

HLA Class I and II Allele Group Distributions in a Senegalese Kidney Transplantation Cohort

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Abstract

Background: HLA diversity is poorly characterised in West African transplantation programmes. We described harmonised first-field HLA class I and II allele-group assignments, locus-specific typing losses and interlaboratory concordance in a Senegalese transplantation cohort. **Methods:** Participants were recruited through the MHO-Le Dantec kidney-transplantation programme, resulting in an analytical cohort of 72 individuals (38 recipients and 34 potential donors). HLA-A, -B, -C, -DRB1, -DQA1 and -DQB1 were typed using LABType reverse sequence-specific oligonucleotide assays on a Luminex platform at the Blood Bank, Immunology and Histocompatibility Laboratory of MHO. For the primary analysis, allele assignments were harmonised at the first-field level. Calls with unresolved higher-field information were retained when the first-field group was unambiguous, whereas non-interpretable results were handled separately for each locus. Assignment categories and Hardy-Weinberg equilibrium (HWE) were analysed independently, with a sensitivity analysis retaining one participant per related donor-recipient pair. In addition, eight samples from four donor-recipient pairs were compared with results from a Turkish laboratory at the highest resolution shared by both laboratories. **Results:** The most frequent first-field groups were HLA-A*02, HLA-B*35/HLA-B*53, HLA-C*07, HLA-DRB1*13, HLA-DQA1*01/HLA-DQA1*05

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and HLA-DQB1*03. Retained genotype counts were 71, 69, 49, 69, 67 and 68 for these six loci, respectively, with corresponding primary allele-assignment denominators of 142, 138, 98, 138, 134 and 136. No locus showed a significant departure from HWE after correction, and the sensitivity analysis did not change the interpretation. All 40 comparable sample-locus genotypes were concordant between laboratories at first-field resolution. **Conclusion:** This study provides a transparent cohort-level description of HLA diversity and typing completeness in a Senegalese kidney-transplantation programme. The findings are not national population-frequency estimates; larger population-based studies using high-resolution typing and haplotype analysis are required.

Keywords

HLA Typing, Allele Group, rSSO, Histocompatibility, Kidney Transplantation, Senegal, West Africa

1. Introduction

The human leukocyte antigen (HLA) system is a polymorphic immunogenetic system that forms part of the human major histocompatibility complex (MHC) [1]. It is located on the short arm of chromosome 6 at 6p21.3 and encodes highly polymorphic molecules that play central roles in antigen presentation, immune regulation and histocompatibility [2] [3]. Classical HLA class I molecules, encoded by the HLA-A, HLA-B and HLA-C genes, are expressed on nearly all nucleated cells and predominantly present endogenous peptides to CD8⁺ T cells [4] [5]. HLA class II molecules, including HLA-DR, HLA-DQ and HLA-DP, are expressed mainly on professional antigen-presenting cells and present exogenous peptides to CD4⁺ T cells [6] [7]. Because of its extensive polymorphism, the HLA system enables presentation of a broad repertoire of peptides, but it is also a major barrier to donor-recipient compatibility [1] [8].

Most HLA polymorphisms are concentrated in the peptide-binding region, thereby influencing antigen-presentation specificity and tissue compatibility [1] [7] [8]. HLA genes are inherited as haplotypic blocks from both parents. Each parent carries two HLA haplotypes, and each child inherits one. Siblings therefore share zero, one, or two parental HLA haplotypes. This inheritance pattern contributes to HLA diversity in families and in populations [9]. Because of its high diversity, the HLA system is a powerful marker of migration history and population structure [10] [11]. HLA diversity reflects a long evolutionary history shaped by natural selection, admixture, migration, founder effects, and genetic drift [10]. Sub-Saharan African populations exhibit high HLA diversity [12], consistent with the African origin of modern humans [13]. HLA diversity has declined outside Africa, with lower levels observed in Oceanic and Native American populations, consistent with serial founder effects [14].

During organ transplantation, the recipient immune system can recognise donor HLA molecules through direct, indirect, and semi-direct allorecognition pathways, which may induce an alloimmune response [15]. T-cell activation promotes cytokine and chemokine production and may recruit innate immune components such as NK cells, macrophages and the complement system [16]. HLA mismatches, especially involving HLA-B and HLA-DR, have been associated with transplant outcomes; HLA-DR mismatches have been found to be particularly important for early graft survival, whereas HLA-B mismatches may play a role in long-term graft survival [17]-[20].

Beyond transplantation, HLA variation is associated with susceptibility or resistance to many autoimmune and infectious diseases [21]-[23]. For instance, HLA-B*27 is strongly associated with spondyloarthritis and related rheumatic or ocular inflammatory diseases [24]. In a Senegalese study, the authors found HLA-B*27 expression among patients with spondyloarthropathies [25] [26]. HLA-B*51 and Behçet's disease have also been associated with HLA-DRB1*04 lineages [27]. Disease association can only be interpreted in a case-control setting and with an appropriate typing resolution.

This study aimed to describe the allele group distribution of HLA class I and II in a Senegalese kidney-transplantation cohort, clarify locus-specific typing, and compare genotype consistency through an interlaboratory comparison. The study also aimed to establish preliminary local evidence for histocompatibility services and define the methodological requirements for future high-resolution HLA studies in Senegal.

2. Materials and Methods

2.1. Patient Selection and Sample Collection

An initial pool of 87 candidate individuals was identified through the MHO-Le Dantec kidney-transplantation pathway. After 10 potential donors did not attend sample collection and five recipients had inconclusive HLA typing, the final cohort comprised 72 participants: 38 recipients and 34 potential donors. Participants were eligible if they were evaluated within the transplantation programme and provided a blood sample (Figure 1). For transplantation, we assessed eligibility through clinical and biological evaluations conducted as part of the MHO-Le Dantec Consortium (Military Hospital of Ouakam and Aristide Le Dantec Hospital) [28]. Ministerial Order No. 008677 of 10 April 2020 approved the programme. The Senegalese National Ethics Committee for Health Research granted ethical approval of the research protocol (00159/MSAS/CNERS/Sec, 21 August 2020.). All participants gave informed consent before sample collection.

