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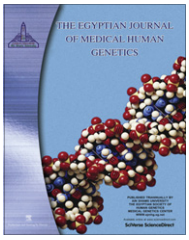

ORIGINAL ARTICLE

Genetic study of phenylthiocarbamide (PTC) taste perception among six human populations of Jammu and Kashmir (India)

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KEYWORDS

Phenylthiocarbamide (PTC);
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Abstract *Background:* The ability to taste phenylthiocarbamide (PTC), a bitter chemical has long been known to be a bimodal autosomal trait inherited in a simple Mendelian recessive pattern which is being widely used for both genetic and anthropological studies. The frequency of taster and non-taster allele is found to vary in different populations. The present paper deals with the distribution of PTC tasting ability as a marker to study the genetic structure among Muslim populations of Jammu; as no detailed information is available.

Aim: To investigate the prevalence and gene frequencies of PTC taste sensitivity among male and females.

Subjects and methods: We have undertaken a survey of gene frequencies of PTC taste ability for six different endogamous groups including tribal population. PTC serial dilution method was used to assess the PTC taster and non-taster phenotypes. Hardy–Weinberg method was used to determine allele frequencies.

Results: Gujjar and Bakarwal population showed highest PTC threshold while Syed had the least. The phenotypic frequency for PTC taste ability varies within six populations; Syed were observed

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with highest taster frequency while Gujjar and Bakarwal had lowest taster frequency. The taster frequency of six different populations showed that the percentage of taster frequency was more frequent than that of the non-tasters. Also, females ($\chi^2 = 4.563$, df = 5, $p = 0.471$) had more PTC tasters than males ($\chi^2 = 5.254$, df = 5, $p = 0.385$), being statistically significant. The allelic frequencies in Gujjar and Bakarwal for non-taster (t) males and females were 55.86 and 54.55, respectively. In Syed population, t-allele frequencies for males and females were 45.75 and 37.79, respectively, while the other four populations showed intermediate t-allele frequencies. The heterozygosity showed little variation among all of the six populations.

1. Introduction

The North Indian human population and population from Jammu and Kashmir provide historical, linguistic, cultural, and socioreligious significance to the Indian subcontinent. Throughout the ages many population groups have migrated toward India along North-eastern and North-western routes [1]. Ethnic history of India reveals that Indians belong to two different categories: Dravidians (aborigines) and the Aryans or Sanskrit-speaking group (with mixed groups known as the Musalmans) [1]. Empirical studies indicate variable patterns of association among castes and tribes inhabiting wide geographic regions [2–4]. For example, Dravidian and Austro-Asiatic speaking tribes inhabiting different geographic regions show wide genetic diversity thus supporting the hypothesis of their heterogeneous origin, geographic isolation and migration history [2,4,5], whereas geographically proximate tribes and sub tribes within a region reflect close genetic affinity irrespective of their cultural and linguistic differences [6]. Diversity among Indian Muslims also shows close affinity because caste system is not rigid and they are not strictly reproductively isolated [7].

Muslims of India make up more than 13% of the population, and they belong to various castes based on linguistic and ethnic groups, besides a few tribes. According to the Indian census 2001, the human population of Jammu and Kashmir consists of 66.97% Muslims, 29.63% Hindus, 2.04% Sikhs, 1.12% Buddhists, 0.20% Christians, 0.024 Jains and 0.012% others. Muslims of Jammu and Kashmir belong to various castes such as Syed, Mughal, Malik, Mir, Bhatt, Khan, Lone, Pathan, Qureishi, Sheikh and many others based on their occupations. Gujjar and Bakarwal belong to Muslim population and is the major tribe of the state, densely populated in Rajouri and Poonch districts.

To understand the extent of biological affinity and diversity among the regional castes and tribes, we explored PTC classical genetic marker [8]. Genetic studies rely on variation, and substantial variation has been found in normal human taste abilities [9], opening the possibility of using genetic methods to improve our understanding of the sense of taste. The experience of bitterness occurs after certain chemicals contact taste receptors located in cells on the surface of the tongue. Some investigators hypothesize that this sense provides information so that people do not ingest bitter-tasting toxic chemicals [10]. Responses of humans to some bitter compounds show a bimodal distribution that distinguishes two phenotypes, tasters and non-tasters. The best-studied example of these is the ability to taste phenylthiocarbamide (PTC) and structurally related compounds [11]. Investigators reported that PTC-insensitive parents tended to produce PTC-insensitive children, and in many families where both parents were sensitive, 25% of their children were not [12]. Among population groups of India, the frequency of taster allele (T) is higher among population groups of Islands followed by North and South India and is low in West and Central India, as well as among scheduled tribes [13].

