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Research Article

Frequency of *CYP1A1*2A* polymorphisms and deletion of the *GSMT1* gene in a Peruvian mestizo population

Angel Tito Alvarado[1], Ana María Muñoz[2], María Saravia Bartra[1], Milton Valderrama-Wong[1], Daniela González[3], Luis Abel Quiñones[3], Nelson Varela[3], María Rocío Bendezú[4], Jorge Antonio García[4], Berta Loja-Herrera[4]

1 *International Research Network in Pharmacology and Precision Medicine, Human Medicine, San Ignacio de Loyola University, Lima, Peru*
2 *Research Unit in Nutrition, Functional Foods for Health and Nutraceuticals, San Ignacio de Loyola University, Lima, Peru*
3 *Laboratory of Chemical Carcinogenesis and Pharmacogenetics, Department of Basic and Clinical Oncology, Faculty of Medicine, University of Chile, Santiago de Chile, Chile*
4 *Faculty of Pharmacy and Biochemistry, San Luis Gonzaga National University of Ica, Ica, Peru*

Corresponding author: Angel Tito Alvarado (eaa.alvarado@hotmail.com)

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Abstract

The polymorphic variants of *CYP1A1* and the deletion of *GSTM1* are present in the Peruvian mestizo population. Wild type and mutated genotypes (WT/*2A and *2A/ *2A) were identified, whose allele frequencies are 0.31 (T allele) and 0.69 (C allele), respectively; 53% with wild type *GSTM1* (+) and 47% with null *GSTM1*. The frequency in Iquiteño emigrants was 0.72 *CYP1A1*2A* and 25% *GSTM1* (-); from Lima 0.67 *CYP1A1*2A* and 33% of *GSTM1* (-). The Hardy-Weinberg equilibrium test for the studied population showed that both frequencies are out of balance, $p > .05$.

The presence of the risk allele of the *CYP1A1*2A* polymorphism and the deletion in the *GSTM1* gene are high, which could be indicative of a phase I and II metabolic imbalance in this group of Peruvian populations, with potential risks of activating agents procarcinogens thus affecting the incidence of tumor pathologies with an environmental component.

Keywords

Allelic variants, Mestizo, Mutagens, Peru, Procarcinogens

Introduction

Cancer is a priority disease for national and global public health; being the second cause of death worldwide. The year 2020 registered 19.3 million new cases and 9.9 million deaths related to cancer, many of these cancers have an environmental component (Sung et al. 2021); in Peru, mortality from cancer in 2018 was 33,098 deaths (17,039 women and 16,059 men), the first cause of death was stomach cancer (13.8%), followed by lung cancer (8.6%). Estimating for the same year, 42,849 prevalent cases of cancer, 23,734 women and 19,115 men. In men the most prevalent locations were prostate, followed by colorectal, stomach and leukemia, while in women they were breast, followed by cervix, thyroid and colorectal (Vallejos-Sologuren et al. 2020).