2.2. HLA rSSO Typing

Low and intermediate-resolution HLA typing was performed using LABType RSSO assays (One Lambda, Thermo Fisher Scientific) on the Luminex platform as described by the manufacturer. The assay is based on hybridisation of PCR-amplified

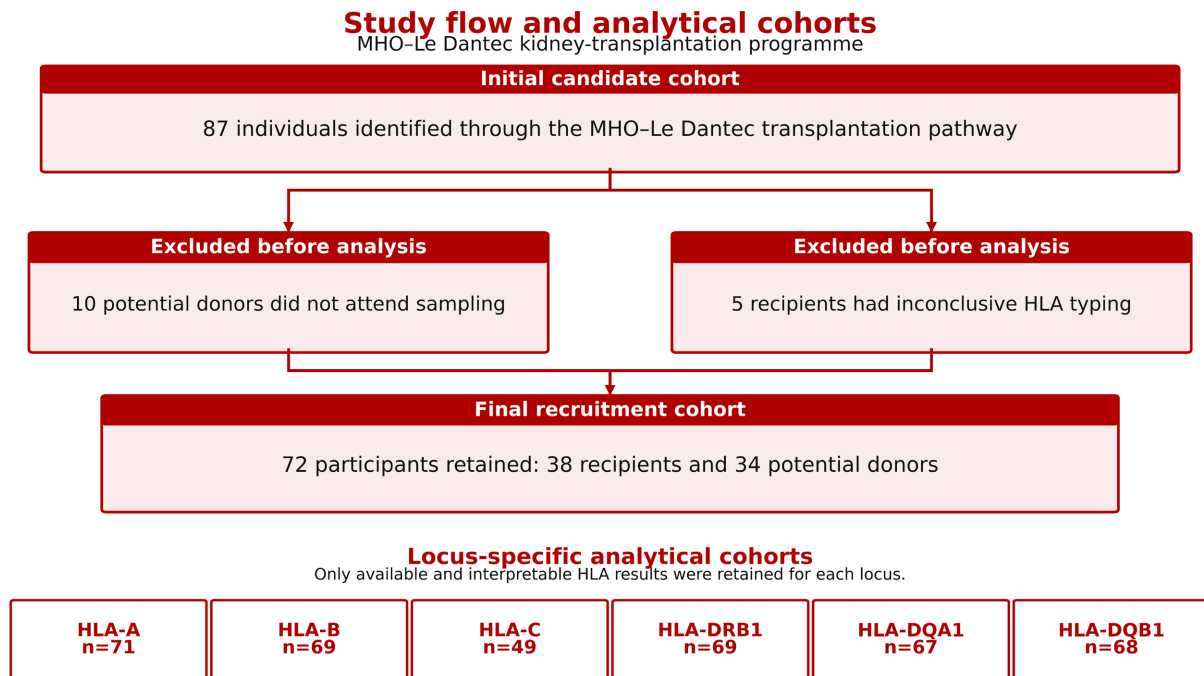


Figure 1. Study flow from donor-recipient pairing records to the final recruitment and locus-specific analytical cohorts.

DNA to sequence-specific oligonucleotide probes targeting HLA alleles.

2.2.1. DNA Extraction and Separation

Genomic DNA was extracted from EDTA-anticoagulated blood using the QI-Aamp Blood Mini Kit (QIAGEN, cat. 61104) according to the manufacturer’s instructions. We briefly lysed blood cells using a chaotropic, guanidine-containing buffer to denature proteins and release DNA. We loaded lysates onto silica columns, washed with AW1 and AW2 buffers to remove contaminants, and eluted in a low-salt buffer. We used the DNA immediately for PCR or stored it at –20°C until analysis.

2.2.2. Amplification of HLA Alleles

We amplified HLA-A, HLA-B, HLA-C, HLA-DR, and HLA-DQ using One Lambda (Thermo Fisher Scientific) LABType SSO PCR kits (A1, B1, C1, DR, and DQ, respectively). We added 2 µL of DNA to each well, then added a PCR mix containing 4 µL of primers, 13.8 µL of D-Mix, and 0.2 µL of Taq polymerase to a final volume of 20 µL. We sealed the plates and amplified them on an Applied Biosystems thermal cycler using the rSSO-PCR programme. We checked amplification products by electrophoresis on a 2.5% agarose gel and visualised them using the Photogel system. DP primers were available in the original panel, but DPA1/DPB1 data were not retained for analysis because only two complete DP records were available; therefore, no DP results are reported.

2.2.3. Denaturation and Hybridisation

During hybridisation, 2.5 µL of denaturation buffer and 5 µL of amplified DNA

were added to each well of a new plate. After mixing, the plate was incubated at room temperature for 10 minutes. Subsequently, 5 μ L of neutralisation buffer were added to each well. The denatured PCR products were then hybridised to sequence-specific oligonucleotide probes coupled to fluorescent microspheres, followed by three washing steps with wash buffer.

2.2.4. Labelling

LT-SAPE (streptavidin conjugated with R-phycoerythrin, cat. 0917012) was used to label biotinylated PCR products for fluorescence detection. Signal acquisition was then performed on the Luminex platform according to the manufacturer's instructions.

