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ORIGINAL ARTICLE

Baseline Data and HLA Alleles and Haplotypes Diversity and Panel Reactive Antibody in Kidney Transplant Candidates in Southwest China

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SUMMARY

Background: **To investigate the baseline data characteristic, human leukocyte antigen (HLA) polymorphisms, and panel reactive antibody (PRA) in end-stage kidney disease (ESKD) patients awaiting kidney transplantation in Southwest China.**
Methods: **HLA genotyping was performed using the real-time PCR sequence-specific primer. PRA was detected by enzyme-linked immunosorbent assay. The patients' medical records were extracted from the hospital information database.**
Results: **A total of 281 kidney transplant candidates with ESKD were analyzed. The average age was 35.7 ± 13.8 years. There were 61.6% patients had hypertension, 40.2% patients had dialysis ≥ 3 times per week, 47.3% patients had moderate or severe anemia, 30.2% patients with albumin < 35 g/L, 49.1% patients had serum ferritin < 200 ng/mL, 40.5% patients had serum calcium in target range (2.23 - 2.80 mmol/L), 43.4% patients had serum phosphate in target range (1.45 - 2.10 mmol/L), and 93.6% patients with parathyroid hormone > 88.00 pg/mL. In total, 15 HLA-A, 28 HLA-B, 15 HLA-DRB1, and 8 HLA-DQB1 allelic groups were identified. The most frequent alleles for each locus were HLA-A*02 (33.63%), HLA-B*46 (14.41%), HLA-DRB1*15 (21.89%), and HLA-DQB1*05 (39.50%). The most frequent haplotypes were HLA-A*33-B*58-DRB1*17-DQB1*02. A total of 9.60% of patients tested positive for PRAs - Class I or Class II.**
Conclusions: **The data from this study provide some new insights into baseline data, the distribution of HLA polymorphisms, and PRA results in the population of Southwest China. This is of great significance in this region, and indeed in the country as a whole, in comparison with other populations and in the process of organ transplant allocation.**
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KEYWORDS

end-stage kidney disease, baseline data, HLA polymorphism, panel reactive antibody

INTRODUCTION

End-stage kidney disease (ESKD) is a rapidly increasing global health problem, and the burden of health care is a great challenge for patients and governments, especially in developing countries [1]. The incidence and prevalence of ESKD vary between geographic re-

gions and countries, and it is prevalent in Asia [2]. In China, the world's most populous country, the incidence of crude ESKD is much higher than other developed countries [3,4].

Currently, kidney transplantation using organs from relatives or donors is the most cost-effective treatment for ESKD as it reduces costs and improves survival and quality of life [5]. With the rapid increase in the incidence of ESKD, the need for transplants has increased dramatically, resulting in a smaller number of available kidneys than the number of kidney transplant candidates [6]. As of 2017, there are approximately 1 million patients with ESKD in China, and only 52 percent of them have received kidney replacement therapy [3]. The histocompatibility test is the key step in the immune compatibility of donor and recipient in organ transplantation, and is crucial to determine the success of renal transplantation [7]. The human leukocyte antigen (HLA) region, consisting of approximately 3 MB on the short arm of chromosome 6 (6p21.3), determines the compatibility of the transplanted kidney with the recipient [8]. In addition, panel reactive antibodies (PRAs) are anti-HLA antibodies produced in the sera of patients. PRA positive (> 10%) patients are sensitized and at high risk of kidney transplant failure [9].

The genes encoding HLA class I (A, B, and C) and class II (DR, DQ, and DP) molecules are the most polymorphic loci in the human genome, and the frequencies of HLA alleles and haplotypes vary in different regions. Ethnic diversity may complicate the search for the most immune compatible donors. Several studies of HLA allelic diversity have been conducted globally [10-13], including in China [9,14,15]. However, to the best of our knowledge, few studies have investigated HLA allele and haplotype diversity in kidney transplant candidates from Southwest China, especially Guangxi. Therefore, we performed a retrospective analysis of patients awaiting kidney transplantation in Southwest China from 2019 to 2022 to determine the diversity and distribution of HLA alleles and PRA data in this population. We also report data on baseline demographic, clinical, laboratory and therapeutic characteristics of patients with ESKD patients awaiting kidney transplantation. Understanding baseline data and the diversity of HLA alleles and PRA results in this population, may aid the organ transplant allocation process.