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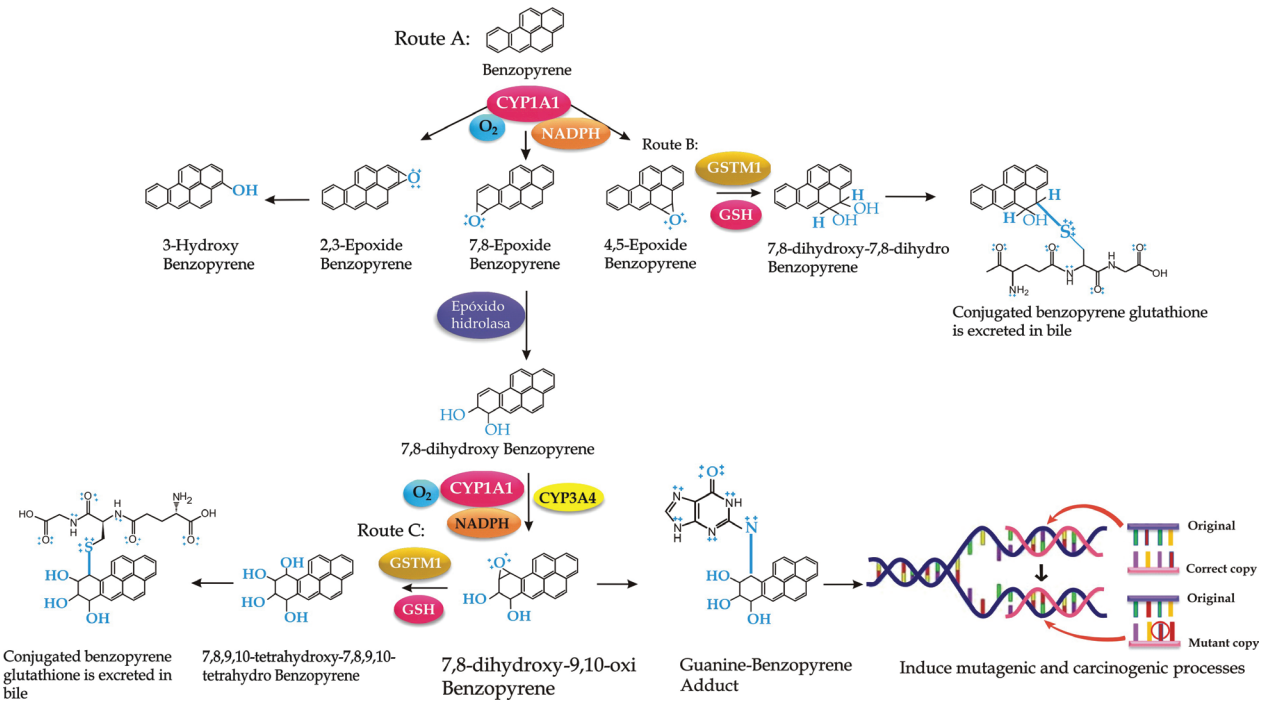

Figure 1. Mechanism of action of CYP1A1 and GSTM1.

The *CYP1A1*, *CYP2C19*, *CYP2D6* and *CYP17* genes that encode their respective isoenzymes are associated with different types of cancer (Lee et al. 2006), by participating in the phase I metabolism of procarcinogens [polycyclic aromatic hydrocarbons (benzopyrene), arylamines, N-nitrosamines and dioxins] forming reactive metabolites that produce DNA adducts (Lee et al. 2006; Attia 2010; Jin et al. 2011; Rahal et al. 2013; Acevedo et al. 2014; Wongpratate et al. 2020); of them, the *CYP1A1* gene (Santes-Palacios et al. 2016), has greater susceptibility to various types of cancer (Wongpratate et al. 2020), such as gastric, colorectal, buccal, esophageal, laryngeal, mammary, cervix, lung , thyroid, prostate and kidney (Jin et al. 2011; Balaji et al. 2012; Meng et al. 2015; Li et al. 2016; Ding et al. 2017).

The *CYP1A1* gene is located on the arm of chromosome 15 in region 24.1 (15q24.1) and consists of seven exons and six introns (Masson et al. 2005); which presents four single nucleotide polymorphisms (SNPs), called *CYP1A1*m1, m2, m3 and m4 (Acevedo et al. 2014). The *CYP1A1*1A* (m1, T3801C, rs4646903) genotype contains a thymine (T) for cytosine (C) substitution at nucleotide 3801 (T3801C) of the 3' noncoding region of polyadenylation resulting in a restriction site for MspI endonuclease (CYP1A1 MspI or CYP1A1*2A) associated with increased enzyme activity. The *CYP1A1*2A* polymorphism generates three genotypes, one wild-type that is a homozygous *1A/*1A allele without the MspI site (genotype A, T/T, m1/m1), a heterozygous *1A/*2A allele (genotype B, T/C, m1/m2) and a rare homozygous recessive *2A/*2A allele with the MspI site (genotype C, C/C, m2/m2) (Zhuo et al. 2012; Khlifi et al. 2013; Acevedo et al. 2014; Rosero et al. 2016).

