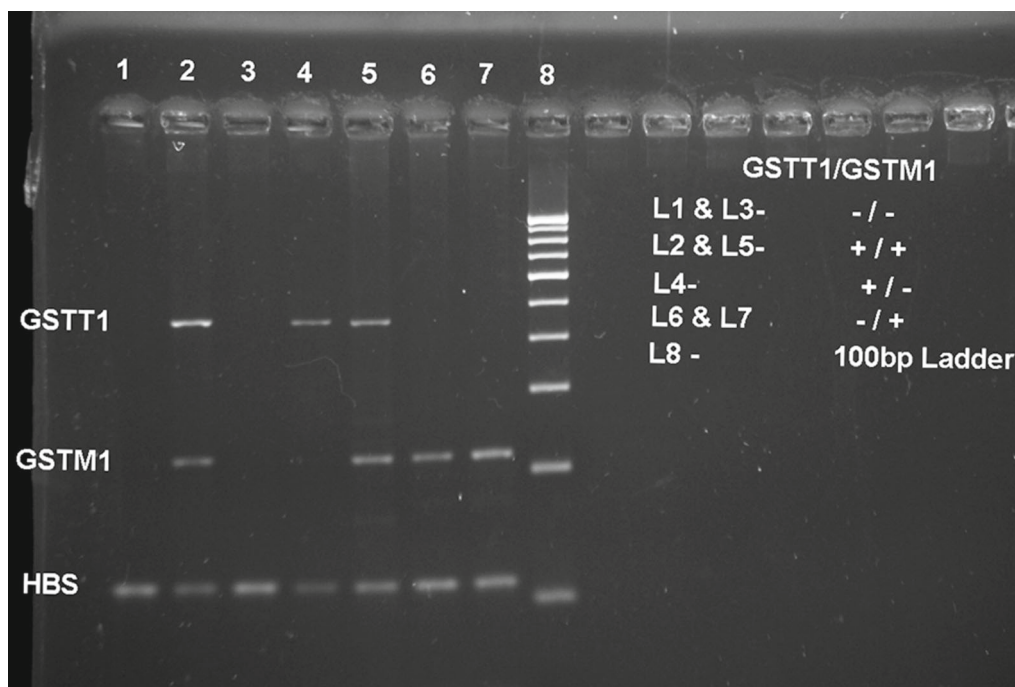


Figure 1. Displays genotypes through lanes 1 to 7. Lanes 1 and 3 shows null, lanes 2 and 5 show both present, lane 4 *GSTT1* present and *GSTM1* null, lanes 6 and 7 *GSTM1* present and *GSTT1* null, lane 8 show 100-bp DNA ladder. Distinctive samples were selectively run along with *HBS* gene as internal control on 2% agarose gel stained with ethidium bromide at the concentration of 0.5 $\mu\text{g/ml}$. Product size of *GSTT1*, *GSTM1* and *HBS* were 459 bp, 219 bp, and 110 bp respectively.

gene, forward primer: 5'-TTC CTT ACT GGT CCT CAC ATC TC-3' and reverse primer: 5'-TCA CCG GAT CAT GGC CAG CA-3' with product size of 459 bp. *HBS* gene, forward primer: 5'-ACA CAA CTG TGT TCA CTA GC-3' and reverse primer: 5'-CAA CTT CAT CCA CGT TCA CC-3' with product size of 110 bp.

PCR mix was optimized for 10 μL reaction as 1 \times PCR buffer (10 mM Tris-HCl (pH 9.0 at 25°C) 50 mM KCl and 0.01% gelatin (Merck Genei, Mumbai, India), 1.25 mM MgCl_2 (Merck Genei), 200 μM dNTPs (Sigma Aldrich, St Louis, USA), forward and reverse primers 5 μM each (Sigma Aldrich), 0.5 U of *Taq* DNA polymerase (Merck Genei) and 3 μL of DNA was used. PCR reaction for each of the primer was optimized as initial denaturation at 95°C for 5 min, secondary denaturation at 94°C for 1 min, annealing at 55°C for *GSTM1*, 59.5°C for *GSTT1* and 50°C for *HBS* gene loci (internal control) for 1 min, extension at 72°C for 2 min, final extension at 72°C for 10 min and ended at 4°C.