2.2.5. Sample Acquisition

Samples were acquired on the Luminex FLEXMAP-3D platform (Ref. APX1342) using xPONENT software version 4.2. The assay employs fluorescent microspheres coupled to sequence-specific oligonucleotide probes. xPONENT identifies bead regions and measures mean fluorescence intensity (MFI), and HLA Fusion 4.7.1 software interprets probe-reactivity patterns to generate HLA assignments. We included positive and negative controls to validate each run.

2.2.6. HLA Assignment, Quality Control and Validation

Following data acquisition with xPONENT, we interpreted the results using HLA Fusion software version 4.7.1 (Thermo Fisher Scientific) and the lot-specific interpretation database associated with each LABType kit. Before interpretation, we reviewed the internal control beads and verified that the positive and negative controls, internal quality-control parameters and HLA Fusion validity flags met the manufacturer's cutoff and ratio criteria. No manual assignment overrides were applied.

When controls failed, signal intensity was insufficient or no solution was obtained, the run was repeated once using the original DNA when sufficient material was available. Persistent failures were reported as "no solution" and excluded only from the corresponding locus-specific analysis. Kit lot numbers and database identifiers were recorded in the laboratory worksheet.

HLA assignments were retained at the available low- or intermediate-resolution level and standardised according to the official IPD-IMGT/HLA nomenclature. Because rSSO typing may produce unresolved probe-reactivity patterns, manufacturer ambiguity codes and unresolved alternative allele groups were classified as ambiguous assignments. These categories were analysed separately for each HLA locus in the secondary analysis. Ambiguity proportions were calculated from the number of distinct reported assignment categories and should not be interpreted as patient-level ambiguity rates.

2.3. External Interlaboratory Comparison

The external interlaboratory comparison included eight samples from four donor-recipient pairs. Results generated by the Senegalese and Turkish laboratories were

compared at the highest resolution shared by both laboratories. Concordance was assessed for HLA-A, HLA-B, HLA-C, HLA-DRB1 and HLA-DQB1, corresponding to 40 sample-locus comparisons at first-field resolution.

2.4. Statistical Analysis

For the primary analysis, HLA assignments were harmonised at the first-field level and reported as allele groups rather than specific alleles. Partially resolved calls with a unique first-field assignment were retained for allele-group frequency calculations. These calls were considered a subset of the evaluable genotypes and were not added to the total number of evaluable genotypes. Two-field designations and manufacturer-generated ambiguity codes were retained separately for the secondary assignment-category analysis. First-field allele-group frequencies used the number of retained allele assignments as the denominator, whereas secondary category frequencies used the number of distinct reported assignment categories.

Bar plots were initially generated using ggplot2 in R/RStudio. **Figure 2** and **Figure 3** were subsequently formatted using Python version 3.12.14 with Matplotlib version 3.10.8 and Pillow. **Figure 4** was generated using Python version 3.12.14 with Matplotlib version 3.10.8. The formatting process did not modify the underlying data, assignment categories, numerical values or bar lengths.

Hardy-Weinberg equilibrium (HWE) was assessed separately for HLA-A, HLA-B, HLA-C, HLA-DRB1, HLA-DQA1 and HLA-DQB1. The primary analysis included all eligible individuals with complete locus-specific genotypes. Because the recruitment pathway included biologically related donor-recipient pairs, a sensitivity analysis retained one participant per documented relationship, with the recipient retained. For each analysis, we calculated the number of individuals, the number of distinct allele groups, homozygous and heterozygous genotype counts, observed heterozygosity (H_o), expected heterozygosity (H_e), the inbreeding coefficient (FIS) and the HWE p-value. Given the multiallelic nature of the HLA loci, HWE was evaluated using the HWPerm.mult function from the HardyWeinberg package version 1.7.8 in R version 4.3.2, with 100,000 permutations. A p-value < 0.05 was considered statistically significant. After Bonferroni correction for six locus-specific tests, the adjusted significance threshold was set at 0.0083.

3. Results

3.1. Characteristics of the Study Cohort

The analysed recruitment cohort comprised 72 Senegalese individuals: 38 recipients and 34 potential donors. Ten potential donors did not attend sample collection, and five recipients were excluded because HLA typing was inconclusive. These exclusions occurred before locus-specific accounting; participants with a valid result at one locus could therefore remain in another locus-specific analysis.

Table 1 summarises the locus-specific analytical denominators. The number of evaluable genotypes ranged from 49 for HLA-C to 71 for HLA-A. The corresponding

Table 1. Locus-specific accounting of the final 72-participant cohort.

Locus	Cohort (n)	Evaluable genotypes (n)	Partially resolved but retained at first field (n)*	Excluded or non-interpretable genotypes (n)	Retained first-field allele assignments (n; primary denominator)	Distinct assignment categories (n; secondary analysis)
HLA-A	72	71	1	1	142	25
HLA-B	72	69	0	3	138	41
HLA-C	72	49	1	23	98	33
HLA-DRB1	72	69	0	3	138	17
HLA-DQA1	72	67	1	5	134	5
HLA-DQB1	72	68	2	4	136	8

denominators for first-field allele-group frequencies were 142 assignments for HLA-A, 138 for HLA-B, 98 for HLA-C, 138 for HLA-DRB1, 134 for HLA-DQA1 and 136 for HLA-DQB1. These differences reflect locus-specific missing or non-interpretable results and do not represent different recruitment cohorts. Two-field assignments were reported separately but were collapsed to their corresponding first-field allele group in the primary frequency analysis.