2. Subjects and methods

Jammu and Kashmir is situated between 32.17° and 36.58° North latitude and 37.26° and 80.30° East longitude. To its North is China and Russian Turkistan. On its East is Chinese Tibet. On the South and Southwest lie the Indian states of Punjab and Himachal Pradesh. On the West are the North West Frontier Provinces of Pakistan. The state of Jammu and Kashmir is 640 km in length from North to South and 480 km from East to West. The mountain chains that adorn the region include the Karakoram range, Nun Kun range, the Zanskar range, and Nanga Parbat. The survey was conducted from July 2011 to August 2011 for PTC taste ability in Rajouri and Poonch districts of Jammu and Kashmir. Nine hundred and eighty (980) individuals with the age range of 10–30 years were randomly selected from six populations viz., Gujjar and Bakarwal ($n = 241$), Mughal ($n = 142$), Khan ($n = 173$), Malik ($n = 145$), Mir ($n = 151$) and Syed ($n = 128$).

2.1. PTC threshold analysis

Taste sensitivity to PTC was ascertained using the serial dilution method by Harris and Kalmus [14]. A stock solution containing 0.13% phenylthiocarbamide was prepared in distilled water and serial dilutions were made up to the number thirteen. The least diluted solution was numbered as dilution number 14 and the most diluted solution was numbered as dilution number 1. If an individual could not taste any solution including 14, then he/she was designated a non-taster. The experiment was commenced with the weakest PTC solution in the order of increasing concentrations. Threshold levels for PTC were then recorded for males and females of each population.

2.2. Statistical analysis

Chi-square (χ^2) test is used for statistical analysis:

$$\chi^2 = \sum \frac{(\text{Observed frequency} - \text{Expected frequency})^2}{\text{Expected frequency}}$$

2.3. Gene frequency analysis

Genotype and allele frequencies for each population were calculated by Hardy–Weinberg method and heterozygosity was determined.

3. Results

3.1. PTC thresholds

Fig. 1 presents the threshold values for PTC among six populations which ranged from 4.98 to 7.25 in males, 4.07 to 6.08 in females and 4.72 to 6.79 as combined. The Gujjar and Bakarwal shows the highest one (7.25 in males and 6.08 in females), Syed the lowest (4.98 in males and 4.07 in females) and Khan, Malik, Mir showed intermediate PTC threshold values.

3.2. Phenotypic frequency

Table 1 presents χ^2 differences among the number of phenotypes of different human populations and Table 2 shows the percentage of phenotypes for PTC. The taster frequency of six different populations showed that the percentage of taster was higher than that of the non-tasters, and is statistically significant ($\chi^2 = 9.644$, df = 5, $p = 0.085$). The least PTC taster phenotypic frequencies were found among Gujjar and Bakarwal (68.79% in males and 70.24% in females) with high non-taster frequencies (31.21% in males and 29.76% in females). The highest PTC taster phenotypic frequencies were observed in Syed (79.07% in males and 85.71% in females) who also had the least non-taster frequencies (20.93% in males and 14.28% in females). The PTC phenotypic frequencies for Mughal, Khan, Malik and Mir lie between these two populations. We also observed that females ($\chi^2 = 4.563$, df = 5, $p = 0.471$) were more PTC tasters than males ($\chi^2 = 5.254$, df = 5, $p = 0.385$), the difference is statistically significant.

3.3. Gene frequency

Table 3 shows the taster (T) and non-taster (t) allelic distribution in males ($\chi^2 = 2.99$, df = 5, $p = 0.701$), females ($\chi^2 = 6.675$, df = 5, $p = 0.245$) and combined group ($\chi^2 = 3.733$, df = 5, $p = 0.588$) and these are statistically significant among six populations. Allelic frequency for the non-tasters (t) varies in different populations. The allelic frequencies in Gujjar and Bakarwal for non-taster (t) male and females were 55.86 and 54.55, respectively. In the Syed population t-allele frequencies for males and females were 45.75 and 37.79, respectively. The t-allele frequencies of other four populations almost lie between Gujjar and syed.

