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HLA Class I and II allelic diversity among Ecuadorian transplant candidates: A comprehensive retrospective analysis

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ABSTRACT

The Major Histocompatibility Complex (MHC) comprises over 220 genes encoding proteins that are vital for the functioning of the immune system. These genes are divided into three classes: HLA class I, II, and III. The polymorphism of MHC genes serves to enhance the immune response by increasing the diversity of antigen presentation. In Ecuador, a country with a diverse population comprising numerous ethnic groups, it is crucial to comprehend the distribution of HLA alleles in order to facilitate several health approaches such as personalized medicine and organ transplantation. The present study employed data from Ecuador's National Institute of Organ, Tissue, and Cell Donation and Transplantation (INDOT) from 2017 to 2022. The data were analyzed to determine the distribution of HLA class I (HLA-A, HLA-B, HLA-C) and class II (HLA-DRB1, DRB3, DRB4, DQB1) alleles. A total of 1530 HLA alleles were identified among the 2352 patients included in the study. The highest variability was observed in Class I alleles, with HLA-A02 (32 %) and HLA-B35 (21 %) being the most common. In the case of class II, the most prevalent alleles were DRB104 and DQB103, with frequencies of 25.1 % and 48 %, respectively. It is notable that significant regional variations in allele frequencies were observed across Ecuador. The findings of this comprehensive study provide valuable insights into Ecuador's HLA allele distribution, contributing to genetic research, personalized medicine, and organ transplant matching. However, the results also highlight the need for further studies to better understand genetic diversity and improve public health strategies.

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1. Introduction

The Major Histocompatibility Complex (MHC) comprises over 220 genes responsible for encoding three distinct groups of proteins: HLA class I, II, and III (Matzaraki et al., 2017). These proteins are essential for immunological activities. More specifically, they are involved in the recognition and presentation of self and foreign antigens (Matzaraki et al., 2017). HLA class I proteins present principally endogenous peptides, whether of autologous or pathogenic origin, to CD8+T cells. In contrast, HLA class II proteins present exogenous antigens which are introduced into the cell through endosomes, to CD4+T cells (Nakamura et al., 2019).

The genes of the MHC are highly polymorphic. This phenomenon represents an evolutionary adaptation designed to enhance antigen presentation repertoire, thereby fostering a more robust immune response against pathogens. In fact, more than 500 alleles have been discovered for HLA-A, 2800 for HLA-B and 1362 for HLA-C proteins (Chen et al., 2023; Robinson et al., 2020). Additionally, in MHC class II, 2581 alleles have been identified for HLA-DRB1, 1718 for HLA-DQB1, 1449 for HLA-DPB1, 183 for HLA-DQA1, 132 for HLA-DPA1 and 7 for HLA-DRA (Robinson et al., 2020).

The abundance of HLA genes over a short genetic distance has resulted in the massive transmission of alleles located at nearby loci, generating linkage disequilibrium (Evseeva et al., 2010). Interestingly, both genetic polymorphism and linkage disequilibrium are essential tools to reconstruct the history of human migration, providing a better understanding of ongoing phylogenetic phenomena and origin of populations (Gourraud et al., 2014). Consequently, comparison of the distribution of HLA loci between ethnic groups and calculation of genetic distances are essential to determine ancestry and population admixtures (Gourraud et al., 2014).

According to Paz y Miño et al. Ecuador is characterized by its ethnic diversity, whose composition is distributed as follows: 71.9 % of mixed ancestry, 7.4 % of Montubios (group of mixed ancestry in the coastal regions), 7.2 % of Afro-descendants, 7.0 % Indigenous, 6.1 % of European ancestry, and 0.4 % identified as "others" (e.g., Asian origin). This ethnic distribution is heterogeneous throughout Ecuador (Paz-Y-Miño et al., 2016).

Within the ethnic Ecuadorian populations HLA genotyping offers invaluable insights into human evolution and potential migratory patterns. Nevertheless, its significance extends beyond this realm. For instance, analyzing the distribution of HLA alleles holds pivotal importance in personalized medicine and biomedical research (Lim et al., 2022), particularly in organ transplantation. Information about both donor and recipient HLA profiles is indispensable for graft success, and even more crucial to predict/estimate the probability of potential rejection episodes over time.