3.2. Distribution of HLA Assignment Categories

The intermediate-resolution HLA typing by rSSO-Luminex generated allele assignments for all loci examined. The composition of the distinct assignment categories varied across loci (**Table 2**). HLA-C had the highest proportion of different categories that were ambiguous (13 of 33 categories, 39.4%); HLA-B had 8 of 41 (19.5%); HLA-A had 4 of 25 (16.0%); and HLA-DQB1 had 1 of 8 (12.5%). No ambiguous categories were observed among the 17 categories in HLA-DRB1 or the five categories in HLA-DQA1. These proportions reflect the distribution of distinct reported categories and should not be interpreted as patient-level ambiguity rates.

Table 2. Distribution of distinct unambiguous and ambiguous HLA assignment categories by locus.

Assignment category	HLA-A	HLA-B	HLA-C	HLA-DRB1	HLA-DQA1	HLA-DQB1
Ambiguous, n (%)	4 (16.0)	8 (19.5)	13 (39.4)	0 (0.0)	0 (0.0)	1 (12.5)
Unambiguous, n (%)	21 (84.0)	33 (80.5)	20 (60.6)	17 (100.0)	5 (100.0)	7 (87.5)
Total distinct categories, n	25	41	33	17	5	8

3.3. Hardy-Weinberg Equilibrium Analysis

We detected no statistically significant deviation from HWE at any of the six loci examined. The recipient-per-pair sensitivity analysis included 35 - 37 complete recipient genotypes per locus and did not change the interpretation; the corresponding permutation p-values were 0.696, 0.288, 0.432, 0.464, 0.715 and 0.884 for HLA-A, HLA-B, HLA-C, HLA-DRB1, HLA-DQA1 and HLA-DQB1, respectively. No lo-

cus crossed the Bonferroni-adjusted threshold of 0.0083. Observed heterozygosity was highest at HLA-B (0.942), followed by HLA-A (0.845), HLA-C (0.816), HLA-DQA1 (0.806), HLA-DRB1 (0.797) and HLA-DQB1 (0.706) (**Table 3**).

Expected heterozygosity values were generally close to observed heterozygosity values. Estimated H_e values were 0.881 for HLA-A, 0.919 for HLA-B, 0.868 for HLA-C, 0.813 for HLA-DRB1, 0.727 for HLA-DQA1, and 0.724 for HLA-DQB1. The F_{IS} values were small. Slight heterozygote deficits were observed for HLA-A, HLA-C, HLA-DRB1 and HLA-DQB1, whereas slight heterozygote excesses were observed for HLA-B and HLA-DQA1. None of the loci showed a statistically significant departure from HWE.

Table 3. Hardy-Weinberg equilibrium analysis by HLA locus.

Locus	n analysed	n excluded	Distinct allele groups	Homozygous, n	Heterozygous, n	H_o	H_e	F_{IS}	HWE p-value	Adjusted p-value	Interpretation
HLA-A	71	1	15	11	60	0.845	0.881	0.040	0.308	1.000	No significant deviation
HLA-B	69	3	28	4	65	0.942	0.919	-0.025	0.258	1.000	No significant deviation
HLA-C	49	23	13	9	40	0.816	0.868	0.060	0.475	1.000	No significant deviation
HLA-DRB1	69	3	13	14	55	0.797	0.813	0.019	0.081	0.486	No significant deviation
HLA-DQA1	67	5	6	13	54	0.806	0.727	-0.109	0.969	1.000	No significant deviation
HLA-DQB1	68	4	6	20	48	0.706	0.724	0.024	0.972	1.000	No significant deviation

3.4. HLA Class I Allele Group Frequencies

3.4.1. HLA-A Locus

At the HLA-A locus, HLA-A*02 was the most common allele group (17.7% of all allele group assignments). It was followed by HLA-A*23 (13.8%), HLA-A*33 (13.1%), HLA-A*30 (12.3%) and HLA-A*68 (10.0%). These five allele groups accounted for approximately two-thirds of HLA-A assignments, while the remaining resolved allele groups each had frequencies below 7%. We found four coded ambiguous assignments, each at 0.8% (**Figure 2(A)**).

3.4.2. HLA-B Locus

The HLA-B locus had a more diverse distribution of allele groups. The most common among them were HLA-B*53 and HLA-B*35, each accounting for 12.4% of assignments, followed by HLA-B*07 (10.1%). HLA-B*08, HLA-B*72 and HLA-B*58 had a frequency of 5.4% each, while HLA-B*49 had 4.7%. HLA-B*27 and HLA-B*51 had frequencies of 3.9% and 1.6%, respectively. Eight coded ambiguous assignments were identified at this locus. The most frequent ambiguous as-

signment was associated with the HLA-B*08 allele group (2.3%), while the other ambiguous assignments in the HLA-B*35, HLA-B*40, HLA-B*52 and HLA-B*78 allele groups each occurred at 0.8% (**Figure 2(B)**).

3.4.3. HLA-C Locus

At HLA-C, we found 33 different assignments: 20 unambiguous categories and 13 coded ambiguous assignments. HLA-C*07 was the most common allele group (21.1% of assignments), followed by HLA-C*04 (15.6%), HLA-C*02 (11.1%), HLA-C*10 (7.8%), and HLA-C*06 (5.6%). The other unambiguous assignments were all at 3.3% or less. Each of the remaining 12 coded ambiguous assignments occurred at a rate of 1.1%. HLA-C had the highest proportion of distinct assignment categories classified as ambiguous among the class I loci, with 13 of 33 categories classified as ambiguous (39.4%) (**Figure 2(C)**).