The *GSTM1* gene is located on the short arm of chromosome 1 in region 13.3 (1p13.3), and has four polymorphisms, called GSTM1*A, GSTM1*B, both due to changes in a single nitrogen base; GSTM1*1 × 2 which is a duplication and the GSTM1*0 generated by a deletion (Heredia et al. 2017). These genes encode different glutathione S-transferase (GST) isoenzymes classified into seven families (GST alpha, kappa, mu, pi, sigma, theta and zeta) that differ from each other due to their sequencing and functional activity (Strange et al. 2001; Usategui-Martín et al. 2014). *GSTM1* (GST mu), *GSTP1* (GST pi) and *GSTT1* (GST theta) are the most frequent, which are expressed in the gastrointestinal tract (Board and Menon 2013; Usategui-Martín et al. 2014; Rosero et al. 2016; García-Martínez et al. 2017). GSTM1mu is encoded by five genes that constitute the isoforms GSTM1, GSTM2, GSTM3, GSTM4, and GSTM5 (Xu 1998). The GSTM1*0 variant is the product of a homozygous deletion, due to an unequal recombination between two highly conserved regions of 4.2 kb that are located at the 5' and 3' ends of the gene respectively, generating a null allele that expresses an enzyme without activity (Board and Menon 2013; Rosero et al. 2016; Heredia et al. 2017), which leads to genomic instability that predisposes to various types of cancer (Heredia et al. 2017; Satinder et al. 2017). Figure 1 outlines the action of the CYP1A1 enzyme (expressed by the *CYP1A1* gene) on benzopyrene (Route A), which converts it into a bioactive metabolite (7,8-dihydroxy-9,10-oxy-benzopyrene) that binds to the guanine of DNA generating the benzopyrene guanine adduct that induces mutagenic and carcinogenic processes (Lee et al. 2006; Acevedo et al. 2014; Wongpratate et al. 2020); at the same time, the mechanism of conjugation of 4,5-benzopyrene epoxide (Route B) and 7,8,9,10-tetrahydroxy-7,8,9,10-tetrahydro benzopyrene (Route C) is represented by action of reduced glutathione (GSH g-Glu-Cys-Gly) which is expressed by *GSTM1*;

additionally, GSH conjugates different reactive oxygen species (ROS), protecting cells from cytotoxic effects and oxidative stress (Board and Menon 2013; Usategui-Martín et al. 2014; García-Martínez et al. 2017).

After reviewing the PubMed-NCBI database of polymorphic studies of the *CYP1A1* and *GSTM1* gene in Peruvian populations, it is evident that they are still scarce, so it is necessary to know and describe the frequencies of these polymorphisms. In this sense, we have decided to study *CYP1A1*2A* and *GSTM1*, which were selected for being the most frequent in various populations and for being related to susceptibility to different types of cancer.

Our objective was to identify and describe the frequency of *CYP1A1*2A* polymorphisms and the deletion of the *GSTM1* gene in a sample of a Peruvian mestizo population and compare them with data previously reported in Caucasian, African and Asian populations, which are part of the migratory offspring of Peruvians.

Materials and methods

Study type and design

Observational, descriptive, cross-sectional study with prospective recruitment between January 2019 and December 2020. The residents of Lima were summoned to the Molecular Pharmacology Laboratory of the School of Medicine, San Ignacio de Loyola University (USIL), to inform about the objectives and importance of the study, after that, the volunteers were selected by type sampling non-probabilistic and for convenience. The sample size was 81 Peruvian individuals residing in Lima (22 women; 59 men). It was distributed into two groups according to the place of origin and based on the declaration of each participant: 30 migrant individuals from the jungle area of Iquitos and 51 migrants from other provinces of Peru.

Inclusion and exclusion criteria

To establish the inclusion criteria, we have used the migratory pattern, linguistic tree, surnames and the percentage of Peruvian mestizos.