Currently, numerous databases detail MHC profiles of various populations, including the United Network for Organ Sharing (UNOS) (UNOS) or the Allele Frequency Net Database (AFND) (The Allele Frequency Net Database, 2024). These repositories have revolutionized patient monitoring on organ donor waiting lists, ensuring optimal graft allocation. However, these databases predominantly represent Caucasian and Asian populations. In this context, analyzing HLA allele diversity is not only clinically relevant but also essential for anthropological studies. Its distribution reveals human migration and admixture patterns, highlighting the genetic contributions of Indigenous, European, and African populations in Ecuador. Clinically, these variations are crucial for improving organ transplant compatibility and advancing personalized medicine tailored to the Ecuadorian population.

The significant genetic diversity and HLA polymorphisms reported combined with the limited genetic information available for Ecuadorian populations highlight the need to conduct studies to address these gaps. Our study aims to characterize the genetic composition of Ecuadorians in HLA class I and class II, from the cohort of patients from the national organ transplant waiting list. Then, we are leveraging a comprehensive dataset of HLA allele frequencies and their demographic distribution in Ecuador. Notably, this research represents the largest HLA class II sampling among Latin American countries.

2. Methods

2.1. HLA and genotyping

This is a retrospective study based on the data obtained from the National Institute of Organ, Tissue and Cell Donation and Transplantation (INDOT, in Spanish) of Ecuador between 2017 and 2022. Data was collected as a requirement for patient admission to the waiting list for solid organ transplantation.

Genomic DNA was extracted from blood samples using the QIAamp DNA Mini Kit (Qiagen, Hilden, Germany) following the manufacturer's protocol. DNA quality was assessed through spectrophotometry (NanoDrop) and agarose gel electrophoresis to ensure integrity and purity before proceeding with amplification. HLA allele identification was performed via PCR with sequence-specific primers (PCR-SSP) using the Olerup SSP HLA Typing Kit (Olerup, Stockholm, Sweden) (Galarza et al., 2018). PCR cycling conditions followed the manufacturer's recommendations, and allele assignment was conducted using a reference database. PCR amplifications were visualized on agarose gels to confirm the presence of specific amplification products. Internal and external controls were included in each PCR-SSP reaction to ensure specificity and detect potential contamination.

Genotyping was performed for three HLA class I genes (HLA-A, HLA-B and, HLA-C) and four HLA class II genes (DRB1, DRB3, DRB4, and DQB1). Alleles were described according to the WHO Nomenclature Committee for HLA System Factors (https://hla.alleles.org/nomenclature/committee.html), and the data alleles was organized in an Excel spreadsheet.

2.2. Ethics Committee approval

The Human Research Ethics Committee of the Universidad de las Americas (UDLA) granted research permission with code 2023-EXC-009. Investigators involved in the present study signed data management confidentiality agreements. The databases generated for this manuscript used coded and anonymized information provided by the Ecuadorian transplant regulatory entity INDOT to eliminate any sensitive or traceable data associated with individuals on the organ waiting list.

2.3. Data processing and analysis

Specific demographic information such as age, clinical history, and genetic data was dichotomized. Relevant variables for this study were filtered by organ, province, and HLA alleles (Supplementary Table 1). Statistical approaches were performed using frequency tables for all qualitative demographic and genetic variables. We mapped the four most frequent alleles of each HLA gene studied at the province level using official Ecuadorian shapefiles to depict spatial frequencies which were depicted using natural breaks.

Frequency tables were generated with programming language R version 4.2.1 (2022–06–23). Maps were -+generated through R version 4.2.1 and QGIS 3.26 Buenos Aires.

3. Results

A total of 2352 patients were included in the study. Genotyping resulted in a total of 153 HLA alleles. HLA class I presented the greatest variety of alleles representing 73.2 %. (n = 112/153). The distribution of HLA class I alleles was as follows: HLA-A with 34.8 % (n = 39/112), HLA-B with 49.1 % (n = 55/112), and HLA-C with 16.1 % (n = 18/112). On the other hand, HLA class II alleles comprised 26.7 % (n = 41/153) of

the total alleles identified. The distribution of HLA class II alleles was: DRB1 with 51.2 % (n = 21/41), DQB1 with 26.8 % (n = 11/41), DRB3 with 9.8 % (n = 4/41), and DRB4 with 12.2 % (n = 5/41).