HLA class I allele-group frequencies in the Senegalese kidney-transplantation cohort

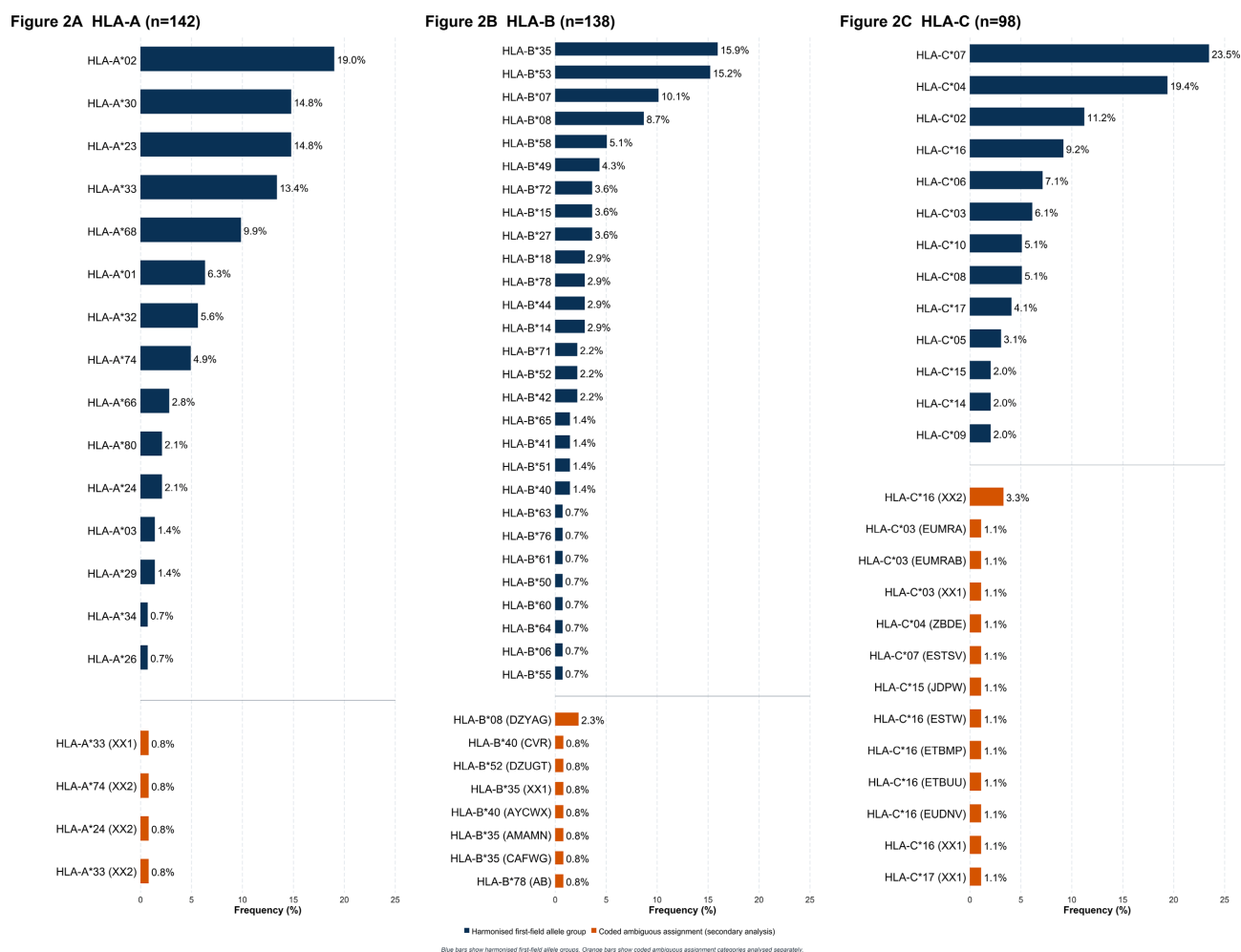


Figure 2. Distribution of HLA class I assignments in the Senegalese kidney transplantation cohort.

3.5. HLA Class II Allele Group Frequencies

Class II assignment distributions were more concentrated than those observed at

the class I loci. Seventeen distinct assignment categories were reported at HLA-DRB1.

3.5.1. HLA-DRB1 Locus

The most frequent HLA-DRB1 assignment was HLA-DRB1*13, accounting for 32.3% of evaluable assignments. HLA-DRB1*03 and HLA-DRB1*08 each accounted for 12.1%, followed by HLA-DRB1*11 at 11.3%. HLA-DRB1*09, HLA-DRB1*04 and HLA-DRB1*10 occurred at frequencies of 7.3%, 6.5% and 5.6%, respectively, whereas the remaining assignments each accounted for 2.4% or less (**Figure 3(A)**).

3.5.2. HLA-DQ Loci

At the HLA-DQ locus, the α -chain was dominated by the HLA-DQA1*01 and HLA-DQA1*05 allele groups, whereas HLA-DQA1*03 and HLA-DQA1*04 were less frequent. For the β -chain, HLA-DQB1*03 was the most common first-field allele group, followed by HLA-DQB1*02, HLA-DQB1*05 and HLA-DQB1*06. We did not count the two-field designations HLA-DQB1*03:19 and HLA-DQB1*05:01 as separate primary groups; we reported them only as secondary-resolution examples. We retained one manufacturer-coded ambiguous DQB1 assignment in the secondary assignment-category analysis (**Table 2; Figure 3(C)**).

At the common first-field resolution, genotype concordance was 8/8 (100%) for each of the five comparable loci: HLA-A, HLA-B, HLA-C, HLA-DRB1 and HLA-DQB1. All 40 sample-locus comparisons were concordant between laboratories and there was no difference in the first-field genotype between the Senegalese and Turkish reports (**Figure 4**).