3.4. Genotype frequency

Table 4 presents the dominant (TT), recessive (tt) and heterozygous (Tt) genotypic frequencies and their χ^2 difference in male ($\chi^2 = 4.976$, df = 10, $p = 0.892$), female ($\chi^2 = 13.29$, df = 10, $p = 0.207$) and combined group ($\chi^2 = 7.458$, df = 10, $p = 0.681$) which are significant statistically among six populations. The frequency of heterozygotes of all populations lies between 49.00 to 50.00, which showed little differences, however dominant and recessive genotypes for combined group showed greater differences as in Gujjar and Bakarwal (TT = 19.87 and tt = 30.71) and in Syed (TT = 32.14 and tt = 18.74).

3.5. Homozygosity and heterozygosity

Table 5 presents homozygosity and heterozygosity among six populations. The observed heterozygosity showed little variations among these populations.

4. Discussion

The human sense of taste consists of five different modalities, bitter, sweet, sour, salt, and umami (the taste elicited by glutamate), that are critical for nutrition and survival. Of these, bitter perception has a particularly important role, as it protects us from ingesting naturally toxic substances which typically taste bitter [10]. Variation in taste sensitivity to the bitter compound phenylthiocarbamide (PTC) is one of the best known

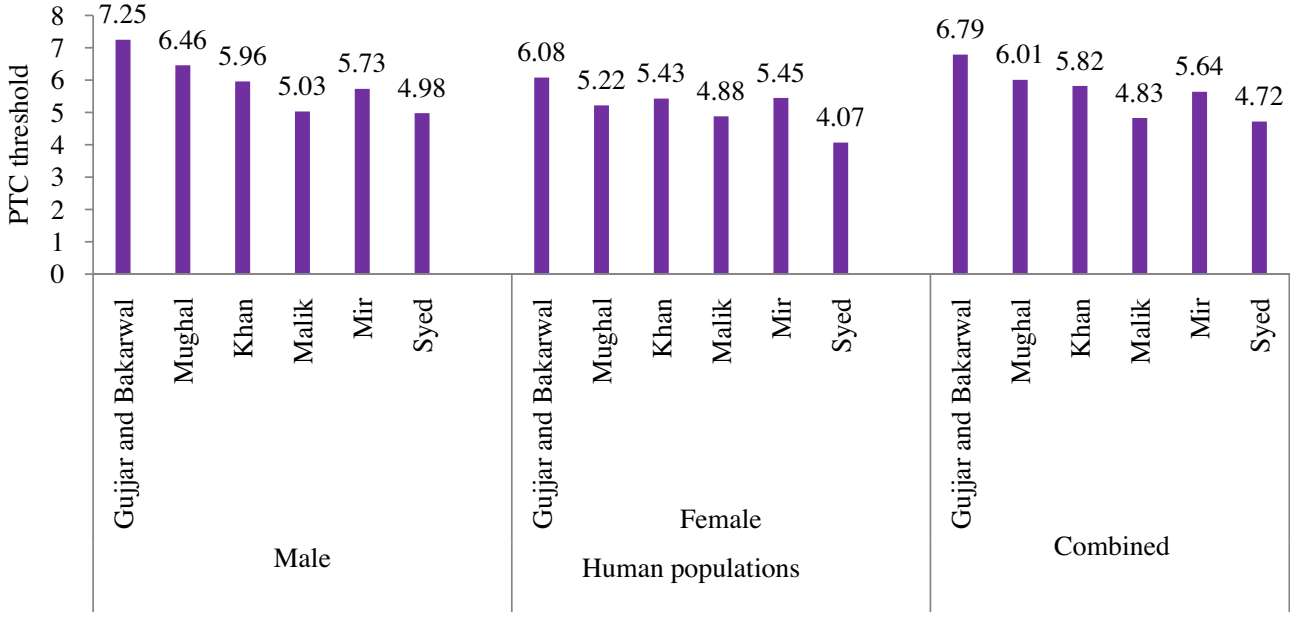

Figure 1 Threshold values among different human populations for PTC tasting.

Table 1 The χ^2 differences among number of phenotypes of different human populations.

Population	*n*	Male		Female		Combined	
		Taster	Non-taster	Taster	Non-taster	Taster	Non-taster
Gujjar and Bakarwal	241	108(1.2)	49(2.025)	59(0.254)	25(2.722)	167(1.399)	74(4.414)
Mughal	142	66(0.352)	23(0.00)	40(0.243)	13(0.364)	106(0.037)	36(0.117)
Khan	173	85(0.012)	26(0.143)	49(0.355)	13(0.00)	134(0.031)	39(0.097)
Malik	145	78(0.342)	23(0.042)	36(0.105)	08(0.818)	114(0.145)	31(0.457)
Mir	151	84(1.08)	22(0.36)	36(0.1)	09(0.364)	120(0.217)	31(0.694)
Syed	128	68(0.25)	18(0.428)	36(0.272)	06(1.6)	104(0.505)	24(1.581)

Parentheses = chi-square value (χ^2) and *n* = number of individuals.
The chi-square (χ^2) values for number of phenotypes in male ($\chi^2 = 5.254$, df = 5, $p = 0.385$), female ($\chi^2 = 4.563$, df = 5, $p = 0.471$) and combined group ($\chi^2 = 9.644$, df = 5, $p = 0.085$), are statistically significant.