For the HLA-A gene, HLA-A*02 and HLA-A*24 alleles were the most frequently identified in the population with 32 % and 22 % respectively. For the HLA-B gene, the allele HLA-B*35 was the most abundant at 21 %. For the HLA-C gene, both HLA-C*07 and HLA-C*04 alleles were equally prevalent, each accounting for 11 % of the alleles. Regarding HLA class II alleles, DRB1*04 and DQB1*03 were the most frequently detected, with a 25.1 % and 48 % prevalence, respectively (Table 1).

Within each HLA class, we observed a large diversity of alleles across the country (Table 2). In our population, for HLA class I genes, we identified 40 HLA-A alleles. Among these, HLA-A*02 was distributed across 16 provinces (Fig. 1A and Table 2). For HLA-B, we identified a total of 56 alleles. Among the six most frequent alleles, HLA-B*35 was distributed in 12 provinces, primarily in the Andean and Coastal regions of Ecuador (Fig. 1B and Table 2). For HLA-C, we found a total of 19 alleles, with HLA-C*04 being the most frequent. This allele was prevalent in the Andean region as well as in the northern areas of the Coast and Amazonia (Fig. 1C and Table 2).

For HLA class II genes, 22 and 12 alleles were identified for HLA-DRB1 and HLA-DQB1, respectively. In particular, the most frequent alleles across the country were HLA-DRB1*04 in 20 provinces and HLA-DQB1*03 in 19 provinces (Fig. 2 and Table 2).

Finally, HLA-DRB3*01 and HLA-DRB4*01 alleles were identified as the most prevalent, appearing in 21 % and 25 % of the population, respectively. Of the 2352 individuals subjected to HLA typing, only 21.13 % showed the presence of DRB3 alleles, while DRB4 was detected in 27 % of cases. This can be explained by the auxiliary or haplotype-dependent nature of these HLA genes (Table 3). Thus, the number of individuals (n) presenting the HLA DRB3 and DRB4 genes was considerably lower compared to the other HLA genes (Table 3) and most of them presented allele 1 for each gene so it was not considered relevant to estimate the geographic distribution for their alleles.

4. Discussion

This is the first study presenting the diversity and geographic distribution of class I and class II HLA alleles in the Ecuadorian population as identified through donors of the national transplant waiting list.

The evolving genetic composition of the HLA class I and II complex has been documented across the globe exhibiting the most polymorphic regions in the human genome (Sanchez-Mazas and Meyer, 2014). These alleles have been instrumental in advancing our understanding of evolutionary patterns in population genetics and genetic profiling, with significant implications for medical purposes such as organ transplantation (Sanchez-Mazas and Meyer, 2014; Single et al., 2007; Sanchez-Mazas et al., 2013). Although the class I and class II HLA lineages are regarded as having been conserved for millions of years by humans and primates, it is noteworthy that specific polymorphisms identified across human populations have a more recent evolutionary event (Leffler et al., 2013). The presence of such polymorphisms may be influenced by changes in the environment to which these populations have adapted (Leffler et al., 2013; von Salomé et al., 2007).

A recent massive study analyzed HLA alleles from over 200 populations represented from all continents and suggested that a general variation in global demographics is present (Arrieta-Bolaños et al., 2023). The study analyzed 50 class I HLA-A and HLA-B alleles and 13 class II DRB1 alleles (Arrieta-Bolaños et al., 2023). The findings indicate that the variation of class I alleles is significantly influenced by geographic distribution, whereas class II exhibits population-specific characteristics less contingent on geographical location (Arrieta-Bolaños et al., 2023). In this context, HLA-A*02 and HLA-A*24 alleles have the highest frequency in human populations worldwide, with predominance in Oceania, Southeast Asia, and North and South America (Arrieta-Bolaños et al., 2023). Our findings align with this data, as the same alleles exhibit the highest frequency in the Ecuadorian studied population. More specifically, HLA-A*02 exhibited a 32 % prevalence and HLA-A*24 a 22 % prevalence across the country (Tables 1 and 3, Fig. 2). According to Arrieta-Bolaños et al., there is a considerable prevalence of HLA-A*31, HLA-A*68, and HLA-A*11 alleles in South American populations (Arrieta-Bolaños et al., 2023), however, we found none of the mentioned alleles in our study. Actually, HLA-A*31 presented the 5.5 % of individuals, HLA-A*68 in 3 %, and HLA-A*11 in 1.9 % (Table 1). This low prevalence may be due to the absence of an Ecuadorian population in the study by Arrieta-Bolaños et al. (2023).

