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Original Article

Prevalence of the SNP rs10774671 of the OAS1 gene in Mexico as a possible predisposing factor for RNA virus disease

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Abstract: The COVID-19 pandemic has revealed the susceptibility of certain populations to RNA virus infection. This variety of agents is currently the cause of severe respiratory diseases (SARS-CoV2 and Influenza), Hepatitis C, measles and of high prevalence tropical diseases that are detected throughout the year (Dengue and Zika). The rs10774671 polymorphism is a base change from G to A in the last nucleotide of intron-5 of the OAS1 gene. This change modifies a splicing site and generates isoforms of the OAS1 protein with a higher molecular weight and a demonstrated lower enzymatic activity. The low activity of these OAS1 isoforms makes the innate immune response against RNA virus infections less efficient, representing a previously unattended risk factor for certain populations. Objective: Determine the distribution of rs10774671 in the open population of Mexico. Methods: In 98 healthy volunteers, allelic and genotypic frequencies were determined by qPCR using allele specific labeled probes, and the Hardy-Weinberg equilibrium was determined. Results: The A-allele turned out to be the most prevalent in the analyzed population. Conclusions: Our population is genetically susceptible to RNA virus disease due to the predominant presence of the A allele of rs10774671 in the OAS1 gene.

Keywords: Innate immunity, 2',5'-oligoadenylate synthetase, single nucleotide polymorphism, RNA virus infections, coronavirus infections

Introduction

There are three main components in most infectious diseases: an infectious agent, a host, and the transmission environment [1]. Some pathogens are carried by vectors or require intermediate hosts to complete their life cycle. Adequate climatic conditions and distribution are both necessary for the survival and subsequent access of the pathogen-carrying vector to the host [2]. Some studies suggest that long-term warming is an event that favors the geographic spread of vector-borne diseases; while extreme weather events create opportunities for the emergence of new diseases [1, 2].

The first scenario is observed in the American continent where the spread from south to north of tropical diseases transmitted by vectors such as Dengue and Zika has been progressive.

In addition to diseases transmitted by vectors, infectious diseases with animal hosts and mutation-prone such as influenza and SARS CoV2, are favored by current human dynamics where overcrowding and coexistence with domestic and farm animals provide an environment with potential for generation of a pandemic.

The inherent factors of the host such as its genetic landscape, determine the susceptibility of each individual to diseases.

In recent years, seasonal viral diseases such as those transmitted by vectors have emerged

as a major public health problem. In the particular case of the tropical disease agents Dengue (DENV) and Zika (ZIKV) viruses, efforts to combat them have focused in controlling the Aedes aegypti and Aedes albopictus vectors. Originally endemic to tropical areas, climate change and human migration have caused proliferation and establishment of the vector in almost the whole territory of Latin America.

On the other hand, Influenza virus and SARS-CoV2, prevail nowadays as the most common respiratory disease agents.

Due to the antigenic variability of the agent, Influenza remains as one of the most prevalent respiratory diseases around the world. Influenza Virus A (IVA) represents a latent threat for the generation of a pandemic, due to its diverse animal reservoirs that permanently carry viruses that occasionally spread to humans after undergoing rearrangements in their genome. In 2009, an IVA (H1N1) derived from a strain of swine influenza originated what is known as the first pandemic of the 21st century, with Mexico as the origin of the outbreak [3, 4].

The appearance of new Influenza subtypes prevents the preexisting immunological memory and therefore the innate immune response take on a high importance.

Recently, the impact of SARS-CoV2 as the etiological agent of COVID19, has dramatically affected health systems around the world [5].

This disease represents the greatest current health concern worldwide, presenting as of today 111 million reported cases and 2.46 million deaths. In the United States, there have been 28.1 million cases and 498 thousand deaths due to this disease. In Mexico on the other hand, reported cases scale to 2.04 million, while deaths have reached 180,000. Both data (global and national) comes from the Johns Hopkins University Center for Systems Science and Engineering (JHU CSSE).

The innate immune response (IIR) is the first to develop against infectious agents, it is not antigen-specific and does not generate immunological memory [6-10]. As part of IIR, the production of type I interferons (IFN-α/IFN-β) occurs almost immediately in response to the presence of viral proteins or nucleic acids. Type I interferons through their receptors stimulate two actions that inhibit the synthesis of viral proteins, the first is the phosphorylation of eIF-2 by the action of PKR and the second is the activation of RNAse L through the activity of the proteins of Oligoadenylate synthetase (OAS) [6, 7].