The internal migration pattern of Peruvians is a complex phenomenon, which is generated by natural disasters, internal security, displacement from the countryside to the city, by the economic crisis (Yamada 2010; Carrillo-Larco et al. 2017), for continuing studies university students and by the aspiration to seek better socioeconomic levels or living conditions (Carrillo-Larco et al. 2017); to be considered as a migrant, the citizen indicated his or her place of birth, previous place of residence, duration of current residence and place of residence on a fixed date; having reported that 11.9% of residents in Lima are migrants from various provinces of Peru, and within them, 16.1% are from the city of Iquitos (INEI 2020); the linguistic tree (built with phonemes) was considered, which is a non-molecular marker of miscegenation and the surnames that indicate their historical migratory patterns, population structure and phylogenetic relationships between populations (Herrera-Paz 2013). At the same time, the percentage of mestizos in Peru was considered, with 67.7% of mestizos living in Lima and 75.9% in Iquitos (INEI 2018).

In this sense, the present study included all Peruvians who declared to be mestizo with a surname of Spanish, African, Chinese and Japanese descent, originally from Iquitos (jungle area) and other provinces of Peru who resided in Lima for a time greater than one year, both sexes, over 18 years of age and without a family relationship. At the clinical examination, by a surgeon, the participants had to be in good health (systolic blood pressure of 110–139 mm Hg and diastolic blood pressure of 60–89 mm Hg, abdominal circumference less than 95 cm in men and 82 cm in women and not having a diagnosis of diabetes), not consuming drugs of abuse or alcohol, which was established through an interview, six months before taking the sample, not to consume medications and give written consent. All subjects who could not give their consent and those who did not meet the inclusion criteria were excluded from the study (Alvarado et al. 2019).

Ethical considerations

The study was developed in strict compliance with national ethical standards, criteria of the Belmont Report, Declaration of Helsinki of 1975 with the current revision and based on the informed consent approved by the Methodological Research Committee of the Santa Rosa Hospital by means of certificate No. 16-19-CMI-HSR. All were assigned a code to ensure anonymity and confidentiality.

Obtaining genomic DNA

The buccal sample of non-keratinized stratified flat epithelial tissue was obtained by swabbing, rubbing the inner cheek mucosa six times with the swab to guarantee an adequate amount of scaly cells, from which genomic DNA (DNAg) was extracted. Subsequently, the swab was immersed for 60 seconds in 300 µL of lysis buffer solution and the resulting mixture was refrigerated at 4 °C for a time not exceeding 18 hours. The DNAg was extracted using the innuPRE DNA Master kit (Analytik Jena), following the manufacturer's protocol, a procedure performed at the Molecular Pharmacology Laboratory of the School of Medicine, USIL. The DNAg was quantified by spectrophotometry using Denovix equipment (model DS-11, FX, Spectrophotometer Series, USA). Samples with absorbance ratios of 260/280 nm and 260/230 nm equal to or greater than 1.8 were considered suitable for the study. The samples were stored at -20 °C until analysis (Alvarado et al. 2019).

Genotypic analysis

After extracting the DNAg, it was amplified by polymerase chain reaction and subsequent digestion with restriction enzymes (Lee et al. 2006; Yun et al. 2014).

Detection of the polymorphism of the CYP1A1 gene

The restriction fragment length polymorphism technique based on polymerase chain reaction (PCR-RFLP) was used to detect the *CYP1A1*2A* polymorphism, using primer sequences such as the first forward 5'-CAGTGAAGAGGTGTAGCCGCT-3' and first reversed 5'-TAGGAGTCTTGTCTCATGCCT-3'. After an initial denaturation at 94 °C for 3 min, the samples were subjected to 30 cycles for 30 s at 94 °C, 30 s at 55 °C, and 1 min at 72 °C, followed by the final extension at 72 °C for 5 min. Subsequently, the amplicons were digested with MspI enzyme (GIBCO BRL, Life Technologies, Inc. Gaithersburg, MD) at 37 °C for 3 hours (Acevedo et al. 2014). The digestion system contained 5 µL of PCR products, 1 µL of 10xT buffer, 1 µL of 0.1% BSA, 0.6 µL of MspI, 2.4 µL double-distilled water (Yun et al. 2014). The digested products were separated by 2% agarose gel electrophoresis and then visualized under ultraviolet light. The presence of the wild genotype *1A/*1A (T/T) is observed by a single band of 340 bp, the genotype *1A/*2A (T/C) is identified by three bands 340, 200 and 140 bp and the genotype *2A/*2A (C/C) is identified by two bands of 200 and 140 bp (Lee et al. 2006; Yun et al. 2014).