MATERIALS AND METHODS

Study subjects

The First Affiliated Hospital of Guangxi Medical University, the largest hospital in Guangxi in southwestern China, was selected to provide representative data. Unrelated patients diagnosed with ESKD and awaiting kidney transplantation at this hospital between December 2019 and June 2022 were enrolled in this study.

Inclusion criteria were the availability of complete HLA class I and II typing data and PRA results. None of the participants came from the same family. Patients' medical records, such as age, gender, BMI and other details, were extracted from the hospital's laboratory and hospital information system databases. The entire study protocol was approved by the Ethics Committee of the First Affiliated Hospital of Guangxi Medical University.

DNA extraction

Whole blood samples were collected and stored at -20℃ until DNA extraction. Genomic DNA was extracted from EDTA anticoagulant whole blood using the QIAamp DNA Blood Mini Kit (QIAGEN GmbH, Hilden, Germany) according to the manufacturer's instructions. The purity of extracted DNA should meet the conditions that OD260/OD280 > 1.6. The extracted DNA was stored at -20℃ until used.

PCR amplification and HLA genotyping

HLA class I (HLA-A and -B) and HLA class II (HLA-DRB1 and -DQB1) genotyping were performed by the real-time PCR sequence-specific primer (PCR-SSP) method using HLA-ABCDRB1DQ Typing test kit (Beijing Genome Precision Technology CO., Ltd.). The ABI 7500 Thermocycler (Applied Biosystems, Foster City, CA, USA) was used for PCR amplification of target DNA. The amplification cycles were set as follows: predenaturation with 5 minutes at 96℃; then five cycles of 25 seconds at 96℃, 5 seconds at 70℃, and 30 seconds at 72℃; and finally 32 cycles of 25 seconds at 96℃, 45 seconds at 65℃, and 30 seconds at 72℃ (fluorescence signal collection). The cyclic threshold (CT) value of the sample was used to judge the amplification result (16 - 28 was positive). The HLA typing results were analyzed by GeneFinderTM HLA typing software.

ELISA screening for panel reactive antibody (PRA)

PRA was detected by enzyme-linked immunosorbent assay (ELISA) using the Lambda Tray TM HLA-Specific IgG Antibody Detection Kit (One Lambda Biotechnology Co., Ltd.) according to the manufacturer's instructions. One Lambda Analysis Software was used to analyze the PRA results.

Statistical analysis

Continuous variable data were described as mean ± standard deviation (SD) or median (25th, 75th), and categorical data were described as percentage. Independent sample *t*-test or chi-squared` test were used to analyze gender differences. HLA-A, -B, -DRB1, and -DQB1 allele frequencies (AF) were calculated by directly counting the frequency of each allele in ESKD patients using the following formula: AF (%) = (n/2N) x 100, where n represents the sum of specific alleles and N represents the total number of individuals. The Arlequin program, version 3.5, was used to test Hardy-Weinberg equilibrium and calculate allele and haplotype frequencies and significant linkage disequilibrium parameters for the HLA-A-B-DRB1-DQB1 loci haplotypes [16]. IBM SPSS Statistics 23.0 software was used for other statisti-

cal calculations.

RESULTS

Baseline data characteristic of study participants

Table 1 showed the demographic characteristics of the study population. A total of 281 ESKD patients awaiting kidney transplantation were retrospectively analyzed. There were 191 males and 90 females with an average age of 35.7 ± 13.8 years (range, 2 - 75 years). Among kidney transplant candidates, males were significantly dominant (68.0%). The mean BMI of all patients was 21.3 ± 3.3 kg/m^2. The average BMI of male patients (21.9 ± 3.6 kg/m^2) was higher than that of female patients (20.02 ± 2.32 kg/m^2). Among the kidney transplant candidates, 76 (27.0%) smoked and 63 (22.4%) drank alcohol. The main ethnic group was Han (71.9%), followed by Zhuang (26.3%).