PCR plates were prepared using PCR coolers in aseptic condition under laminar air flow bench. Routine agarose (Sigma Aldrich) and Agarose Low EEO Superior grade type II (SRL) were used at the concentration of 2% stained with ethidium bromide. Deletions confirming the null genotype were detected after the agarose gel electrophoresis in 1 \times TAE gel running buffer (40 mM Tris-acetate and 1 mM EDTA) by analysing all the amplicons on Alpha Innotech Multi Image II gel documentation System (figure 1).

Reference information on worldwide frequency distribution of both the genetic polymorphism were generated from eligible publications according to the inclusion criteria, i.e. frequency distribution of *GSTM1* and *GSTT1* both from individual locus study or multigenes study with respect to the worldwide geographical zones, ethnicity, tribal groups etc.

Results

The frequency distribution of *GSTM1* null genotype among four tribal groups of western India has been appended in table 1. The study shows the frequency of *GSTM1* null genotype to be the highest among the Mina tribal group, i.e. 66.9% followed by the Garasia (43.4%), the Damor (36.5%) and the Saharia (22.6%). Table 1 also includes the comparative frequencies of this genotype among various population groups of India. The Mina population from our study shows the highest frequency of *GSTM1* null genotype among all the population groups so far studied in India. The lowest frequency (14.7%) has been reported in Hyderabad, south India. Reference data suggest that north India is consistently showing on an average 35% *GSTM1* null genotype frequency in various population groups. Rest of the Indian populations show variable pattern of distribution. Frequency distribution of *GSTM1* null genotype among the currently studied tribal groups of western India has been compared with the other

Table 1. Comparative frequency distribution of *GSTMI* null genotype in India.

India zone	Area	N	<i>GSTMI</i> Null	Reference
East India	Kolkata	67	27.0	Sikdar et al. (2005)
Northeast India		217	60.4	Chatterjee et al. (2009)
Northeast India	Sikkim, Guwahati, Aizawl	154	42.9	Ihsan et al. (2014)
Northeast India		236	38.1	Borah et al. (2011)
North India	Lucknow	238	37.8	Shukla et al. (2013)
North India	Lucknow	200	36.5	Konwar et al. (2010)
North India		200	36.5	Bid et al. (2010)
North India		144	35.4	Srivastava et al. (2003)
North India	Kashmir	124	35.0	Bhat et al. (2012)
North India	Delhi	500	33.6	Sharma et al. (2012)
North India		370	33.0	Mishra et al. (2004)
West India	Mina from Rajasthan	115	66.9	Present study
West India	Garasia from Rajasthan	191	43.4	Present study
West India	Damor from Rajasthan	115	36.5	Present study
West India	Saharia from Rajasthan	279	22.6	Present study
West India	Maharashtra	729	37.0	Anantharaman et al. (2007)
West India	Maharashtra	450	24.0	Buch et al. (2002)
West India	Gujarat	504	20.0	Senthilkumar and Thirumurugan (2012)
South India	South India	162	43.8	Sultana et al. (2011)
South India	Karnataka	110	36.4	Naveen et al. (2004)
South India	Andhra Pradesh	115	33.0	Naveen et al. (2004)
South India	Kerala	122	31.9	Naveen et al. (2004)
South India		146	26.7	Sreeja et al. (2005)
South India	Pondicherry, Tamil Nadu	170	23.5	Naveen et al. (2004)
South India		255	22.4	Vettriselvi et al. (2006)
South India		500	22.0	Samson et al. (2007)
South India	Hyderabad	102	14.7	Roya et al. (2009)

Table 2. Comparative frequency distribution of *GSTMI* null genotype among various tribal groups worldwide.

Country/zone	Tribe	N	<i>GSTMI</i> null	Reference
Western India	Mina	115	66.9	Present study
Western India	Damor	115	36.5	Present study
Western India	Garasia	191	43.4	Present study
Western India	Saharia	279	22.6	Present study
Northeast India	Deori	95	61.1	Chatterjee et al. (2009)
Northeast India	Sonowal, Kachari	60	60.0	Chatterjee et al. (2009)
Africa	Hausa	98	37.0	Ebeshi et al. (2011)
Africa	Yoruba	101	31.0	Ebeshi et al. (2011)
Africa	Ibo	101	23.0	Ebeshi et al. (2011)
Africa	Xhosa	128	21.1	Kurose et al. (2012)
Brazil	Surui	21	43.0	Gaspar et al. (2002)
Brazil	Ache	67	35.8	Gaspar et al. (2002)
Brazil	Munduruku	47	27.0	Klautau-Guimaraes et al. (2005)
Brazil	Wai-Wai	26	26.9	Gaspar et al. (2002)
Brazil	Parakana	79	20.0	Arruda et al. (1998)
Brazil	Xavante	33	18.2	Gaspar et al. (2002)
Brazil	Zoro	28	14.3	Gaspar et al. (2002)
Brazil	Gaviao	31	12.9	Gaspar et al. (2002)
Brazil	Guarani	51	3.9	Gaspar et al. (2002)
Brazil	Kayabi	79	0.0	Klautau-Guimaraes et al. (2005)