Table 2 PTC taste frequency in percentage phenotypes among different human populations.

Population	Male		Female		Combined	
	Taster	Non-taster	Taster	Non-taster	Taster	Non-taster
Gujjar and Bakarwal	68.79	31.21	70.24	29.76	69.29	30.71
Mughal	74.15	25.85	75.47	24.52	74.65	25.35
Khan	76.58	23.42	79.03	20.97	77.46	22.54
Malik	77.23	22.77	81.82	18.18	78.62	21.38
Mir	79.25	20.75	80.00	20.00	79.47	20.53
Syed	79.07	20.93	85.71	14.28	81.25	18.75
M ± SE	75.85 ± 1.36	24.15 ± 1.36	78.71 ± 1.31	21.29 ± 1.31	76.79 ± 1.34	23.21 ± 1.34

M = mean and SE = standard error.

Table 3 Gene frequency distribution among different human populations for PTC tasting.

Population	Male		Female		Combined	
	T	t	T	t	T	t
Gujjar and Bakarwal	44.16	55.86	45.45	54.55	44.58	55.42
Mughal	49.16	50.84	50.48	49.52	49.65	50.35
Khan	51.61	48.39	54.21	45.79	52.52	47.48
Malik	52.28	47.72	57.36	42.63	53.76	46.24
Mir	54.45	45.55	55.28	44.72	54.69	45.31
Syed	54.25	45.75	62.21	37.79	56.7	43.3

The chi-square (χ^2) differences for gene frequencies in male ($\chi^2 = 2.99$, df = 5, $p = 0.701$), female ($\chi^2 = 6.675$, df = 5, $p = 0.245$) and combined group ($\chi^2 = 3.733$, df = 5, $p = 0.588$) among six populations, are statistically significant.
T and t are dominant and recessive alleles respectively.

Table 4 Genotype frequency among different human populations for PTC tasting.

Population	Male			Female			Combined		
	TT	Tt	tt	TT	Tt	tt	TT	Tt	tt
Gujjar and Bakarwal	19.50	49.33	31.20	20.65	49.58	29.75	19.87	49.41	30.71
Mughal	24.16	49.98	25.84	25.48	49.99	24.52	24.65	49.99	25.35
Khan	26.63	49.95	23.41	29.38	49.64	20.96	27.58	49.87	22.54
Malik	27.33	49.89	22.77	32.90	48.91	18.17	28.90	49.71	21.38
Mir	29.65	49.60	20.74	30.56	49.44	19.99	29.90	49.56	20.52
Syed	29.43	49.63	20.93	38.70	47.01	14.28	32.14	49.10	18.74

The chi-square (χ^2) values for genotype frequencies in male ($\chi^2 = 4.976$, df = 10, $p = 0.892$), female ($\chi^2 = 13.29$, df = 10, $p = 0.207$) and combined group ($\chi^2 = 7.458$, df = 10, $p = 0.681$) among six populations, are significant statistically.
TT, Tt and tt represent dominant, heterozygous and recessive genotypes.

Mendelian traits in human populations, ranking alongside eye color and blood types in the canon of classic examples.

The major gene TAS2R38 on chromosome 7 responsible for this trait was identified as a member of the TAS2R bitter taste

Table 5 Herterozygosity and homozygosity among different human populations for PTC tasting.