The OAS gene family, although initially described as an antiviral activator of restriction enzymes against dsRNA viruses, has been also identified as a predisposing factor for ssRNA viruses and critical illness due to COVID-19 in a GWAS performed in patients in intensive care [11]. Association of this family with IVA is also well documented [12]. This family is made up of 4 genes called OAS1, OAS2, OAS3 and OAS-L. OAS1, OAS2 and OAS3 having one, two and three OAS domains respectively, while OAS-L is catalytically inactive [10, 13, 14]. By alternative splicing, the OAS1 gene can generate five isoforms (p42, p44, p46, p48 and p52), the p52 isoform of OAS1 is generated when the last nucleotide of intron 5 changes G to A [13], being rs10774671 the single nucleotide polymorphism (SNP) at this position. The presence of the A allele causes the splice acceptor site to travel a position that removes the first base of exon 6, thereby modifying the open reading frame. The activity of the p52 and p48 isoforms is lower with respect to the p46 isoform and therefore they activate RNAse L in a less efficient way [7, 10]. The rs10774671 polymorphism of OAS1 has been linked to alteration in alternative splicing of OAS1, resulting in decreased activity in peripheral blood mononuclear cells (PBMC) and susceptibility to West Nile virus (WNV) and Hepatitis C virus (HCV) infection in homozygous for the A allele, compared to those with the G allele that generates the OAS1p46 isoform [15-18]. Due to this stablished relationship with Flavivirus, associations with DENV and ZIKV have also been proposed.

In the present study, the allelic and genotypic frequency for the rs10774671 polymorphism of OAS1 was determined in 98 Mexican volunteers residing in the State of Nuevo León, to understand the state of vulnerability of this population in one of the main defense mechanisms of the innate immune response against RNA virus infections.

Methods

Study design

A cross-sectional, descriptive, observational study was performed in Mexican volunteers to establish the prevalence of the rs10774671.

Recruitment of volunteers

This study was approved by the UANL school of Medicine and University Hospital's Ethics Committee with the number BI12-005.

98 volunteers (49 men and 49 women) were recruited with the following inclusion criteria:

Men or women between 18 and 35 years old with previously informed consent, a previously answered form regarding socio-demographic data for ethnicity establishment and a 5 ml blood sample donation collected in an EDTA tube.

On the other hand, unavailability or contraindication for blood sample taking and apparent illnesses at the time of taking were considered as exclusion criteria (See **Table 1** for general information and clinic feature of recruited patients).

Nucleic acids isolation

Using 500 µl of peripheral blood, genomic DNA (gDNA) was obtained by the TSNT method. DNA was quantified in a Nanodrop-2000 spectrophotometer (Thermo Fisher) and its integrity was visually verified by electrophoresis in 0.8% agarose gels.

Genotyping

Genotype analysis was performed by real time PCR. Specific oligonucleotides (5'-TGAATCCAGCTGCAATGCAGG-3'/5'-ATGAGGGTACTCATGTGTTCC-3') were designed in regions flanking the SNP rs1077467; in addition to allele-specific fluorescent probes (5' HEX-CCCTTTCAGGCTGAA-IBFQ 3'/5' FAM-CCCTTTCAAGCTGAA-IBFQ 3') labeled with the fluorophores HEX (allele G) and FAM (allele A) (Integrated DNA Technologies). 50 ng of total gDNA, 20 pmol of each oligonucleotide and 2.5 pmol of each probe were used in a Prime Time Gene Expression Master Mix 2X reaction mix (Integrated DNA Technologies). The PCR was performed in a CFX-100 thermal cycler (Bio Rad). The thermocycling program consisted of 39 cycles with an alignment temperature of the probes and oligonucleotides of 55°C.

Statistical analysis

All data were deposited and processed in Microsoft Office Excel 2007 spreadsheets to generate graphs of allelic frequency, genotypic frequency, and descriptive statistics of the population. Chi-square test (χ^2) was performed to evaluate Hardy-Weinberg's equilibrium in the IBM SSPS Statistics 20 computational package. A $P<0.05$ was considered statistically significant.