Detection of the GSTM1 gene polymorphism

The detection of the deletion of the *GSTM1* gene was determined using two primers, 5'GAACTCCCTGAAAAGCTAAAGC-3' and 5'-GTTGGGCTCAAATATACGGTGG-3' for 30 cycles of amplification with 1 min at 94 °C for denaturation, 1 min at 59 °C for primer hybridization, 1 min at 72 °C for extension. The amplicons were subjected to electrophoresis in a 2% agarose gel, the presence of positive *GSTM1* was identified by staining with ethidium bromide and analysis under ultraviolet light, observing the 215 bp fragment and the null *GSTM1* was determined by the absence of the mentioned snippet.

Polymorphism nomenclature

The international nomenclature was used for the *CYP1A1* gene, the wild genotype being *1A/*1A, the heterozygous *1A/*2A and the homozygous recessive *2A/*2A (Santes-Palacios et al. 2016). For the *GSTM1* gene, the null genotype [GSTM1 (-)] corresponds to the homozygous deletion of the gene that generates absence of expression and enzymatic activity; the present genotype [GSTM1 (+)] corresponds to the wild variant that has the active gene (homozygous or heterozygous) (Lee et al. 2006).

These analyzes were carried out at the Laboratory of Chemical Carcinogenesis and Pharmacogenetics, Faculty of Medicine, University of Chile.

Statistical analysis

The expected genotype frequencies for *CYP1A1* and *GSTM1* were determined by direct counting from the allele frequencies. To determine if the distribution of the genotypes studied was in Hardy-Weinberg equilibrium (HWE), the Chi-square test (X^2) was used, considering a degree of freedom and a p value <.05. X^2 values greater than 3.88 in the comparison indicated the rejection of the null hypothesis, therefore, the observed frequencies differed significantly from those expected (Alvarado et al. 2019). The analysis included allele frequencies described in populations of Peruvian descent (African, Asian, and Caucasian). The Statistical Software GraphPad Prism 9 was used. Version 9.1.2 (Acevedo et al. 2014; Alvarado et al. 2019).

Results

*CYP1A1*2A* polymorphisms and deletion of *GSTM1* were detected in a population of 81 Peruvian individuals living in Lima for more than one year, of which 30 were migrants from the jungle area of Iquitos who resided in Lima and 51 subjects from the other provinces of the country (Chincha, Ica, Trujillo). Their ages and genders are described in Table 1.

Table 1. Demographic characteristics of the study population of Peruvian mestizo volunteers.

Residents in Lima	Gender	Sample by gender n (%)	Sample by province n (%)	Age (years)	
				Mean	DS
Various provinces	Female	13 (25.49)	51 (62.96)	22.31	±10.51
	Male	38 (74.51)		25.53	±7.30
Iquitos	Female	9 (30.00)	30 (37.04)	25.78	±2.33
	Male	21 (70.00)		24.24	±2.07
	Total		81(100.00)	26.31	±7.08

DS: standard deviation.

Figure 2 shows the analysis of the genotypes studied in 2% agarose gel.

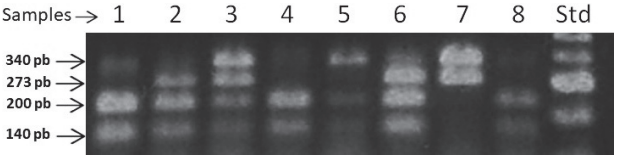

Figure 2. Genotypic analysis of *CYP1A1*2A* and *GSTM1* (-) (2% agarose gel). Std represents the 100 bp molecular weight marker. The 340 bp amplicon represents the undigested *CYP1A1* gene fragment. The 200 bp and 140 bp fragments correspond to the fragments cut with the enzyme Mspl. The 273 bp amplicon corresponds to the presence of *GSTM1*.