4. Discussion

In this study, we described the diversity of HLA class I and class II in a Senegalese population recruited in an emerging kidney transplantation programme. We observed the predominance of HLA-A*02, HLA-B*53/HLA-B*35, and HLA-C*07 among class I assignments; as well as the predominance of HLA-DRB1*13, HLA-DQA1*01/HLA-DQA1*05, and HLA-DQB1*03 among class II assignments; and locus-dependent patterns of typing ambiguity. HLA-C had the highest proportion of ambiguous categories in the assignment list, followed by HLA-B and HLA-A. However, these proportions are based on distinct reported assignment categories, rather than independent patient-level allele calls. We therefore did not directly compare ambiguity across the different loci. The large number of ambiguous classifications at HLA-C should therefore be viewed as a descriptive feature of the assignment range generated by rSSO. A valid inferential comparison would require determining patient-level ambiguity status independently for every sample at each locus. These findings are relevant to developing histocompatibility platforms in Senegal, but should be interpreted as descriptive of a selected clinical cohort rather than as national population-frequency estimates [12] [28].

The Hardy-Weinberg equilibrium (HWE) analysis showed no significant

HLA class II allele-group frequencies in the Senegalese kidney-transplantation cohort

Figure 3A HLA-DRB1 (n=138)

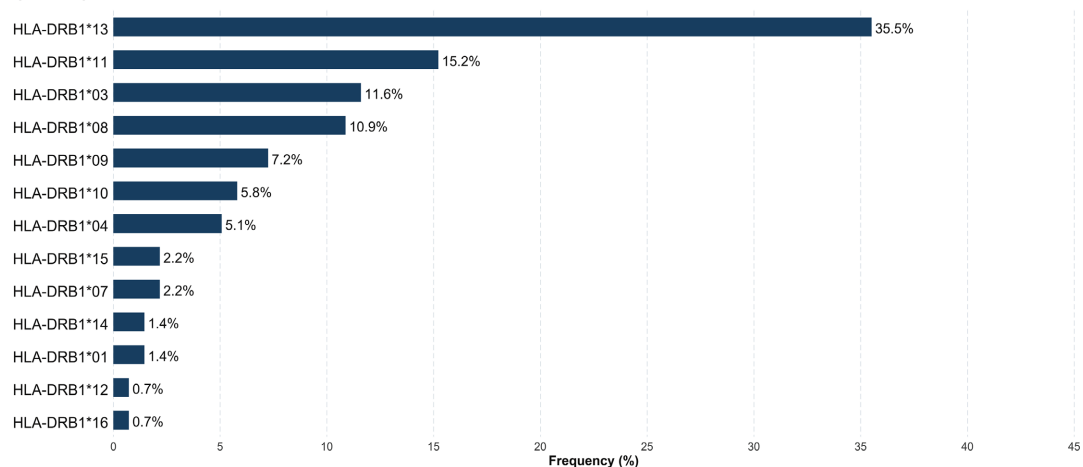


Figure 3B HLA-DQA1 (n=134)

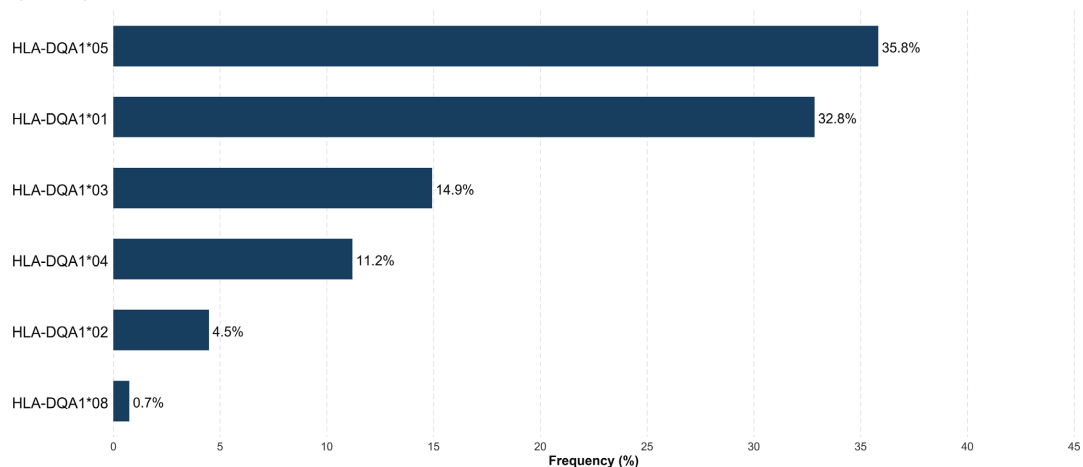


Figure 3C HLA-DQB1 (n=136)

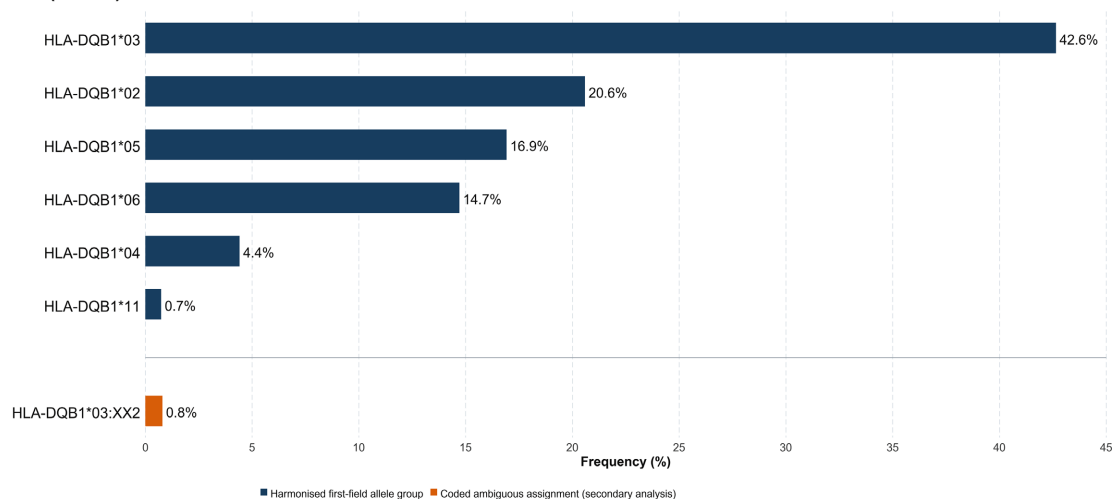


Figure 3. Distribution of HLA class II assignments in the Senegalese kidney transplantation cohort.