In the context of global population, HLA-B alleles displayed the greatest diversity across all ethnic groups (Arrieta-Bolaños et al., 2023). In Ecuador the most frequent alleles were HLA-B*35 (21 %), HLA-B*40 (9.6 %), and HLA-B*39 (9.1 %), which were also previously reported as the most common HLA-B alleles found in North and South American populations. Conversely, these alleles differ greatly from those present in Australian, Polynesian, and European Arctic populations (Arrieta-Bolaños et al., 2023; Main et al., 2001; Edinur et al., 2012).

For HLA class II, the highest global frequencies have been observed for the DRB1*04, DRB1*14, and DRB1*08 alleles (Arrieta-Bolaños et al., 2023), which align with the findings of our study showing frequencies of

Table 1
Frequencies and percentages of HLA class I and II in the Ecuadorian population of the organ waiting list program. Ot. = others, Allele ID = HLA allele, (f) = frequency.

HLA class I									**HLA class II**					
HLA-A (n = 4178)			**HLA-B (n = 4262)**			**HLA-C (n = 2735)**			**DRB1 (n = 4097)**			**DQB1 (n = 3759)**		
Allele ID	%	(f)	Allele ID	%	(f)	Allele ID	%	(f)	Allele ID	%	(f)	Allele ID	%	(f)
02	32	1486	**35**	21	994	**07**	11	537	**04**	25.1	1182	**03**	48	2257
24	22	1032	**40**	9.6	451	**04**	11	528	**14**	11.2	529	**02**	10.1	475
68	5.5	260	**39**	9.1	428	**03**	8.6	404	**08**	8	380	**04**	7.5	354
01	4.9	230	**51**	6.6	309	**01**	5.5	260	**13**	6.5	306	**06**	7.5	354
03	4.4	206	**15**	6.2	290	**08**	5.3	250	**03**	6.3	295	**05**	6	280
29	3.5	165	**48**	4.6	215	**15**	3.9	183	**09**	5.6	263	**07**	0.3	14
31	3	140	**07**	4.1	193	**16**	2.4	115	**07**	5.3	251	**01**	0.3	12
30	2.4	114	**44**	4.1	192	**06**	2.2	104	**01**	5	234	**08**	0.2	8
26	2	96	**18**	3.6	171	**05**	2.2	102	**11**	4.8	227	**09**	0.04	2
11	1.9	89	**14**	3.2	150	**12**	2	96	**15**	4.5	213	**13**	0.04	2
23	1.7	79	**27**	2.2	105	**02**	1.9	87	**16**	2.6	125	**14**	0.02	1
33	1.6	75	**52**	2.2	104	**Ot.**	8.6	69	**Ot.**	2.2	92	-	-	-
Ot.	5	206	**08**	2.1	98	-	-	-	-	-	-	-	-	-
-	-	-	**49**	1.6	76	-	-	-	-	-	-	-	-	-
-	-	-	**38**	1.3	60	-	-	-	-	-	-	-	-	-
-	-	-	**45**	1.3	60	-	-	-	-	-	-	-	-	-
-	-	-	**Ot.**	8.6	366	-	-	-	-	-	-	-	-	-

Table 2
HLA allele diversity by provinces in Ecuadorian population of the organ waiting list program.

	Total, alleles per-gene	Number of most frequent alleles per province (%)	Most frequent alleles HLA	Most distributed allele
HLA-A	40	4 (10 %)	A*01 A*02 A*24 A*68	HLA-A*02 in 16 provinces
HLA-B	56	6 (10.7 %)	B*35 B*39 B*40 B*44 B*51 B*07	HLA-B*35 in 12 provinces
HLA-C	19	5 (26.32 %)	C*04 C*07 C*03 C*01 C*15	HLA-C*04 in 11 provinces
HLA-DRB1	22	5 (22.7 %)	DRB1*04 DRB1*80 DRB1*14 DRB1*03 DRB1*01	HLA-DRB1*04 in 20 provinces
HLA-DQB1	12	3 (25 %)	DQB1*3 DQB1*2 DQB1*6	HLA-DQB1*03 in 19 provinces