tribal populations of the world (table 2). Although, the *GSTMI* null genotype frequency distribution is found to be variable among the tribal populations of the world,

Indian tribes show a high frequency, particularly Mina population show the highest frequency worldwide. Lowest frequency has been reported in Brazilian Amerindian

Table 3. Worldwide frequency distribution of *GSTM1* null genotype.

World zone	Country	N	<i>GSTM1</i> null*	Reference
Europe				
Northern	Norway, Sweden, Denmark, Finland, England, UK	3973	51.8	Hou <i>et al.</i> (2000), Garte <i>et al.</i> (2001), Bu <i>et al.</i> (2007), Zhang <i>et al.</i> (1999), Welfare <i>et al.</i> (1999)
Western	Netherlands, Germany, France	6486	51.0	Garte <i>et al.</i> (2001), Risch <i>et al.</i> (2001), Schneider <i>et al.</i> (2004), Kabesch <i>et al.</i> (2004), Abbas <i>et al.</i> (2004)
Southern	Italy, Spain, Portugal, Slovenia, Greece	5041	50.4	Alberti <i>et al.</i> (1996), Garte <i>et al.</i> (2001), Boccia <i>et al.</i> (2007), D'Alo <i>et al.</i> (2004), Paracchini <i>et al.</i> (2006), Garcia-Closas <i>et al.</i> (2005), Varela-Lema <i>et al.</i> (2008), Lopez-Cima <i>et al.</i> (2012), Conde <i>et al.</i> (1999), Dialyna <i>et al.</i> (2003), Georgiou <i>et al.</i> (2000), Stavropoulou <i>et al.</i> (2007)
Eastern	Turkey, Bulgaria, Poland, Russia, Slovakia	1875	49.2	Ada <i>et al.</i> (2004), Aydemir <i>et al.</i> (2007), Aydos <i>et al.</i> (2009), Toncheva <i>et al.</i> (2004), Kargas <i>et al.</i> (2003), Gajecka <i>et al.</i> (2005), Garte <i>et al.</i> (2001), Gra <i>et al.</i> (2010), Polonikov <i>et al.</i> (2010)
Southeast Asia	Serbia	56	48	Dordevic <i>et al.</i> (2010)
Eastern	China	5367	50.3	Setiawan <i>et al.</i> (2001), Chen <i>et al.</i> (2001), Zhao <i>et al.</i> (2001), Yu <i>et al.</i> (2009), Chen <i>et al.</i> (2002), Chen <i>et al.</i> (2010), Tang <i>et al.</i> (2012), Wu <i>et al.</i> (2013), Xu <i>et al.</i> (2013), Mu <i>et al.</i> (2005), Liu <i>et al.</i> (2009), Zhong <i>et al.</i> (2006), Guo <i>et al.</i> (2008), Lin <i>et al.</i> (2009), Lee <i>et al.</i> (2005)
	Japan	2444	51.1	Inoue <i>et al.</i> (2000), Kihara <i>et al.</i> (1994), Oyama <i>et al.</i> (1997), Kiyohara <i>et al.</i> (2000), Naoe <i>et al.</i> (2000), Ichioka <i>et al.</i> (2009), Murata <i>et al.</i> (2001), Morinobu <i>et al.</i> (1999), Hishida <i>et al.</i> (2005), Tamaki <i>et al.</i> (2011)
	Korea	3963	51.1	Hong <i>et al.</i> (1998), Park <i>et al.</i> (2000), Kim <i>et al.</i> (2000), Hur <i>et al.</i> (2004), Choi <i>et al.</i> (2003), Cho <i>et al.</i> (2005), Piao <i>et al.</i> (2009), Kwon <i>et al.</i> (2011)
South eastern	Mongolia	207	46.6	Fujihara <i>et al.</i> (2009)
	Vietnam, Philippines, Thailand, Indonesia, Malaysia	1555	56.3	Agusa <i>et al.</i> (2010), Rimando <i>et al.</i> (2008), Pakakasama <i>et al.</i> (2005), Sangrajrang <i>et al.</i> (2006), Klinchid <i>et al.</i> (2009), Amtha <i>et al.</i> (2009), Zhao <i>et al.</i> (1995), Alshagga <i>et al.</i> (2011), Lee <i>et al.</i> (1995)
Southern	India			
	North India	1776	35.4	Mishra <i>et al.</i> (2004), Sharma <i>et al.</i> (2012), Naveen <i>et al.</i> (2004), Konwar <i>et al.</i> (2010), Shukla <i>et al.</i> (2013), Bhat <i>et al.</i> (2012), Srivastava <i>et al.</i> (2005), Bid <i>et al.</i> (2010)
	South India	2199	28.5	Naveen <i>et al.</i> (2004), Samson <i>et al.</i> (2007), Roya <i>et al.</i> (2009), Mishra <i>et al.</i> (2004), Vettriselvi <i>et al.</i> (2006), Shehnaz <i>et al.</i> (2011)
	West India	2383	29.7	Senthilkumar and Thirumurugan (2012), Anantharaman <i>et al.</i> (2007), Buch <i>et al.</i> (2002), Present Study
	East India	67	27.0	Sikdar <i>et al.</i> (2005)
	North-east India	390	40.5	Ihsan <i>et al.</i> (2014), Borah <i>et al.</i> (2011)