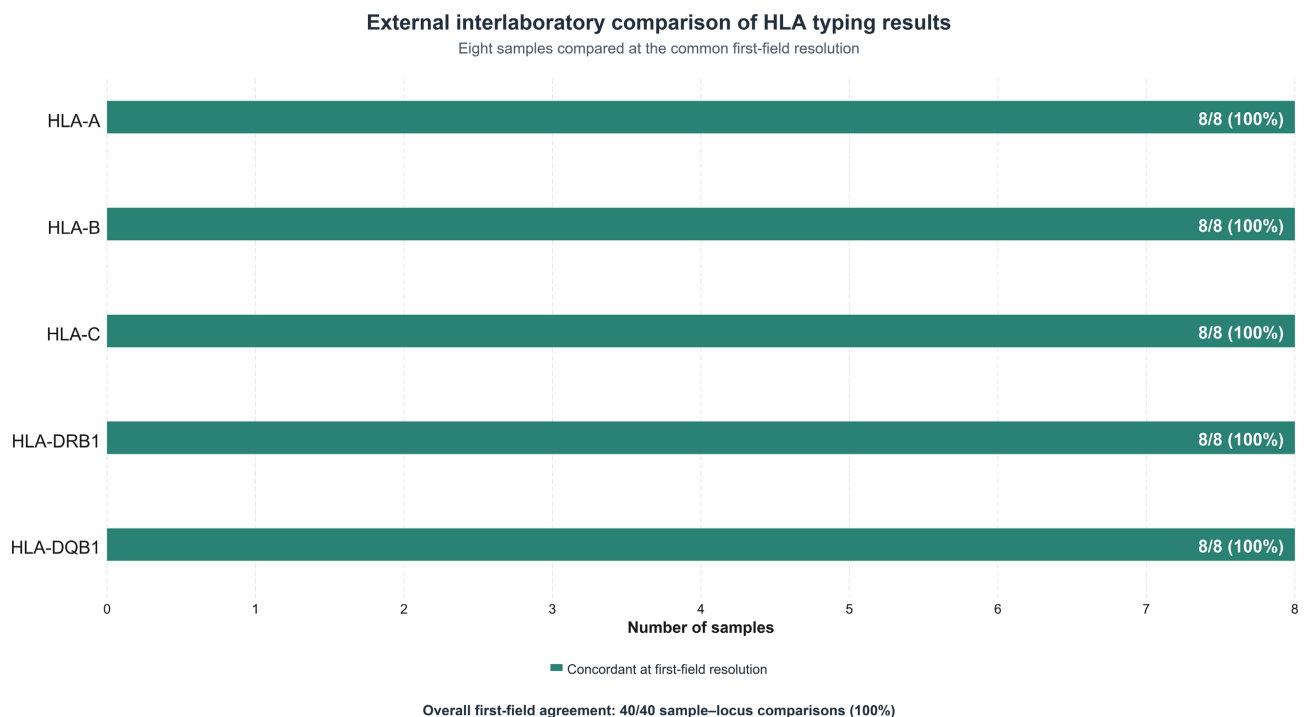


Figure 4. External interlaboratory comparison of HLA typing results between the Senegalese and Turkish laboratories.

deviations across the six HLA loci analysed, indicating that genotype distributions generally matched allele frequencies in this population. Other population-based HLA studies have also applied Hardy-Weinberg equilibrium testing to allele and haplotype frequency analyses in Mauritanian, Tunisian, Lebanese, South African, and Indian populations [29]. Because HLA loci are highly polymorphic and multi-allelic, exact or permutation-based procedures are generally more appropriate than conventional asymptotic chi-square tests, particularly in small samples containing rare genotypes [30]-[32].

However, interpret these results cautiously. The population involved in this study was recruited in a transplantation context and was not a random sample of the Senegalese population. Therefore, the absence of a significant deviation from HWE should not be considered evidence that the population is representative. Instead, it should be viewed as a descriptive indication of the genotype distribution in the study sample.

This cautious interpretation is especially important in HLA studies, as deviations from Hardy-Weinberg equilibrium may result from several factors, including small sample size, population substructure, admixture, relatedness among participants, and unresolved typing ambiguities [33] [34]. On the other hand, the absence of significant deviation does not rule out these factors; it only means that the genotype proportions do not differ significantly from the predicted values based on this test. However, these findings should be treated as a quality-control and descriptive population-genetic assessment, not as evidence that the cohort fully reflects the genetic composition of the Senegalese population.

HLA-A*02 was the most common allele group at the HLA-A locus, followed by

HLA-A*23, HLA-A*33, and HLA-A*30, respectively. The detection of HLA-A*30 is consistent with previous Senegalese studies, but numerical comparisons are difficult due to differences in recruitment, ethnicity, typing technology, and data resolution. At HLA-B, HLA-B*53 and HLA-B*35 were the most common allele groups, followed by HLA-B*07. HLA-B diversity was also observed in Senegal and other sub-Saharan populations, and HLA-B*53 and HLA-B*35 were frequently reported. Population-genetic studies have linked the spatial distribution of HLA-B*53, HLA-B*78, and HLA-A*74 to malaria-endemic regions [35], but this study is not intended to assess whether pathogen selection or disease association is linked to them.