ESKD causes and complications

Among our patients, 215 patients (76.5%) had hypertensive nephropathy, which is the most common complication of ESKD. Meanwhile, most patients (173 patients (61.6%)) had hypertension. There were 105 cases (37.4%) of coronary artery disease, 80 cases (28.5%) of chronic glomerulonephritis, 25 cases (8.9%) of peripheral vascular disease, 25 cases (8.9%) of hyperlipidemia, 20 cases (7.1%) of diabetic nephropathy, 8 cases (2.8%) of cancer, 4 cases (1.4%) of nervous system diseases, 3 cases (1.1%) of congestive heart failure, and 1 case (0.4%) of psychological disorder.

Dialysis frequency

Dialysis is the most commonly used kidney replacement therapy for ESKD. Among our patients, there were 113 (40.2%) with dialysis ≥ 3 times per week, 61 (21.7%) with dialysis two times per week. The proportion of men on dialysis is higher than that of women.

Blood protein

The median hemoglobin of all patients was 91.20 (74.00, 107.90) g/L (Figure 1A). There were 133 (47.3%) patients with moderate or severe anemia (hemoglobin < 90 g/L), 84 (29.9%) patients with mild anemia (hemoglobin in 90 to 110 g/L), 64 (22.8%) patients with hemoglobin within the target range. For serum albumin (Figure 1B), the median for all patients was 38.20 (34.00, 41.80) g/L. There were 85 (30.2%) patients with albumin < 35 g/L, 84 (29.9%) patients in 35 to 39 g/L and 112 (39.9%) patients with albumin > 40 g/L. As for serum ferritin (Figure 1C), 138 patients (49.1%) had serum ferritin < 200 ng/mL, 104 patients (37.0%) had serum ferritin 200 to 500 ng/mL, and 39 patients (13.9%) had serum ferritin > 500 ng/mL. The level of ferritin in females [149.97 (57.32, 312.20) ng/mL] was lower than that in males [229.30 (88.20, 412.20) ng/mL] (p = 0.013).

Biomarkers of chronic kidney disease - mineral and bone disorders

The median serum calcium of all patients was 2.18 (1.98, 2.36) mmol/L (Figure 1D). One hundred fourteen patients (40.5%) had serum calcium in the target range (2.23 to 2.80 mmol/L), 164 patients (58.4%) had calcium < 2.23 mmol/L, and 3 patients (1.1%) had calcium > 2.80 mmol/L. For serum phosphate (Figure 1E), the median level was 1.82 (1.46, 2.25) mmol/L, and 122 patients (43.4%) had serum phosphate in the target range (1.45 to 2.10 mmol/L), 67 patients (23.84%) had serum phosphate < 1.45 mmol/L, and 92 patients (32.74%) serum phosphate > 2.10 mmol/L. Serum parathyroid hormone was not well controlled in our patients, with a median level of 413.10 (222.10, 639.09) pg/mL, and only 16 patients (5.7%) had serum parathyroid hormone levels in the target range (12.00 to 88.00 pg/mL), while 263 patients (93.6%) had parathyroid hormone > 88.00 pg/mL (Figure 1F).

Hepatitis B and C, HIV infection

The hepatitis B infection rate in our patients was 13.5% and the hepatitis C infection rate was 0.7%. No HIV infection was detected.

Allelic and phenotypic frequencies of HLA-A, -B, -DRB1, and DRQ1 loci

Table 2 listed the allelic and phenotypic frequencies of HLA-A, -B, -DRB1, and DQB1 in the total sample. The HLA-A, -B, and -DRB1 loci were in Hardy-Weinberg equilibrium (p = 0.299, 0.108, and 0.079, respectively). The observed heterozygosity of DQB1 was 0.669, and the expected heterozygosity was 0.769. The observed heterozygosity of DQB1 was significantly different from the expected heterozygosity (p = 0.023), that is, only DQB1 was not in Hardy-Weinberg equilibrium (p = 0.023). In total, 15 HLA-A, 28 HLA-B, 15 HLA-DRB1, and 8 HLA-DQB1 allelic groups were identified in all candidates for kidney transplantation. For the HLA-A locus, the first three frequent alleles were HLA-A*02, -A*11, and -A*24, which occurred at a frequency of 33.63%, 32.92%, and 15.12%, respectively. In the HLA-B locus, the top three most frequent alleles detected were HLA-B*46, -B*13, and-B*60, occurring at the frequency of 14.41%, 13.35%, and 11.57%, respectively. Among the HLA-DRB1 alleles detected in our group, the top three were HLA-DRB1*15, -DRB1*14, and -DRB1*16, occurring at a frequency of 21.89%, 13.70%, and 12.46%, respectively. In the HLA-DQB1 locus, the top three most frequent allele groups were HLA-DQB1*05, -DQB1*07, and -DQB1*06, occurring at the frequency of 39.50%, 17.62%, and 15.48%, respectively.