Table 3 (contd)

World zone	Country	N	GSTMI null*	Reference
Middle East	Egypt	411	43.6	Shereen et al. (2010), Amer et al. (2011), Kurose et al. (2012), EL-Said et al. (2013)
	Iran	619	43.0	Safarinejad et al. (2010), Salehi et al. (2011), Saadat et al. (2012), Dadbinpour et al. (2013)
	Syria	172	22.7	Al-Achkar et al. (2014)
America	Chile	220	32.9	Adonis et al. (2005), Quinones et al. (2006)
	Brazil	2316	42.2	Gattas et al. (2004), Rossini et al. (2002), Arruda et al. (1998), Hatagima et al. (2000), Burim et al. (2004), Magno et al. (2009), Possuelo et al. (2013), Pinheiro et al. (2013)
	African Americans	690	41.8	Bailey et al. (1998), Chen et al. (1996), Millikan et al. (2000)
Africa				
West Africa	Nigeria	894	28.3	Kurose et al. (2012), Ebeshi et al. (2011)
East Africa	Namibia	134	11.2	Fujihara et al. (2009)

*Average frequency calculated from the selected sources of study.

Table 4. Comparative frequency distribution of *GSTTI* null genotype in India.

India zone	Area	N	<i>GSTTI</i> null	Reference
East India	Kolkata	67	13.0	Sikdar et al. (2005)
North-East India		236	28.1	Borah et al. (2011)
North-East India	Sikkim, Guwahati, Aizawl	154	27.3	Ihsan et al. (2014)
North-East India		217	25.3	Chatterjee et al. (2009)
North India	Delhi, India	309	27.4	Singh et al. (2003)
North India	Lucknow	238	24.4	Shukla et al. (2013)
North India	Kashmir	124	21.0	Bhat et al. (2012)
North India		144	20.1	Srivastava et al. (2003)
North India		370	18.4	Mishra et al. (2004)
North India	Lucknow	200	14.0	Konwar et al. (2010)
North India		200	14.0	Bid et al. (2010)
North India	Delhi, India	500	12.0	Sharma et al. (2012)
West India	Gujarat	504	35.5	Senthilkumar and Thirumurugan (2012)
West India	Saharia, Rajasthan	279	33.0	Present study
West India	Mina, Rajasthan	115	28.7	Present study
West India	Garasia, Rajasthan	191	20.4	Present study
West India	Damor, Rajasthan	115	19.1	Present study
West India	Maharashtra	729	16.0	Anantharaman et al. (2007)
West India	Maharashtra	450	12.3	Buch et al. (2002)
South India	Andhra Pradesh	115	18.8	Naveen et al. (2004)
South India		255	17.6	Vettriselvi et al. (2006)
South India	Kerala	122	15.6	Naveen et al. (2004)
South India	Andhra Pradesh	212	15.6	Lakkakula et al. (2013)
South India		162	13.8	Sultana et al. (2011)
South India		150	13.3	Suneetha et al. (2011)
South India	Pondicherry, Tamil Nadu	170	13.0	Naveen et al. (2004)

tribe Guarani with 3.9% and Kayabi tribe with no deletion present among them. Worldwide frequency distribution of *GSTMI* null genotype is also shown in table 3 and we

can see a contrasting pattern of *GSTMI* null genotype frequency distribution worldwide. The frequency distribution follows from a higher to lower clinal pattern from

Table 5. Comparative frequency distribution of *GSTT1* null genotype among various tribal groups worldwide.