HLA-C*07, HLA-C*04, and HLA-C*02 were the most frequent HLA-C allele groups. The HLA-C locus also had the highest proportion of ambiguous assignments among the class I loci. This finding should not be interpreted as evidence that HLA-C was intrinsically more polymorphic than HLA-B in this cohort. Rather, it primarily reflects the ability of the low and intermediate-resolution rSSO assay and its probe panel to discriminate the HLA-C variants present in these samples. Likewise, the observed frequencies of HLA-B*27 and HLA-B*51 cannot be used to infer autoimmune disease risk because participants were not recruited through a disease-association design and the typing results were predominantly reported at one-field resolution [36]–[38].

For HLA class II, HLA-DRB1*13 was the predominant reported allele group. This is consistent with the high frequency of DR13 and DRB1*13 lineages previously described in Senegalese Serere and Mandenka populations [39]. In particular, high-resolution studies in Mandenka identified HLA-DRB1*13:04 as a frequent allele, but the present rSSO data do not support assigning that specific two-field allele to all HLA-DRB1*13 results. The concentration of HLA-DQA1 assignments in HLA-DQA1*01 and HLA-DQA1*05, and of HLA-DQB1 assignments in HLA-DQB1*03 and HLA-DQB1*02, further supports the presence of recurrent class II profiles in this cohort. Definitive characterisation of these patterns requires phased, high-resolution allele and haplotype analysis [39]–[42].

These ambiguities reflect the limited discriminatory power of low- to intermediate-resolution rSSO typing, as different allelic combinations can yield the same probe-reactivity pattern. High-resolution sequencing could resolve many of these assignments and enable more consistent reporting at two or more HLA fields [9] [38] [43] [44].

In transplantation, these results offer locally relevant information that may help guide laboratory planning, donor-recipient matching, and the development of Senegalese HLA reference sets. However, allele group frequencies alone cannot measure compatibility, predict graft rejection or identify mismatch problems. For this purpose, individual genotypes, haplotype and linkage disequilibrium estimates, anti-HLA antibody data, donor-specific antibody information, and future clinical outcomes need to be obtained. The role of HLA-DQ should not be underestimated, because mismatches and antibodies directed against these loci can be

clinically relevant in kidney transplantation [17] [19] [45] [46].

The bilateral interlaboratory comparison further assessed the reproducibility of the Senegalese HLA typing results. All 40 comparable sample-locus genotypes were concordant between the two laboratories at first-field resolution. This agreement supports the reproducibility of the HLA-A, HLA-B, HLA-C, HLA-DRB1 and HLA-DQB1 assignments in the eight samples evaluated. Nevertheless, this one-off comparison cannot be considered equivalent to a formal external proficiency-testing programme, because it involved a small selected subset, did not document blinding or predefined acceptance criteria, and did not include repeated testing rounds [47] [48]. The result should therefore be interpreted as evidence of first-field interlaboratory agreement in the tested subset rather than as proof of the overall analytical accuracy of the typing platform [49].

5. Conclusion

In conclusion, this study provides a preliminary cohort-level HLA profile for a Senegalese kidney transplantation cohort and identifies recurrent allele groups and locus-specific weaknesses in rSSO typing. Its main value lies in providing local evidence and laying the groundwork for the methodological work still needed. A larger population-based study with high-resolution typing, standardised allele reporting and haplotype analyses is required before these findings can be used as a national HLA reference or translated into population-level transplantation policy.

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Data Availability Statement

The datasets generated and analysed during the current study are available from the corresponding author on reasonable request, subject to institutional and ethical restrictions.

Ethics Statement

This study was conducted in line with the Declaration of Helsinki. The Senegalese National Ethics Committee for Health Research (Comité National d'éthique pour la Recherche en Santé, CNERS) and the Ministry of Health and Social Action reviewed and approved the study protocol (approval No. 00159/MSAS/CNERS/Sec, August 21, 2020). We obtained written informed consent from all participants before enrolment and sample collection.

Use of AI-Assisted Tools

OpenAI ChatGPT and Codex (GPT-5 series) assisted with English-language edit-

ing, sentence restructuring, consistency checking, reference formatting, manuscript organisation, and the preparation of code for figure formatting. They did not generate primary data, assign HLA genotypes, make clinical decisions, or independently analyse participant-level data. The authors critically reviewed and verified all AI-assisted content against the source data, laboratory reports, statistical outputs, and the IPD-IMGT/HLA Database. We used only de-identified or aggregated data. The authors take full responsibility for the accuracy, integrity, and final content of the manuscript.

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Author Contributions

Moussa Ndour and Moustapha Mbow conceived and designed the study. Ndeye Magatte Kebe, Cheikhna Ndiaye, Mairam Mignel Diop, Adama Diaw, Cheikh Dieng and Moussa Ndour performed the experiments. Maria Faye, Baratou Coundoul, Bacary Ba, Ibrahima Lyra Sarr, Babacar Mbodj and Sidy Mouhamed Seck recruited patients and collected clinical data. Moussa Ndour, Cheikhna Ndiaye, Ndeye Magatte Kebe, Marouba Cisse, and Moustapha Mbow analysed and interpreted the data. Moustapha Mbow, Youhanidou Thierno Wone, and Babacar Diao contributed to reagents, materials and analytical tools. Babacar Mbengue, Mame Cheikh Seck, and Serigne Abdou Ahad Mbacke Gueye participated in coordination. Moussa Ndour and Moustapha Mbow drafted the manuscript. Moussa Ndour, Marouba Cisse, Babacar Mbengue, Moustapha Mbow, and Babacar Diao reviewed the manuscript critically for important intellectual content. All authors approved the final version of the manuscript.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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