Population	Male		Female		Combined	
	H_t	H_o	H_t	H_o	H_t	H_o
Gujjar and Bakarwal	0.4933	0.5067	0.4958	0.5042	0.4941	0.5059
Mughal	0.4998	0.5002	0.4999	0.5001	0.4999	0.5001
Khan	0.4995	0.5005	0.4964	0.5036	0.4987	0.5013
Malik	0.4989	0.5011	0.4891	0.5109	0.4971	0.5029
Mir	0.4960	0.504	0.4944	0.5056	0.4956	0.5044
Syed	0.4963	0.5037	0.4701	0.5299	0.4910	0.5090
Mean	0.4973	0.5027	0.4909	0.5090	0.4961	0.5039

H_t and H_o represent heterozygosity and homozygosity respectively.

receptor gene family consisting of a single coding exon 1002 bp long, encoding a 333 amino acid, 7-transmembrane domain G-protein-coupled receptor [15], that responds to bitter stimuli [16–20] and the milestones of this discovery have been summarized [21]. Two major forms of this bitter receptor gene were identified in most of the world's populations, designated as the 'major taster' form and the 'major non-taster' form. These two forms differ in 3 amino acid positions, numbers 49, 262, and 296 [22]. The major taster form contains a proline at position 49, an alanine at position 262, and a valine at position 296 (constituting the PAV form), while the non-taster form contains an alanine, a valine, and an isoleucine at these 3 positions, respectively (constituting the AVI form). These two forms, called alleles, account for the bimodal distribution of taste thresholds and the classic recessive inheritance pattern is observed. Based on the example of PTC perception, it appears likely that inter-individual differences in taste response to other bitter compounds come from allelic or haplotype variations between individuals. Individual differences in bitterness sensitivities are reliable [8,23]. Investigators have observed that younger subjects are more sensitive than older subjects to the bitterness of 6-n-propylthiouracil (PROP) or PTC, with some suggesting that age modifies the genotype-phenotype relationship [12,24]. Since allele frequencies do not differ between children and adults, the explanation for age-related differences in bitter perception must lie elsewhere. Previous investigators noted that people who were less sensitive to this class of bitter compounds seemed to lose their sensitivity faster as they got older, concluding that gene penetrance might differ by age and genotype [25]. Much of PTC's appeal arises from the fact that it is nearly impossible to guess one's phenotype until explicitly tested, yet, when tested, the phenotype is so striking as to be amusing.

The objective of this study aimed to observe the phenylthiocarbamide (PTC) sensitivity and to determine gene frequency distribution among different human populations. Allele frequencies for the bitter taste gene, TAS2R38 vary by racial/ethnic group and therefore when two racial groups are compared, they differ in phenotype as they differ in genotype [26]. Factors like mutation, natural selection, inbreeding, genetic drift and miscegenation are known to play an important role in producing gene frequency differences in different human populations. The populations of India and other South Asian countries offer great opportunities for studying socio-cultural and genetic variability. Perhaps, nowhere in the world people are distributed in such a large number of ethnic, castes, religious and linguistic groups even in a small geographic area as, living in India for thousands of years and maintaining their separate entities by practicing endogamy.

Our investigation on PTC taste perception of six different populations revealed that the percentage of taster frequency is significantly more than that of the non-tasters which is in total agreement with other studies [8,18]. We found that females of six populations are more PTC taster phenotypes than males as reported by others [27]. PTC taste thresholds vary among six populations and females are found to taste PTC at lower thresholds than males, a small number of specific differences in taste ability have long been known and well-studied [11]. The frequency of non-taster allele t is about 50% among European populations it varies from 25% to 57%. In India the frequency of t-allele shows variation in different ethnic groups and castes [7,13]. Our study shows little variation in non-taster allele among six populations. Heterozygosity increases the sensitivity to PTC as reported by Mennella et al. [28], i.e., more heterozygous children perceived bitterness at the lowest concentrations than did adults with the same genotype, with adolescents intermediate between adults and children. Our study shows more PTC heterozygous (Tt) genotypes as compared to dominant (TT) and recessive (tt) homozygous genotypes. Whereas little variation in heterozygosity lies in between populations, the dominant and recessive homozygosity values show remarkable differences. Understanding of the multiple sequence variations in the PTC gene will allow examination of the details of the genetic basis of food preferences and the relationship between bitter taste sensitivities and perhaps their possible health outcomes. On a larger scale, the PTC gene may be illustrative of ancient genetic variation that has been proposed to save the tasters and to make non-tasters susceptible to common disease [29]. The PTC non-taster allele is common, as it is very old and yet it appears to confer selective advantage, at least in the heterozygous state. Finally, PTC presents a unique opportunity in the field of bitter taste transduction. Having a known gene with a strong effect on phenotype in vivo provides many opportunities for studies of taste physiology, biochemical function, and molecular structure elucidation in the human taste sensitivity.

In conclusion, this study presents the gene frequencies of PTC taste sensitivity among six populations of Jammu. The data, with some more genetic markers to be studied in future, can throw fresh light on the origin and evolution of the population under study.

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