Results

Establishment of Mexican ancestry in the study population

Of the 98 volunteers that made up the study population, 84% (82/98) of the study subjects mentioned being from the Nuevo León state.

To establish whether the volunteers had Mexican ancestry, the place of birth of their grandparents was asked. 47% (184/392) of the grandparents of the study population were born in the Nuevo León state, while 48% (188/392) were born in another state of the country, 2% (7/392) were not Mexicans and for 3% (13/392) the place of birth was unknown.

Allelic and genotypic distribution of the rs10774671 polymorphism

The rs10774671 polymorphism presents as an ancestral allele a G in the last base of intron 5 and as a mutated allele the change for an A base. We analyzed for each volunteer the possibility of presenting each of the possible alleles by means of qPCR with allele specific fluorescent probes, thus, we analyzed 196 possible alleles for the rs10774671 polymorphism of OAS1. Of the total alleles analyzed, 79.6% of the alleles were identified as mutated alleles while only 20.4% of the alleles were identified as ancestral alleles (**Table 2**).

Similarly, the ancestral homozygous (G/G), mutated homozygous (A/A) and heterozygous (G/A) genotypes were analyzed for each individual. It was found that the G/G genotype is present in 2% of the population, while the heterozygous genotype is in 36.7%. The most prevalent genotype in the study population was homozygous mutated with a frequency of 61.2% (**Table 3**).

Both the frequencies of the A and G alleles and the possible phenotypes are uniformly distributed between men and women, with no identified differences between genres (**Tables 2** and