HLA-A-B-DRB1-DQB1 haplotype frequencies

A total of 1,564 HLA-A-B-DRB1-DQB1 haplotypes were detected using the EM algorithm. The top ten most frequent HLA haplotypes were listed in Table 3. The most three frequent haplotypes were HLA-A*33-B*58-

Table 1. The baseline demographic and laboratory characteristics data of ESKD patients waiting for kidney transplantation.

Variables	All	Gender		p
		Male	Female	
Sample patients [N (%)]	281 (100.0)	191 (68.0)	90 (32.0)	
Demographic parameters				
Age (years, mean ± SD)	35.7 ± 13.8	35.3 ± 14.0	36.49 ± 13.3	0.504
BMI (kg/m^2, mean ± SD)	21.3 ± 3.3	21.9 ± 3.6	20.02 ± 2.32	< 0.001 *
Smokers [N (%)]	76 (27.0)	74 (26.3)	2 (0.7)	< 0.001 *
Drinkers [N (%)]	63 (22.4)	63 (22.4)	0	< 0.001 *
Ethnicity [N (%)]				< 0.001 *
Han	202 (71.9)	138 (49.1)	64 (22.8)	
Zhuang	74 (26.3)	50 (17.8)	24 (8.5)	
Other	5 (1.8)	3 (1.1)	2 (0.7)	
ESKD causes and comorbidities [N (%)]				
Chronic glomerulonephritis	80 (28.5)	54 (19.2)	26 (9.3)	0.915
Diabetic nephropathy	20 (7.1)	18 (6.4)	2 (0.7)	0.028 *
Hypertensive nephropathy	215 (76.5)	143 (50.9)	72 (25.6)	0.344
Hypertension	173 (61.6)	107 (38.1)	66(23.5)	0.005 *
Coronary artery disease	105 (37.4)	70 (24.9)	35 (12.5)	0.717
Congestive heart failure	3 (1.1)	1 (0.4)	2 (0.7)	0.196
Cancer	8 (2.8)	4 (1.4)	4 (1.4)	0.269
Hyperlipidemia	25 (8.9)	14 (5.0)	11 (3.9)	0.179
Neurologic disease	4 (1.4)	2 (0.7)	2 (0.7)	0.438
Peripheral vascular disease	25 (8.9)	21 (7.5)	4 (1.4)	0.072
Psychologic disorder	1 (0.4)	1 (0.4)	0	1.000
Dialysis frequency [N (%)]				
2 times per week	61 (21.7)	34 (12.1)	27 (9.6)	0.021 *
≥ 3 times per week	113 (40.2)	87 (30.9)	26 (9.3)	0.008 *
Laboratory parameters (Median±IQR)				
Hepatitis B infection [N (%)]	38 (13.5)	28 (10.0)	10 (3.5)	
Hepatitis C infection [N (%)]	2 (0.7)	0	2 (0.7)	
HIV infection [N (%)]	0	0	0	
Hemoglobin (g/L)	91.20 (74.00, 107.90)	94.40 (74.00, 108.60)	87.95 (71.78, 105.78)	0.440
Serum albumin (g/L)	38.20 (34.00, 41.80)	38.90 (34.70, 41.80)	37.65 (32.73, 41.73)	0.125
Ferritin (ng/mL)	203.41 (78.75, 381.40)	229.30 (88.20, 412.20)	149.97 (57.32, 312.20)	0.013 *
Serum calcium (mmol/L)	2.18 (1.98, 2.36)	2.18 (1.98, 2.36)	2.17 (1.96, 2.37)	0.678
Phosphate (mmol/L)	1.82 (1.46, 2.25)	1.88 (1.47, 2.42)	1.75 (1.38, 2.20)	0.418
Parathyroid hormone (pg/mL)	413.10 (222.10, 639.09)	412.20 (215.60, 643.60)	429.85 (228.07, 635.56)	0.922
Urea (mmol/L)	22.46 (14.95, 30.72)	23.93 (15.77, 31.24)	20.01 (11.04, 28.77)	0.029 *
Creatinine (μmol/L)	985.00 (598.00, 1,294.50)	1063.00 (754.00, 1,344.00)	840.00 (445.00, 1,198.25)	0.007 *