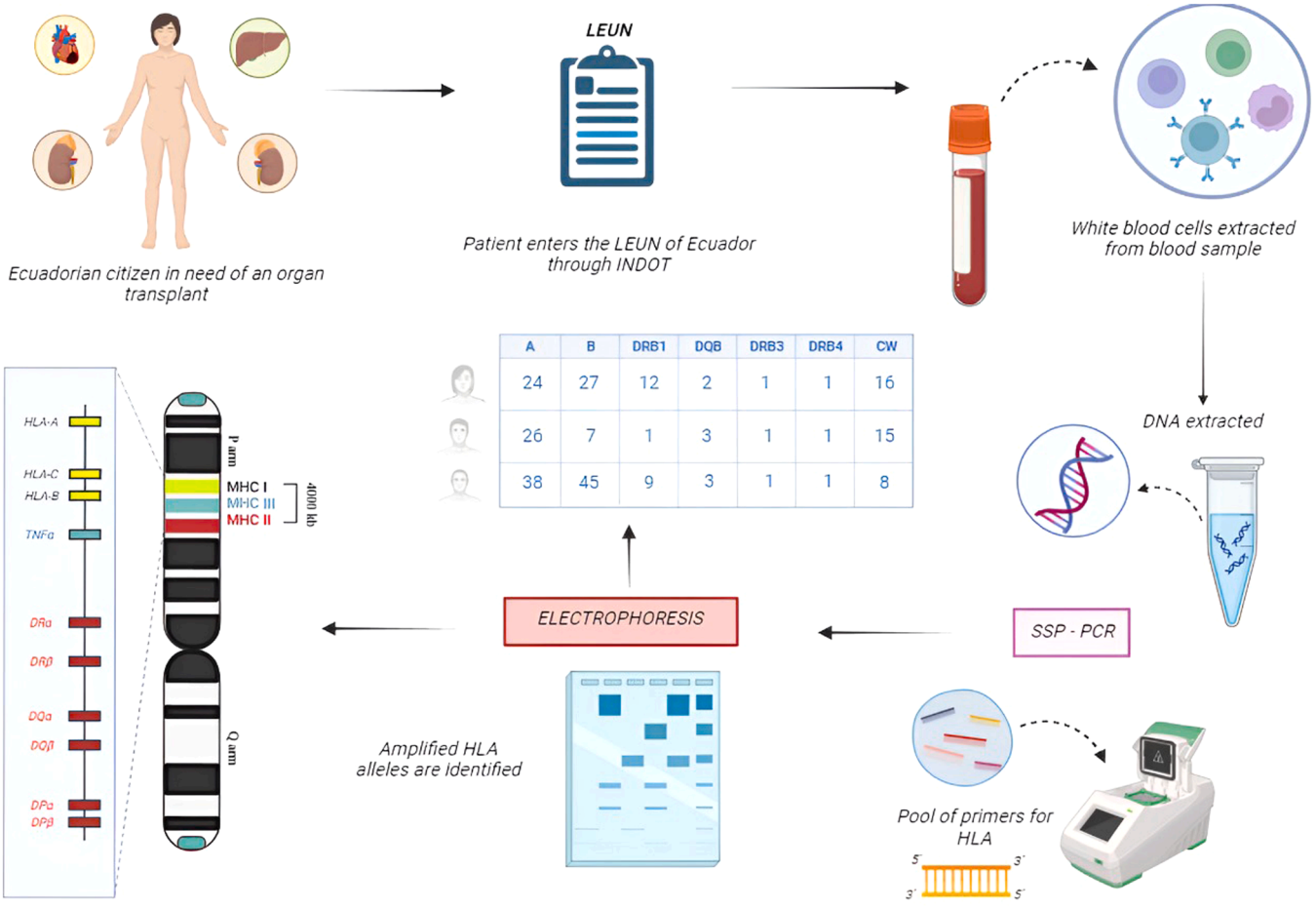

Fig. 1. The following flowchart illustrates the methodology employed in the study. It also depicts the process for HLA allele typing for individuals on the organ waiting list in Ecuador, which is conducted via PCR-SSP (Polymerase Chain Reaction with Sequence-specific primers). The figure was prepared by the authors for this study using Biorender software.