Country/zone	Tribe	N	<i>GSTT1</i> null	Reference
Western India	Saharia	279	33.0	Present study
Western India	Mina	115	28.7	Present study
Western India	Garasia	191	20.4	Present study
Western India	Damor	115	19.1	Present study
Northeast India	Deori	95	45.1	Samson <i>et al.</i> (2007)
Northeast India	Sonowal-Kachari	60	5.0	Chatterjee <i>et al.</i> (2009)
South India	Sugali	27	22.2	Lakkakula <i>et al.</i> (2013)
South India	Mala	45	20.0	Lakkakula <i>et al.</i> (2013)
South India	Madiga	17	17.6	Lakkakula <i>et al.</i> (2013)
South India	Reddy	46	13.0	Lakkakula <i>et al.</i> (2013)
South India	Balija	34	11.8	Lakkakula <i>et al.</i> (2013)
South India	Muslim	43	11.6	Lakkakula <i>et al.</i> (2013)
Africa	Hausa	98	41.0	Ebeshi <i>et al.</i> (2011)
Africa	Xhosa	128	40.6	Kurose <i>et al.</i> (2012)
Africa	Ibo	101	36.0	Ebeshi <i>et al.</i> (2011)
Africa	Yoruba	101	35.0	Ebeshi <i>et al.</i> (2011)
Brazil	Xavante	33	30.3	Gaspar <i>et al.</i> (2002)
Brazil	Munduruku	47	29.0	Klautau-Guimaraes <i>et al.</i> (2005)
Brazil	Kayabi	79	27.0	Klautau-Guimaraes <i>et al.</i> (2005)
Brazil	Ache	67	17.9	Gaspar <i>et al.</i> (2002)
Brazil	Zoro	28	14.3	Gaspar <i>et al.</i> (2002)
Brazil	Guarani	51	11.8	Gaspar <i>et al.</i> (2002)
Brazil	Parakana	79	11.0	Arruda <i>et al.</i> (1998)
Brazil	Gavião	31	6.5	Gaspar <i>et al.</i> (2002)
Brazil	Wai-Wai	26	0.0	Gaspar <i>et al.</i> (2002)
Brazil	Surui	21	0.0	Gaspar <i>et al.</i> (2002)

Europe (north Europe, 51.8%; south Europe, 50.4%; west Europe, 51.0%; east Europe, 49.2%); east Asia (Korea, 51.1%; Japan, 51.1%; China, 50.3%); Middle East (Egypt, 43.6%; Iran, 43.0%), Southeast Asia (58.4%) and South America (Brazil, 42.2%) have considerably higher frequencies than South Asia (western India and northeast India, 40.5%; north India, 35.4%; western India, 29.7%; south India, 28.5%; east India, 27.0%) and Africa (west, 28.3%; east, 11.2%).

Table 4 describes the *GSTT1* null genotype frequency among the four studied populations. The Saharia tribal population is showing the highest frequency of *GSTT1* (33%) followed by Mina (28.7%), Garasia (20.4%) and Damor population (19.1%). The comparative analysis shows the highest frequency of *GSTT1* null genotype occurs in western India (Gujarat, 35.5%; Rajasthan: 33.0% and 28.7%) and lowest frequency has been reported in north India (Delhi, 12.0%). Although there is an inconsistent variability of frequency distribution of *GSTT1* all over India but south India shows a consistent frequency distribution of around 15.0%.