Table 2 describes the identified genotypes: wild type (T/T) and mutated genotypes (heterozygous T/C (WT/*2A) and homozygous C/C (*2A/*2A), whose allelic frequencies are 0.31 (T allele) and 0.69 (C allele), respectively; 53% with active wild type *GSTM1* (+) and 47% with *GSTM1* null (-) due to homozygous deletion of the gene (del/ del). The HWE showed that both frequencies are out of balance (X^2 value greater than 3.84, 1 degree of freedom and p > .05).

In migrants from the jungle area of Iquitos, it is observed that the frequency of the *CYP1A1*2A* polymorphism (X^2 value 1.60) and *GSTM1* (X^2 value 3.33) are in HWE; while

Table 2. Genotype frequencies for *CYP1A1*2A* and *GSTM1* in a sample of a Peruvian mestizo population.

	Genotype	Polymorphic variant	n	Genotypic frequency	Allele	n	Allelic frequency	X^2	p-Value
*CYP1A1*2A*	T/T	*1A/*1A	4	4.94	T	8	0.31	4.30	0.119
	T/C	*1A/*2A	43	53.09	C	86	0.69		
	C/C	*2A/*2A	34	41.98		68			
	Total		81	100.00		162	1.00		
GSTM1	GSTM1 +		43	53.00				7.60	0.017
	GSTM1 -		38	47.00					
	Total		81	100.00					

X^2, Chi square; Homozygous wild type T/T genotype; Heterozygous genotype T/C; Homozygous genotype C/C. *GSTM1* (+) wild type genotype; Null *GSTM1* (-) genotype.

the inhabitants come from other provinces of the country that reside in Lima, it is observed that the frequency of the *CYP1A1*2A* polymorphism is in HWE (value X^2 2.82) and the deletion of GSTM1 is not (value X^2 4.32) (Table 3).

Table 3. Frequencies of *CYP1A1*2A* polymorphisms and deletion of the *GSTM1* gene in a sample of residents of Lima and Iquitos.

Genotype	Lima n (%)	Iquitos n (%)	Frequency Lima	X^2	Frequency Iquitos	X^2
*1A/*1A	3 (5.88)	1 (3.33)	0.33	2.82	0.28	1.60
*1A/*2A	28 (54.90)	15 (50.00)	0.67		0.72	
*2A/*2A	20 (39.22)	14 (46.67)				
Total	51 (100.00)	30 (100.00)	1.00		1.00	
GSTM1 +	28 (54.90)	15 (50.00)	77.00	4.32	75.00	3.33
GSTM1 -	23 (45.10)	15 (50.00)	33.00		25.00	
Total	51 (100.00)	30 (100.00)	100.00		100.00	

Table 4 shows the frequency of combined genotypes of *GSMT1* (+), *GSMT1* (-) with *CYP1A1*2A* of migrants from Iquitos and other provinces residing in the city of Lima, observing that the global frequency is 0.26 (*GSMT1* null + *CYP1A1*2A* T/C) and 0.17 (*GSMT1* null + *CYP1A1*2A* C/C).

Table 4. Frequencies of the combined genotypes of *GSMT1* (+), *GSMT1* (-) with *CYP1A1*2A* in a Peruvian mestizo population sample.

Genotypes		Iquitos	Lima	Global Peru
GSMT1	***CYP1A1*2A***	**f (n)**	**f (n)**	**f (n)**
+	T/T	0.03 (01)	0.00 (00)	0.01 (01)
+	T/C	0.20 (06)	0.31 (16)	0.27 (22)
+	C/C	0.27 (08)	0.24 (12)	0.25 (20)
-	T/T	0.00 (00)	0.06 (03)	0.04 (03)
-	T/C	0.30 (09)	0.24 (12)	0.26 (21)
-	C/C	0.20 (06)	0.16 (08)	0.17 (14)
Total		1.00 (30)	1.00 (51)	1.00 (81)

f, frequency; n, number of individuals.