ESKD end-stage kidney disease, BMI body mass index, SD standard deviation; IQR interquartile range
*** - Differences were significant.**

Table 2. The frequencies of HLA-A, -B, -DRB1, and DRQ1 alleles and phenotype in ESKD patients waiting transplantation.

	HLA- A				HLA- B				HLA-DRB1					HLA-DQB1			
	n	Fa	Fp		n	Fa	Fp		n	Fa	Fp			n	Fa	Fp
A*01	8	0.0142	0.0285	B*07	10	0.0178	0.0356	DRB1*01	4	0.0071	0.0142	DQB1*02		62	0.1103	0.2206
A*02	189	0.3363	0.6726	B*08	1	0.0018	0.0036	DRB1*03	1	0.0018	0.0036	DQB1*03		1	0.0018	0.0036
A*03	9	0.0160	0.0320	B*13	75	0.1335	0.2669	DRB1*04	50	0.0890	0.1779	DQB1*04		30	0.0534	0.1068
A*11	185	0.3292	0.6584	B*18	1	0.0018	0.0036	DRB1*06	1	0.0018	0.0036	DQB1*05		222	0.3950	0.7900
A*13	2	0.0036	0.0071	B*22	1	0.0018	0.0036	DRB1*07	12	0.0214	0.0427	DQB1*06		87	0.1548	0.3096
A*24	85	0.1512	0.3025	B*27	7	0.0125	0.0249	DRB1*08	16	0.0285	0.0569	DQB1*07		99	0.1762	0.3523
A*26	10	0.0178	0.0356	B*35	10	0.0178	0.0356	DRB1*09	43	0.0765	0.1530	DQB1*08		19	0.0338	0.0676
A*29	5	0.0089	0.0178	B*37	6	0.0107	0.0214	DRB1*10	7	0.0125	0.0249	DQB1*09		42	0.0747	0.1495
A*30	5	0.0089	0.0178	B*38	43	0.0765	0.1530	DRB1*11	17	0.0302	0.0605					
A*31	8	0.0142	0.0285	B*39	16	0.0285	0.0569	DRB1*12	63	0.1121	0.2242					
A*32	1	0.0018	0.0036	B*44	2	0.0036	0.0071	DRB1*13	28	0.0498	0.0996					
A*33	52	0.0925	0.1851	B*46	81	0.1441	0.2883	DRB1*14	77	0.1370	0.2740					
A*34	1	0.0018	0.0036	B*48	7	0.0125	0.0249	DRB1*15	123	0.2189	0.4377					
A*68	1	0.0018	0.0036	B*50	1	0.0018	0.0036	DRB1*16	70	0.1246	0.2491					
A*74	1	0.0018	0.0036	B*51	15	0.0267	0.0534	DRB1*17	50	0.0890	0.1779					

Table 2. The frequencies of HLA-A, -B, -DRB1, and DRQ1 alleles and phenotype in ESKD patients waiting transplantation (continued).