Table 1. General Information and clinic features of recruited patients

ID	Age (years)	Gender	Height (m)	Weight (kg)	BMI	Education	Origin	Maternal grandfather origin	Maternal grandmother origin	Paternal grandfather origin	Paternal grandmother origin	Allele 1	Allele 2	Genotype	AA	AG	GG
ATT0002	21	Female	1.62	Unknown	Unknown	2.4	NL	NL	NL	NL	NL	A	A	HOMOZYGOUS	1		
ATT0004	22	Female	1.67	75	26.89	2.5	NL	NL	NL	NL	NL	A	A	HOMOZYGOUS	1		
ATT0005	25	Female	1.6	49	19.14	2.5	NL	NL	NL	NL	NL	A	A	HOMOZYGOUS	1		
ATT0011	23	Female	1.58	46	18.43	2.5	NL	NL	NL	NL	NL	A	A	HOMOZYGOUS	1		
ATT0014	18	Female	1.75	96	31.35	2.3	COAH	COAH	NL	SLP	COAH	A	G	HETEROZYGOUS		1	
ATT0016	21	Female	1.7	62	21.45	2.5	NL	NL	NL	SLP	SLP	A	A	HOMOZYGOUS	1		
ATT0017	24	Female	1.62	60	22.86	2.5	NL	NL	NL	SLP	SLP	A	A	HOMOZYGOUS	1		
ATT0021	23	Female	1.63	67	25.22	2.5	NL	Unknown	Unknown	NL	DGO	A	G	HETEROZYGOUS		1	
ATT0023	19	Female	1.57	48	19.47	2.5	NL	NL	NL	NL	NL	A	A	HOMOZYGOUS	1		
ATT0027	24	Female	1.63	55	20.70	2.5	NL	SLP	SLP	NL	NL	A	G	HETEROZYGOUS		1	
ATT0030	19	Female	Unknown	60	Unknown	2.5	CHIH	NL	NL	NL	NL	A	G	HETEROZYGOUS		1	
ATT0031	18	Female	1.6	56	21.88	2.3	NL	NL	NL	NL	NL	A	A	HOMOZYGOUS	1		
ATT0034	26	Female	1.59	Unknown	Unknown	2.5	CDMX	AGS	CDMX	CDMX	JAL	A	A	HOMOZYGOUS	1		
ATT0035	21	Female	Unknown	75	Unknown	2.3	NL	COAH	NL	Unknown	NL	A	G	HETEROZYGOUS		1	
ATT0038	20	Female	1.62	60	22.86	2.3	NL	NL	NL	NL	NL	A	A	HOMOZYGOUS	1		
ATT0045	19	Female	1.55	75	31.22	2.5	NL	NL	NL	NL	NL	A	G	HETEROZYGOUS		1	
ATT0046	21	Female	1.5	51.9	23.07	2.4	NL	COAH	ZAC	ZAC	ZAC	A	A	HOMOZYGOUS	1		
ATT0053	18	Female	1.56	45.4	18.66	2.3	NL	NL	NL	NL	NL	A	G	HETEROZYGOUS		1	
ATT0057	18	Female	1.6	54	21.09	2.3	NL	MEX	MEX	MEX	MEX	A	G	HETEROZYGOUS		1	
ATT0059	21	Female	1.6	55	21.48	2.3	NL	NL	NL	NL	NL	A	G	HETEROZYGOUS		1	
ATT0062	21	Female	Unknown	49	Unknown	2.5	NL	NL	NL	NL	NL	A	A	HOMOZYGOUS	1		
ATT0063	22	Female	1.68	56.9	20.16	2.5	NL	NL	NL	NL	NL	A	A	HOMOZYGOUS	1		
ATT0066	21	Female	1.56	51	20.96	2.3	NL	SLP	NL	SLP	NL	A	A	HOMOZYGOUS	1		
ATT0067	20	Female	1.64	65	24.17	2.3	NL	NL	NL	NL	NL	A	A	HOMOZYGOUS	1		
ATT0069	22	Female	1.7	53.7	18.58	2.3	NL	SON	SON	NL	NL	A	A	HOMOZYGOUS	1		
ATT0073	18	Female	1.49	44.1	19.86	2.3	NL	NL	NL	NL	NL	A	A	HOMOZYGOUS	1		
ATT0075	18	Female	1.55	46	19.15	2.3	NL	NL	NL	NL	NL	G	G	HOMOZYGOUS			1
ATT0087	22	Female	1.54	49.2	20.75	2.5	NL	SLP	ZAC	SLP	SLP	A	G	HETEROZYGOUS		1	
ATT0088	22	Female	1.6	63.5	24.80	2.5	NL	SLP	NL	NL	NL	A	G	HETEROZYGOUS		1	
ATT0089	20	Female	1.6	54	21.09	2.5	NL	NL	NL	NL	NL	A	A	HOMOZYGOUS	1		
ATT0092	22	Female	1.58	58	23.23	2.5	CHA	CHA	CHA	CHA	CHA	A	A	HOMOZYGOUS	1		
ATT0093	22	Female	1.57	65	26.37	2.4	NL	ZAC	ZAC	NL	NL	A	A	HOMOZYGOUS	1		
ATT0094	21	Female	1.67	71	25.46	2.4	NL	NL	NL	SLP	SLP	A	G	HETEROZYGOUS		1	
ATT0095	19	Female	1.56	47.4	19.48	2.5	COAH	COAH	COAH	COAH	COAH	A	G	HETEROZYGOUS		1	
ATT0096	20	Female	1.54	50	21.08	2.3	TAMPS	GTO	GTO	COAH	COAH	A	G	HETEROZYGOUS		1	
ATT0103	18	Female	1.55	62	25.81	2.3	NL	NL	ZAC	SLP	Unknown	A	A	HOMOZYGOUS	1		
ATT0104	18	Female	1.64	60	22.31	2.3	NL	NL	NL	NL	NL	A	A	HOMOZYGOUS	1		