Frequency distribution of *GSTT1* null genotype among tribal populations of western India and comparison with other tribal populations of the world has been presented in the table 5. After comparing with the south Indian tribes and northeast Indian tribes, the deletion frequencies

among the tribal groups were found to be variable. Deori, a northeast Indian tribe has the highest *GSTT1* null genotype frequency, i.e. 45.1% throughout the world, whereas Brazilian Amerindian tribe Surui and Wai-Wai possess no deletion. Further, northeast India tribe Sonowal-Kachari has been reported to have 5.0% deletion for *GSTT1* gene which is comparatively low than the other tribal populations of northeast India. Here we cannot augment any particular variation pattern in the frequency distribution pattern of *GSTT1* null deletion within several tribal population groups around the world. Table 6 presents the frequency distribution of *GSTT1* null genotype among worldwide populations. We find that east Asia and Southeast Asia (Japan, 49.1%; Korea, 49.6%; China 45.2%) show comparatively higher frequency of *GSTT1* null genotype when compared with the studies reported from other parts of the globe. However, comparatively low frequencies of *GSTT1* null genotype have been observed in European nations (west Europe, 20.0%; east Europe, 16.9%; north Europe 16.4%).

Discussion

The present study is an attempt to find out the frequency distribution of *GSTM1* and *GSTT1* among four tribal population groups of Western India. The selected subjects

Table 6. Worldwide frequency distribution of *GSTT1* null genotype.

World zone	Country	N	<i>GSTT1</i> null*	Reference
Europe				
Northern	Sweden, Denmark, Finland, England, UK	2578	16.4	Bu et al. (2007), Garte et al. (2001), Zhang et al. (1999), Welfare et al. (1999)
Western	Netherlands, Germany, France	5562	20.0	Garte et al. (2001), Risch et al. (2001), Schneider et al. (2004), Kabesch et al. (2004), Abbas et al. (2004)
Southern	Italy, Spain, Portugal, Slovenia, Greece	3624	27.7	Boccia et al. (2007), Garte et al. (2001), Dialyna et al. (2003), Georgiou et al. (2000), Garcia-Closas et al. (2005), Lemos et al. (1999), Alves et al. (2002), D'Alo et al. (2004), Volk et al. (2011), Stavropoulou et al. (2007)
Central		194	17.6	Steinhoff et al. (2000), Binkova et al. (2002)
Eastern	Turkey, Bulgaria, Poland, Russia, Slovakia	2077	16.9	Ada et al. (2004), Demir et al. (2005), Oke et al. (1998), Aydos et al. (2009), Kargas et al. (2003), Polonikov et al. (2010), Toncheva et al. (2004), Gajecka et al. (2005), Garte et al. (2001), Gra et al. (2010)
South eastern	Serbia	56	48.0	Dordevic et al. (2010)
Asia				
Eastern	China	4410	45.2	Setiawan et al. (2001), Zhao et al. (2001), Wong et al. (2002), Wu et al. (2007), Chen et al. (2010), Tang et al. (2012), Xu et al. (2013), Wu et al. (2013), Mu et al. (2005), Guo et al. (2008), Liu et al. (2009), Zhong et al. (2006), Fujihara et al. (2009)
	Japan	1746	49.1	Katoh et al. (1996), Murata et al. (2001), Kiyohara et al. (2003), Naoe et al. (2000), Ichioka et al. (2009), Morinobu et al. (1999), Hishida et al. (2005), Tamaki et al. (2011)
	Korea	3900	49.6	Park et al. (2000), Kim et al. (2000), Hur et al. (2004), Choi et al. (2003), Cho et al. (2005), Piao et al. (2009), Kwon et al. (2011), Fujihara et al. (2009)
Southeast	Vietnam, Philippines, Thailand, Indonesia, Malaysia	860	34.8	Agusa et al. (2010), Rimando et al. (2008), Pakakasama et al. (2005), Klinchid et al. (2009), Amtha et al. (2009), Alshagga et al. (2011)
Southern	India			
	North India	2085	18.9	Mishra et al. (2004); Sharma et al. (2012); Singh et al. (2009); Konwar et al. (2010), Shukla et al. (2013), Bid et al. (2010), Srivastava et al. (2005)
	South India	1703	15.5	Naveen et al. (2004); Lakkakula et al. (2013); Shehnaz et al. (2011); Suneetha et al. (2011), Vettriselvi et al. (2006)
	Western India	2383	22.6	Senthilkumar and Thirumurugan (2012), Anantharaman et al. (2007), Buch et al. (2002), Present Study
	East India	67	13.0	Sikdar et al. (2005)
	North-east India	390	27.7	Ihsan et al. (2014), Borah et al. (2011)
Middle East				
	Egypt	1571	27.2	Shereen et al. (2010), Amer et al. (2011), Hamdy et al. (2003), EL-Said et al. (2013)
	Iran	619	20.7	Safarinejad et al. (2010), Salehi et al. (2011), Saadat et al. (2012), Dadbinpour et al. (2013)
	Syria	172	16.7	Al-Achkar et al. (2014)