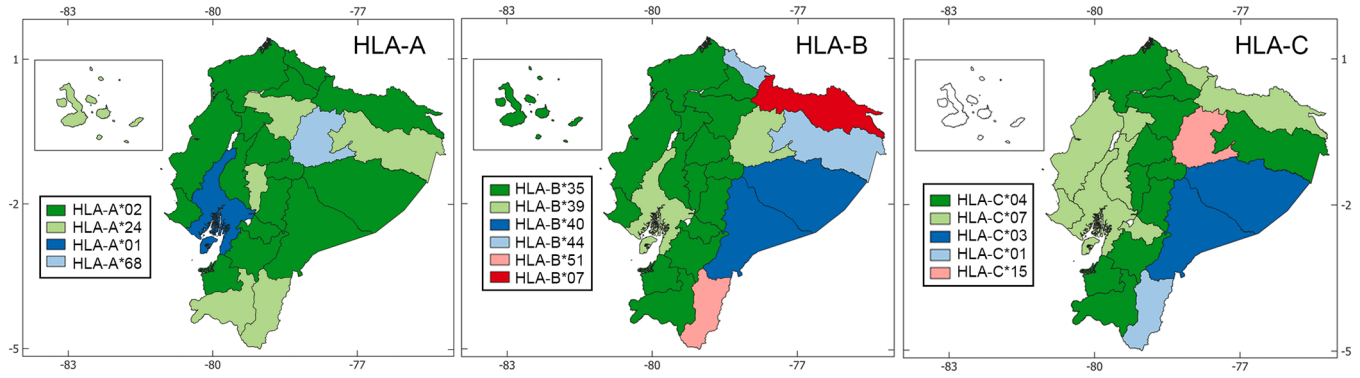

Fig. 2. Geographic distribution of the most frequent alleles of HLA class I in Ecuador according to the studied population. HLA-A (left), HLA-B (middle), and HLA-C (right).

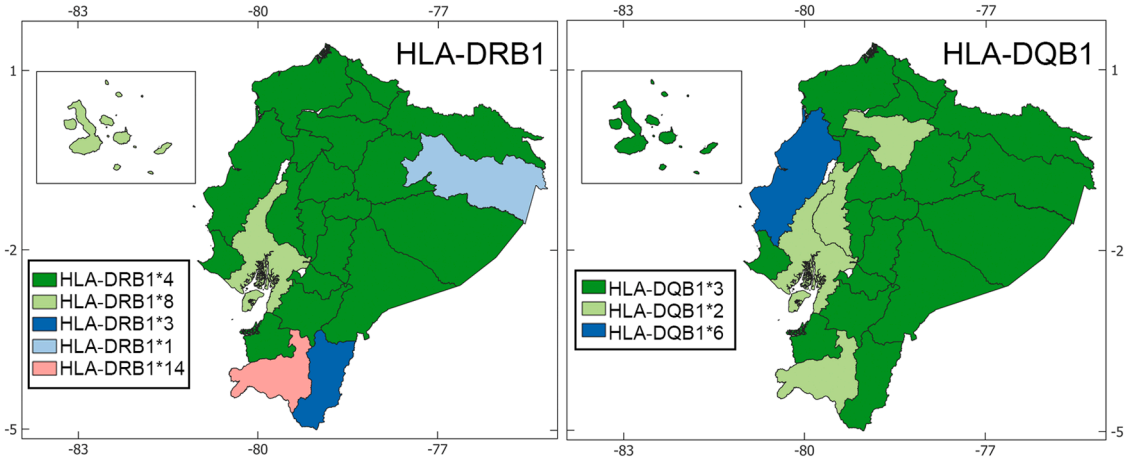

Fig. 3. Geographic distribution of the most frequent alleles of two genes of the HLA class II in Ecuador according to the studied population. HLA-DRB1 (left), HLA-DQB1 (right).

Table 3
Frequencies and percentages of HLA II auxiliary genes in the Ecuadorian population of the organ waiting list program. ID = HLA allele, (f) = frequency.