ATT0106	19	Female	1.58	58.5	23.43	2.3	SLP	SLP	SLP	SLP	NL	A	A	HOMOZYGOUS	1	
ATT0115	21	Female	1.53	70	29.90	2.5	NL	NL	NL	NL	NL	A	G	HETEROZYGOUS		1
ATT0118	19	Female	1.51	81	35.52	2.3	NL	COAH	COAH	NL	MICH	A	A	HOMOZYGOUS	1	
ATT0130	19	Female	1.6	78	30.47	2.3	NL	NL	NL	NL	SLP	A	G	HETEROZYGOUS		1
ATT0133	18	Female	1.58	70	28.04	2.5	COAH	COAH	COAH	COAH	COAH	A	A	HOMOZYGOUS	1	
ATT0136	18	Female	1.6	48	18.75	2.5	NL	NL	NL	COAH	NL	A	A	HOMOZYGOUS	1	
ATT0140	18	Female	1.5	53	23.56	2.5	NL	NL	NL	NL	COAH	A	A	HOMOZYGOUS	1	
ATT0141	19	Female	1.5	55	24.44	2.5	MEX	MICH	MICH	MICH	MEX	A	G	HETEROZYGOUS		1
ATT0151	24	Female	1.58	138	55.28	2.4	NL	NL	NL	COAH	COAH	A	G	HETEROZYGOUS		1
ATT0160	20	Female	1.55	Unknown	Unknown	2.5	NL	NL	SLP	NL	NL	A	G	HETEROZYGOUS		1
ATT0161	19	Female	1.54	52	21.93	2.5	NL	SLP	COAH	VER	VER	A	A	HOMOZYGOUS	1	
ATT0163	20	Female	1.68	76	26.93	2.5	NL	SLP	SLP	SLP	SLP	A	A	HOMOZYGOUS	1	
ATT0003	20	Male	1.8	77.1	23.80	2.3	NL	COAH	TAMPS	SLP	Unknown	A	A	HOMOZYGOUS	1	
ATT0006	26	Male	1.8	92	28.40	2.5	NL	TAMPS	GTO	NL	NL	A	G	HETEROZYGOUS		1
ATT0008	21	Male	1.7	64	22.15	2.3	NL	ZAC	ZAC	NL	NL	A	A	HOMOZYGOUS	1	
ATT0010	22	Male	1.68	78	27.64	2.5	NL	SLP	NL	NL	NL	A	A	HOMOZYGOUS	1	
ATT0015	18	Male	1.73	90	30.07	2.3	NL	TAMPS	TAMPS	MEX	SLP	A	A	HOMOZYGOUS	1	
ATT0018	27	Male	1.75	76	24.82	2.3	CAMP	CAMP	Unknown	YUC	YUC	A	G	HETEROZYGOUS		1
ATT0020	18	Male	1.74	100	33.03	2.3	NL	SLP	VER	NL	SLP	A	G	HETEROZYGOUS		1
ATT0026	20	Male	1.72	57.8	19.54	2.5	TAMPS	NL	NL	NL	NL	A	G	HETEROZYGOUS		1
ATT0028	19	Male	1.8	58.6	18.09	2.5	NL	SLP	SLP	SLP	COAH	A	A	HOMOZYGOUS	1	
ATT0029	21	Male	1.82	105	31.70	2.3	NL	NL	NL	SLP	NL	A	A	HOMOZYGOUS	1	
ATT0032	21	Male	1.74	Unknownn	Unknownn	2.5	NL	SLP	SLP	ZAC	ZAC	A	G	HETEROZYGOUS		1
ATT0044	20	Male	1.7	63	21.80	2.3	NL	NL	NL	TAMPS	NL	A	G	HETEROZYGOUS		1
ATT0048	26	Male	1.75	72	23.51	2.4	NL	ZAC	NL	COAH	COAH	A	A	HOMOZYGOUS	1	
ATT0049	20	Male	1.68	80	28.34	2.5	VER	VER	VER	VER	VER	A	G	HETEROZYGOUS		1
ATT0050	21	Male	1.78	95	29.98	2.3	NL	NL	NL	NL	NL	A	A	HOMOZYGOUS	1	
ATT0052	19	Male	Unknownn	87.9	Unknown	2.5	NL	DGO	GTO	CHIH	NL	A	A	HOMOZYGOUS	1	
ATT0054	19	Male	1.62	82	31.25	2.5	NL	COAH	Unknown	NL	NL	A	A	HOMOZYGOUS	1	
ATT0055	20	Male	1.66	67	24.31	2.3	COAH	COAH	COAH	COAH	COAH	A	A	HOMOZYGOUS	1	
ATT0056	26	Male	1.75	72	23.51	2.4	NL	ZAC	NL	COAH	COAH	A	A	HOMOZYGOUS	1	
ATT0058	21	Male	1.83	77	22.99	2.3	NL	NL	NL	SLP	SLP	A	A	HOMOZYGOUS	1	
ATT0061	20	Male	1.65	60.2	22.11	2.3	NL	NL	NL	NL	NL	A	G	HETEROZYGOUS		1
ATT0064	28	Male	1.72	92	31.10	2.5	NL	SLP	SLP	NL	NL	A	A	HOMOZYGOUS	1	
ATT0065	21	Male	1.75	55.2	18.02	2.3	NL	NL	NL	TAMPS	TAMPS	A	G	HETEROZYGOUS		1
ATT0068	18	Male	1.8	72	22.22	2.3	NL	SLP	SLP	TAMPS	TAMPS	A	A	HOMOZYGOUS	1	
ATT0070	18	Male	1.79	87	27.15	2.3	NL	ZAC	MEX	NL	NL	A	A	HOMOZYGOUS	1	
ATT0071	18	Male	1.77	88	28.09	2.3	NL	CHA	CHA	COAH	COAH	A	G	HETEROZYGOUS		1
ATT0074	18	Male	1.8	73	22.53	2.3	NL	SLP	SLP	DGO	QRO	A	G	HETEROZYGOUS		1
ATT0105	18	Male	1.76	68	21.95	2.3	NL	NL	NL	NL	NL	A	A	HOMOZYGOUS	1	
ATT0107	18	Male	1.5	48	21.30	2.4	NL	NL	NL	NL	NL	A	A	HOMOZYGOUS	1	