Table 6 (contd)

World zone	Country	N	GSTTI null*	Reference
America	Brazil	2501	26.6	Rossini <i>et al.</i> (2002), Gattas <i>et al.</i> (2004), Burim <i>et al.</i> (2004), Magno <i>et al.</i> (2009), Finotti <i>et al.</i> (2009), Possuelo <i>et al.</i> (2013), Pinheiro <i>et al.</i> (2013)
	African Americans	997	19.8	Bailey <i>et al.</i> (1998), Chen <i>et al.</i> (1996), Millikan <i>et al.</i> (2000), Cote <i>et al.</i> (2005), Van Emburgh <i>et al.</i> (2008)
Africa				
West Africa		894	30.1	Kurose <i>et al.</i> (2012), Ebeshi <i>et al.</i> (2011)
East Africa		134	35.8	Fujihara <i>et al.</i> (2009)

*Average frequency calculated from the selected sources of study.

from the populations include healthy individuals to control the effect of any toxicity. Further, the primitiveness of this genotypic configuration among the selected tribal populations allows us to understand the dynamics of the selected polymorphism with respect to other caste groups of India. Our finding shows that Mina population has the highest frequency of *GSTMI* worldwide. We have also found low frequency of *GSTMI* (22.6%) and a high frequency of *GSTTI* (33.0%) among the Saharia. The other three populations show an opposite trend. Such inconsistency of the frequency distribution of these two genetic polymorphisms has also been found with respect to the ethnic as well as geographic background (Houlston 2000; Naoe *et al.* 2000). The gene–gene and gene–environment interactions are said to play key role in the inconsistency of the results (Hamajima *et al.* 2002). We may infer that *GSTMI* substitutes the expression of the *GSTTI* and vice-versa. An *in vitro* study showed that *GSTTI* activity is higher in the individuals carrying the *GSTMI* null genotype (Fuciarrelli *et al.* 2009), thus corroborating our assumption. Other factors such as biocultural adaptation and admixture with other ethnic groups or geographic distribution may explain the differences seen in this study but additional research will contribute to the understanding of such outcome.

The *GSTMI* and *GSTTI* null polymorphism is reported to have associated with various types of cancers, infertility, type-2 diabetes, chronic kidney disease, coronary artery disease, endometriosis and many other diseases (Rebeck 1997; Cotton *et al.* 2000; Shukla *et al.* 2013; Yang and Xian 2014; Hidaka *et al.* 2016). In this back drop, the presence of highest frequency of *GSTMI* among the Mina population sample calls for immediate attention towards the associated risk factors for various diseases like breast cancer etc.

No significant difference between males and females in terms of the genetic frequency of *GSTMI* or *GSTTI* null genotypes were found in any of the studied population. Similar observation has also been found in other studies

(Rossini *et al.* 2002; Sharma *et al.* 2012). Further, the distribution pattern of the two genotype frequency does not follow any distinctive pattern among tribal groups with respect to their geographical territory. Present study shows that the four different tribal populations show intratribal as well as intertribal variation with respect to the frequency distribution while compared with other tribal groups of India, Africa and Brazil.

We have found a contrasting pattern of *GSTMI* and *GSTTI* null genotype frequency distribution worldwide as per the zonal variation. Europe, east Asia, Middle East, Southeast Asia and Brazil have considerably higher frequencies of *GSTMI* null genotype than South Asia, west Africa and east Africa. On the other hand, east Asia has considerably higher frequency of *GSTTI* null genotype than Middle East, European, and Indian regions. Africa, south Europe, South America, northeast India, Middle East has frequency distributed in middle range when compared to east Asia, Europe and South Asia. We have found a clear clinal distribution pattern with respect to *GSTMI* from Europe to Africa. It can be concluded that European populations might be liberated from the strong constraints of UV light toxicity and may contribute towards the elevated frequency of *GSTMI* null genotype. Studies characterized with the clinal variation of population groups throughout the world also describe the same situation (Saitou and Ishida 2015). However no such conclusion can be drawn in terms of the frequency distribution of *GSTTI* null genotypes. Further studies on this dimension, taking into consideration the different tribal as well as caste groups from different parts of India including other null genotypes will add new facet to this study.

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