DRB3*(n = 497)			**DRB4*(n = 640)**		
Allele ID	%	(f)	Allele ID	%	(f)
1	21	483	**1**	25	581
2	0.3	8	**2**	2.1	50
3	0	1	**3**	0.1	3
52	0.2	5	**4**	0.1	3
-	-	-	**53**	0.1	3

25.1 % for DRB1*04, 11.2 % for DRB1*14, and 8 % for DRB1*08. However, variations are expected when comparing different populations. For instance, according to Peterson et al. (2014), the most prevalent alleles in the African population are DQB1*03 (21.79 %), DRB1*11 (11.65 %), DRB3*02 (31.65 %), and DRB4*01 (10.5 %), while in the Asian population, frequencies of DQB1*03 (40.89 %), DRB3*02 (20.27 %), and DRB4*01 (25.72 %) are notably high (14,3221,22). These differences highlight the genetic diversity across populations, yet the high degree of conservation observed for certain alleles within the Ecuadorian population may be attributed to its mestizo genetic composition (Paz-Y-Miño et al., 2016; Galarza et al., 2018).

Due to colonialism, it is expected that patterns of HLA distribution of Western Europe and Latin America were similar. However, the most common HLA-A alleles in Northern and Western Europe differ from the highest frequency alleles in the colonial regions (Colobig et al., 2023). In our study, none of the alleles of HLA class I genes that are more prevalent in Europe occupy more than 5 % of our study population which has been evidenced in other studies as well (Colobig et al., 2023; Arnaiz-Villena et al., 2010). Moreover, the high frequencies of the HLA-A*02 allele found in our study, and in Latin America overall, might suggest that this allele was already dominant in indigenous populations before European colonization.

The high frequency of HLA-B*35, HLA-B*40, and HLA-B*19 alleles in the Ecuadorian population differs completely from any possible African or European lineage (Janse van Rensburg et al., 2021). This finding support the previously described idea that HLA-B has greater uniformity within the American continent when compared to other regions of the world (Arrieta-Bolaños et al., 2023). On the contrary, HLA-C*07, the most prevalent allele in Europe and Africa, is also the most prevalent in this study (Janse van Rensburg et al., 2021; Bergström et al., 2021).

The presence of the genes DRB3 and DRB4 may vary between individuals, but it is estimated that the DRB3 gene is typically present when the DRB1 gene has the following alleles: *03, *11, *12, *13, and *14, while the DRB4 gene is commonly associated with the DRB1 alleles *04, *07, and *09 (Creary et al., 2021). Considering the frequency of DRB1 alleles in our study (Table 2), it is expected that the DRB3 gene should be present in at least 28.8 % and the DRB4 gene in at least 36.6 % of the population. However, our results showed lower values, with 21.13 % presence of the DRB3 gene and 27 % for the DRB4 gene (Table 3). This could suggest that the association between DRB1 alleles and the presence of DRB3 and DRB4 is not as significant in the study population than in the rest of the world.

Previous studies performed in Latin America have identified a clear pattern in HLA frequencies, with HLA-A*02 appearing in more than

30 %, HLA-A*24 appearing in more than 20 %, and HLA-B*35 in more than 15 % of the Argentinian (Emma Laura et al., 2004), Colombian (Rodríguez et al., 2007), Peruvian (de Pablo et al., 2000), Chilean (Solloch et al., 2023), Venezuelan (Solloch et al., 2023), Bolivian (Arnaiz-Villena et al., 2020), Brazilian (Ravazzi-Gauch et al., 2016; Reis et al., 2018), and Uruguayan populations (Alvarez et al., 2006). Studies that included HLA-C alleles found HLA-C*07 and HLA-C*04 to be the most common, with frequencies ranging from 20 % to 40 % across all populations.

This trend aligns strongly with the HLA allele frequencies observed in the Ecuadorian transplant recipient population in our study, supporting the presence of four predominant HLA class I haplotypes across Latin American populations: HLA-A02, HLA-B35, HLA-C07; HLA-A24, HLA-B35, HLA-C07; HLA-A02, HLA-B35, HLA-C04; and HLA-A24, HLA-B35, HLA-C04. The recurrent presence of HLA-B35 in all identified haplotypes suggests a potential immunogenetic selection pressure, possibly mediated by its association with pathogen-driven selection or immunological fitness in response to infectious agents endemic to the region. Furthermore, the strong linkage disequilibrium between HLA-A02 and HLA-B35, as well as between HLA-A24 and HLA-B35, indicates conserved haplotype blocks that might contribute to alloimmune responses during transplantation.

While these haplotypes display high frequencies across diverse Latin American populations, suggesting evolutionary convergence shaped by admixture events and selective pressures, further research is required to ascertain whether this phenomenon can be extended to the wider population.