ATT0108	19	Male	1.8	85.2	26.30	2.4	NL	VER	VER	PUE	CHA	A	A	HOMOZYGOUS	1	
ATT0110	20	Male	1.77	71.4	22.79	2.3	TAMPS	OAX	COAH	COAH	COAH	A	G	HETEROZYGOUS		1
ATT0116	18	Male	1.8	123	37.96	2.3	NL	NL	NL	VER	VER	A	A	HOMOZYGOUS	1	
ATT0117	19	Male	1.78	70	22.09	2.5	NL	COAH	VER	NL	NL	A	A	HOMOZYGOUS	1	
ATT0119	21	Male	1.72	78	26.37	2.5	SIN	SIN	SIN	SIN	SIN	A	A	HOMOZYGOUS	1	
ATT0129	20	Male	1.75	75	24.49	2.5	NL	NL	NL	NL	NL	A	A	HOMOZYGOUS	1	
ATT0131	30	Male	1.69	68	23.81	2.6	NL	NL	NL	CHIH	CHIH	G	G	HOMOZYGOUS		1
ATT0132	21	Male	1.7	71	24.57	2.5	VER	VER	VER	VER	VER	A	A	HOMOZYGOUS	1	
ATT0134	20	Male	Unknown	85	Unknown	2.5	NL	SLP	SLP	SLP	SLP	A	A	HOMOZYGOUS	1	
ATT0135	19	Male	1.79	91	28.40	2.3	NL	NL	DGO	NL	NL	A	G	HETEROZYGOUS		1
ATT0137	21	Male	1.75	90	29.39	2.5	NL	NL	NL	NL	NL	A	A	HOMOZYGOUS	1	
ATT0138	19	Male	1.7	70	24.22	2.5	NL	NL	NL	CDMX	NL	A	A	HOMOZYGOUS	1	
ATT0139	21	Male	1.82	79	23.85	2.5	NL	SLP	SLP	TAMPS	TAMPS	A	A	HOMOZYGOUS	1	
ATT0142	18	Male	1.74	76	25.10	2.5	NL	NL	NL	NL	NL	A	G	HETEROZYGOUS		1
ATT0143	22	Male	1.76	95	30.67	2.5	TAMPS	TAMPS	SIN	TAMPS	SON	A	A	HOMOZYGOUS	1	
ATT0152	22	Male	1.73	68	22.72	2.5	NL	COAH	COAH	NL	NL	A	G	HETEROZYGOUS		1
ATT0158	19	Male	1.8	68	20.99	2.5	NL	SLP	Unknown	SLP	SLP	A	A	HOMOZYGOUS	1	
ATT0162	21	Male	1.73	76.8	25.66	2.5	NL	GTO	GTO	NL	NL	A	G	HETEROZYGOUS		1
ATT0164	20	Male	1.72	61	20.62	2.5	NL	NL	NL	NL	NL	A	A	HOMOZYGOUS	1	
ATT0170	19	Male	1.78	80	25.25	2.5	NL	NL	NL	NL	NL	A	G	HETEROZYGOUS		1

Origin: AGS, Aguascalientes; BC, Baja California; BCS, Baja California Sur; CAM, Campeche; CDMX, Ciudad de México; CHA, Chiapas; CHIH, Chihuahua; COAH, Coahuila; COL, Colima; DGO, Durango; GTO, Guanajuato; GRO, Guerrero; HGO, Hidalgo; JAL, Jalisco; MEX, Estado de México; MICH, Michoacán; MOR, Morelos; NAY, Nayarit; NL, Nuevo León; OAX, Oaxaca; PUE, Puebla; QRO, Querétaro; QR, Quintana Roo. Education: None, 2.1; Elementary School, 2.2; High School, 2.3; Technical School, 2.4; Graduate, 2.5; Postgraduate, 2.6.