HLA- A				HLA- B				HLA-DRB1				HLA-DQB1			
	n	Fa	Fp		n	Fa	Fp		n	Fa	Fp		n	Fa	Fp
				B*52	10	0.0178	0.0356								
				B*53	1	0.0018	0.0036								
				B*54	11	0.0196	0.0391								
				B*55	43	0.0765	0.1530								
				B*56	7	0.0125	0.0249								
				B*57	3	0.0053	0.0107								
				B*58	58	0.1032	0.2064								
				B*60	65	0.1157	0.2313								
				B*61	11	0.0196	0.0391								
				B*62	22	0.0391	0.0783								
				B*72	1	0.0018	0.0036								
				B*75	50	0.0890	0.1779								
				B*76	4	0.0071	0.0142								

n - number of alleles, Fa - allele frequency, Fp - phenotype frequency. The underlined values correspond to the three most frequent alleles in the total sample.

Table 3. The 10 most common HLA-A-B-DRB1-DQB1 haplotype frequencies in the total sample.

No.	HLA haplotype	Frequency
1	A*33-B*58-DRB1*17-DQB1*02	0.0534
2	A*11-B*13-DRB1*15-DQB1*06	0.0430
3	A*02-B*46-DRB1*14-DQB1*05	0.0418
4	A*02-B*46-DRB1*09-DQB1*09	0.0294
5	A*11-B*75-DRB1*12-DQB1*07	0.0244
6	A*02-B*38-DRB1*16-DQB1*05	0.0239
7	A*11-B*60-DRB1*16-DQB1*05	0.0190
8	A*02-B*58-DRB1*17-DQB1*02	0.0160
9	A*11-B*46-DRB1*09-DQB1*09	0.0151
10	A*02-B*38-DRB1*15-DQB1*05	0.0151