Studies for HLA class II involving HLA-DQB1 and DRB1 are limited in Latin America. However, the HLA-DRB1*4 allele shows a frequency of more than 10 % in Mexican (Alaez et al., 2002), Peruvian (de Pablo et al., 2000), Chilean (Solloch et al., 2023), and Brazilian (Ravazzi-Gauch et al., 2016) populations which follows the pattern found in our study. However, with a 25.1 % and 48 %, we report the highest frequencies for HLA-DRB1*4 and HLA-DQB1*3 across Latin American (Alaez et al., 2002; Díaz et al., 2002; Del Río-Ospina et al., 2019).

Brazil and Central American countries accumulate the majority of published studies of HLA-DRB3 and HLA-DRB4 distribution (Petzl-Erler and McDevitt, 1994; Nishimura et al., 2012). According to our findings, there is a high frequency of HLA-DRB3*01 and HLA-DRB4*01 alleles in the region which follows the pattern found in our studied population (Table 3). However, the HLA-DRB3*02 allele in Central America is considerably more prevalent than in our cohort (Arrieta-Bolaños et al., 2011). Nevertheless, few HLA studies include the DRB3 and DRB4 genes, and when they do, the number of individuals typed for these genes is typically low. Our study provides the most extensive typing of these genes in the region.

To the best of our knowledge, there is only one study that examines the demographic distribution of HLA alleles in Ecuador (Galarza et al., 2018). This study analyzed 1101 Ecuadorian individuals from the Coast, Andean, and Amazon regions and concluded that the primary HLA-B genetic components in Ecuador were of Native American and European origin, with African components mostly found on the Coast. Conversely, our study characterized HLA class I and II alleles at the province level and provides the initial description of HLA-C, DRB3, and DRB4 frequencies. The findings of Galarza et al. (2018) identified A*24, B*35, DRB1*04, and DQB1*03 as the most prevalent alleles, which align closely with our results. However, a key difference is that our study found HLA-A*02 to be 10 % more frequent than HLA-A*24.

5. Conclusions

This study represents the first comprehensive analysis of HLA class I and II allele frequencies and their geographic distribution in Ecuador, providing the first available data on HLA-C, DRB3, and DRB4 in the country. Notably, it constitutes the most extensive characterization of HLA-DRB3 and DRB4 in Latin America to date.

The high prevalence of HLA-A*02, HLA-B*35, HLA-C*07, DRB1*04, DQB1*03 in the Ecuadorian population has important implications for donor-recipient matching, potentially improving organ allocation efficiency. Additionally, our findings suggest that HLA-DRB3 and DRB4 loci are less frequent than expected among patients on the organ transplant waiting list, a trend that warrants further investigation to elucidate its immunogenetic and clinical significance.

Beyond its clinical relevance, our findings elucidate the genetic structure of the Ecuadorian population, delineating admixture dynamics and historical migration patterns. HLA characterization in this context refines organ allocation strategies while advancing the study of genetic diversity and evolutionary processes in mestizo populations.

Further research is essential to refine our understanding of the genetic landscape of the Ecuadorian population, particularly regarding the influence of environmental and demographic factors on HLA allele distributions. Expanding these investigations will be crucial for deciphering the complex immunogenetic interactions that shape disease susceptibility and transplant outcomes. By advancing this knowledge, we can better inform precision medicine approaches and public health strategies tailored to the unique genetic profile of Ecuador.

CRediT authorship contribution statement

David Báez-Cevallos: Software, Methodology, Investigation. **Luis Alberto Loyola:** Methodology, Investigation. **Eduardo Espinel:** Methodology, Investigation. **Sofía Espín:** Software, Methodology. **Felipe Ortiz:** Methodology. **María Esther Castillo:** Methodology. **Erick Velasteguí:** Writing – original draft, Methodology, Investigation. **Carlos Bastidas-Caldes:** Writing – review & editing, Writing – original draft, Project administration, Conceptualization. **Isabel Baroja:** Writing – review & editing, Writing – original draft, Validation, Investigation. **Daniel Romero-Alvarez:** Writing – review & editing, Writing – original draft, Visualization, Validation, Software. **Nikolaos C. Kyriakidis:** Writing – original draft, Investigation, Conceptualization.

Conflict of interest

All authors declare that we have no conflict of interest or present any royalty or financial benefit for the publication of this article.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.molimm.2025.03.019.

Data availability

Data will be made available on request.

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