Table 5 shows the comparison of the genotype frequencies of the double mutated genotype of (*2A/*2A), which is present in mixed-breed Peruvian populations, such as

Table 5. Percentages of *CYP1A1* (*2A/*2A) and *GSTM1* (-) polymorphism in populations related to the Peruvian mestizo population.

Genotypes	Alleles	African (%)	Asian (%)	Caucasian (%)	Peruvian Mestizo (%)
*2A/*2A	C	–	33	7–10	41.98
GSTM (-)	Null	33	49–63	50–58	46.91

in Japanese and Caucasians (Sato et al. 1999). For the null genotype of *GSTM1*, the average of the frequencies in our population samples is 46.91%, and it is present in Africans (Dandara et al. 2002), Asians and Caucasians (Heredia et al. 2017), with a great variability between populations.

Discussion

In the present study, the *CYP1A1*2A* genetic polymorphism and the deletion of *GSTM1* were described in samples of 81 mestizo residents living in Lima and of both sexes; when comparing the *CYP1A1*2A* genotype by sex, sex with alleles of *CYP1A1*2A* and sex versus *GSMT1*, Pearson's X^2 test revealed a p value>.05 (0.422, 0.999 and 0.999 respectively), indicating that there is not enough evidence to conclude that the variables are associated; and due to the type of sampling there is likely to be a bias.

In the mestizo Peruvian sample, it has been found that the frequency of the *CYP1A1*2A* polymorphism is 0.69; this variant expresses highly active enzymes that biotransform procarcinogenic substances into mutagenic and carcinogenic metabolites. While the frequency of the deletion of *GSTM1* is 47%; *GSTM1* (-) expresses an enzyme of the glutathione S-transferase family, which cannot conjugate glutathione with procarcinogens; when performing the combination analysis of the global frequencies of the genotypes, we observe that it is 0.26 for the combination *GSMT1* null vs. *CYP1A1*2A* T/C and 0.17 for null *GSMT1* vs. *CYP1A1*2A* C/C, increasing the possibility of mutagenesis, in this group of individuals. Peruvian miscegenation is based on global migration generated between Europeans and American populations, with the current tricontinental miscegenation (European, African and Indo-American) in varying degrees (Hunley et al. 2011; Herrera-Paz 2013), on local miscegenation, linguistic tree, surnames (Herrera-Paz 2013), percentage of mestizos and in native genetics, described by Harris et al. (2018) who have shown that the Peruvian mestizo population (mixtures of multiple Native American communities that occurred before and during the Inca Empire, Spanish dominance and migration among the Peruvian populations of the three geographic regions, mostly from the high Andes to the coast and the low-lying Amazon) have between 60% and 70% native genes, in some more geographic locations 80%.

The reported frequencies of the polymorphism (*CYP1A1*2A*) and of the deletion (*GSTM1*) differ signif-

icantly, indicating that they are not in HWE in the total population studied. In the analysis by migrants and residents, the observed and expected frequencies are the same in Iquiteño emigrants, while, for residents in Lima from other provinces of the country, the test for the *GSTM1* deletion deviates from the HWE; this deviation could be explained by evolutionary selection (Hao and Storey 2019), by mutations (new alleles created), migrations (by immigrants and migrants) (Llorca et al. 2005), probable genotyping errors (Llorca et al. 2005; Hao and Storey 2019) or to alleles not detected by the technique used (Arrunategui et al. 2013). Several studies show that evolution drives an adaptive change in populations, with the environment (consumption of processed foods and environmental chemical agents) being a conditioning factor for allelic variants that can be beneficial in one territory and not in another, increasing or decreasing over the generations, producing a disruptive or deleterious mutation (causing various diseases, premature death or infertility in the individual) or a neutral mutation, which only cause slight changes in the phenotypes that will be expressed as normal variants (Porta and Crous 2005; Herrera-Paz 2013; Carrillo-Larco et al. 2017); Díaz and Glaves (2020), indicate that diet is a critical determinant for cancer risk, estimating that dietary factors are responsible for around 30% of cancers in industrialized countries and 20% in developing countries, like Peru. Molina et al. (2016) mention that the inhabitants of the Peruvian Amazon have stopped consuming their regional products, to introduce various processed and canned foods into their diet. Geography and migration is another factor to consider, since there are differences between individuals in a community, between communities in a territory, between territories in the same geographical area, between areas on the same continent, and between continents (Herrera-Paz 2013). In a study by Thoudam et al. (2010) it was shown that the frequency of the *GSTM1* (-) genotype in the Indian population varies according to geography, being 12.4% in the central population, 16.8% in Indian populations. south, 19% in northern residents and 32.7% in northeastern residents; while in seven Iranian populations the frequencies were reported to range from 43.8 to 53.0% (Nasseri et al. 2015).