Table 2. Allelic frequency of the SNP rs10774671 of the OAS1 gene

Allele	Men (%) (n=49)	Women (%) (n=49)	Men and Women (%) (n=98)
A	80.6% (79/98)	78.6% (77/98)	79.6% (156/196)
G	19.4% (19/98)	21.4% (21/98)	20.4% (40/196)

Table 3. Genotypic Frequency of the SNP rs10774671 of the OAS1 gene

Genotype	Men (%) (n=49)	Women (%) (n=49)	Men and Women (%) (n=98)
A/A	63.3% (31/49)	59.2% (29/49)	61.2% (60/98)
G/A	34.7% (17/49)	38.8% (19/49)	36.7% (36/98)
G/G	2.0% (1/49)	2.0% (1/49)	2.0% (2/98)

3). By the use of the Chi-square test, it was also determined that the rs10774671 polymorphism is in Hardy-Weinberg equilibrium. Therefore, allele and genotypic frequencies are expected to remain unchanged in future generations.

Discussion

In the present study we collected data regarding the OAS1 rs10774671 SNP which G to A change alters a splicing acceptor site resulting in the less efficient allele A isoform. As mentioned above, it has been proposed that certain SNPs of OAS1 could be protective against RNA virus disease. OAS1 gene appears to be a highly relevant element of the innate immune response against SARS-CoV2 as suggested by the identification of SNPs in different exons related with COVID19 susceptibility with opposite effects depending on the SNP, in at least 2 different populations to date (Vietnamese and Chinese) [19, 20]. To the best of our knowledge, there are no reports regarding rs10774671 and SARS-CoV2 infections, however, the relationship between this RNA virus and the aforementioned SNP could be suspected due to the previously suggested associations between rs10774671 and other RNA viruses' susceptibility like WNV, HCV and measles virus (MV) [15-18, 21]. In the Mexican population, the predominant allele was the A allele and the most frequent genotype was the homozygous (AA), so it is suggested that the aforementioned population is genetically susceptible to some RNA viruses.

The global distribution of the rs10774671 polymorphism described on the website (http://www.internationalgenome.org/) of the IGSR (The International Genome Sample Resourse), as part of the data from the "1000 Genomes Project", indicates that the A allele is present with a frequency of 61%, while the G allele represents 39% of the alleles around the world population. Results from the American, Asian and European continents are similar to those reported globally. Interestingly, for the African continent, the distribution is inverse, with the A allele in 36% and the G allele in 64%.

The prevalence of the A allele in the rest of the world population can be explained because the RNAse L system is not the only innate mechanism against viral infections. Furthermore, unlike Africa where the presence of different viruses constantly affects the population as a natural selection of individuals carrying the G allele, in the rest of the world, the absence of such selective pressure could explain the A>G allelic distribution. It can be hypothesized that although the polymorphism is in equilibrium in our population, a global event such as a pandemic caused by a new virus, with high morbidity and mortality rates (as the COVID19 pandemic), can cause a decrease in the homozygous (AA) population due to the fact that these individuals are the most susceptible to disease because of their deficiencies in the innate RNAse L mechanism.

To the best of our knowledge, there is no prevalence data regarding the rs10774671 SNP other than the prevalence given by the aforementioned IGSR, thus our study presents a first insight regarding this SNP in Mexican population.

We can conclude that the prevalence of the OAS1 rs10774671 polymorphism in mexican population makes them a target for emerging diseases and those transmitted by vectors. The proper analysis of this and other SNPs could be useful as a prediction marker for the current pandemic. Our results contribute to a better comprehension of RNA virus disease probability and its association with population and could also serve as an evidence to aug-

ment preventive and control measures to reduce the threat of an epidemic or pandemic that devastates vulnerable populations.

Disclosure of conflict of interest

None.

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