When comparing our results of the mutated homozygous *CYP1A1* genotype (*2A/*2A) with previously published studies, we can observe that, in Asians it is 33% and in Caucasians between 7 and 10% (Sato et al. 1999), being lower than that found in our study (41.98%); likewise, regarding *GSTM1* (-) our results (47%) are closer to those reported for Asians (49–63%) and Caucasians (50–58%) (Heredia et al. 2017), not so with respect to Africans, whose frequency is 33% (Dandara et al. 2002), this is possible due to their natural population evolution, since the arrival of the first Spaniards, Africans, Chinese and Japanese, more than 488 years have passed (Vílchez 2016).

These findings could be useful as a tool for defining cancer risk susceptibility due to exposure to environmental xenobiotics and help in an early diagnosis of it, mainly in individuals who are exposed to polycyclic aromatic hydrocarbons present in cigarette smoke, in processes of incomplete combustion of meat and other organic substances (Lee et al. 2006). For many years, there have been various studies that support that *CYP1A1* polymorphisms are associated with cancer.

The homozygous recessive *2A/*2A genotype increases the risk of oral cancer, as demonstrated by Park et al. (1997) in Caucasian American patients, later (Sato et al. 1999) indicated it in Asian populations. Marques et al. (2006) studied it in a Brazilian population, Cha et al. (2007) described it in a Korean population. In another study (Lee et al. 2006) it was reported that the *1A/*2A and *2A/*2A polymorphisms by themselves are not associated with gastric cancer, but they are in individuals who smoke or drink alcohol. Lakkireddy et al. (2015) reported that the *CYP1A1*2C* (SNP A4889G) polymorphism presents a greater susceptibility to acute lymphoid leukemia (ALL); while Jin et al. (2011) have linked it to colorectal cancer.

The limitations of our study are in the size of the sample (n = 81), which in subsequent studies will need to be increased to achieve greater statistical power and corroborate the results obtained. On the other hand, the selection of volunteers, which despite requiring selection criteria is not necessarily representative of the Peruvian mestizo population. The other variants of the *CYP1A1* gene, the genetic variants of *CYP1A2*, *GSTT1* and *GSTP1*, which are relevant for the analysis of cancer susceptibility, were not studied, so they are being considered in future studies by our research group. Notwithstanding the foregoing, we believe that the results presented in this study are relevant, as a first tool to evaluate the prevention of cancer risk according to genotype and in this way help the early diagnosis of cancer, at the same time as an incentive to reduce consumption cigarettes and processed foods.

Conclusions

In conclusion, our results indicate the presence of *CYP1A1*2A* and *GSTM1* null polymorphisms in high frequency in the Peruvian mestizo population, which varies considerably when considering migrant ethnic groups, in this case from Iquitos. The presence of these genetic variants establishes a metabolic imbalance of phase I and II of xenobiotic metabolism in this group of Peruvian settlers, which denotes a high bioactivation of procarcinogenic agents that translates into mutagenic and carcinogenic metabolites. This motivates us to continue researching in this area in a greater number of inhabitants from different regions of the country, to help prevent cancer inducible by environmental agents.

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