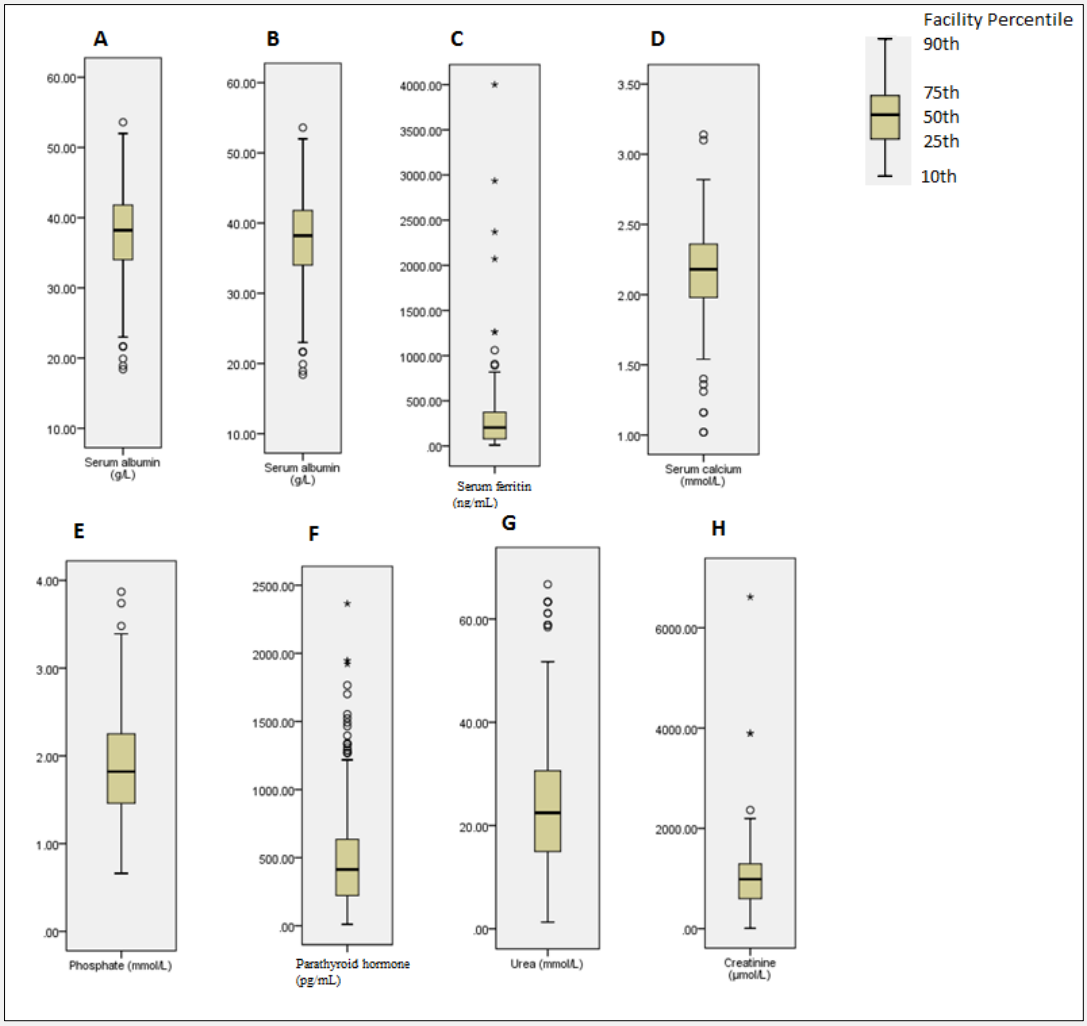

Figure 1. The distribution of laboratory parameters of ESKD patients.

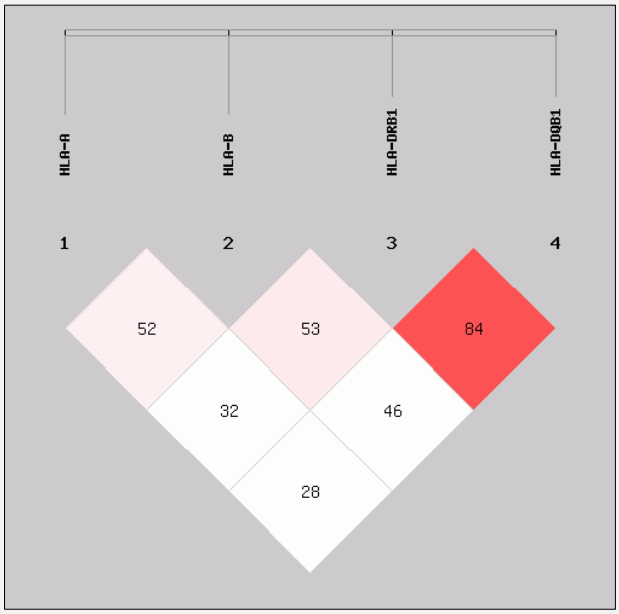

Figure 2. The linkage disequilibrium parameters of HLA HLA-A, -B, -DRB1, and DRQ1 loci.

DRB1*17-DQB1*02, HLA-A*11-B*13-DRB1*15-DQB1*06, and HLA-A*02-B*46-DRB1*14-DQB1*05. Those haplotypes have frequencies of 5.34%, 4.30% and 4.18%, respectively. The linkage disequilibrium parameters for all pairs of four HLA loci were shown in Figure 2. All pairs of loci were in linkage equilibrium.

Analysis of PRA results in ESKD patients

Among the 281 patients, 22 (7.83%) were positive for PRA-Class I, 14 (4.98%) were positive for PRA-Class II, and 9 (3.20%) were positive for both PRA-Class I and II. Among the 191 male patients, 179 (93.72%) were PRA negative and 12 (6.28%) were PRA positive. Among the 90 females, 73 (81.11%) were negative and 17 (18.89%) were positive for PRAs. There was a statistically significant difference in PRA generation between men and women ($\chi^2 = 10.504$, $p = 0.001$).

DISCUSSION

In this study, we report baseline demographic, clinical, therapeutic, and laboratory characteristics data, as well as data on the diversity and distribution of HLA alleles and PRA in ESKD patients awaiting kidney transplantation in southwest China. Several HLA diversity studies have been carried out to investigate the genetic susceptibility of HLA systems to ESKD in different regions of China [9,14,15,17,18]. However, to the best of our knowledge, no study has examined HLA allele and haplotype diversity in kidney transplant candidates in southwest China, especially in Guangxi Zhuang Autonomous Region. This observational and retrospective study, conducted in a representative study population in southwest China, provides some new insights that are more detailed than available data and may contribute to the organ transplant assignment process in this region. The leading cause of ESKD in Chinese is chronic glomerulonephritis, followed by diabetic nephropathy and hypertensive nephropathy [3]. Of our patients, 76.5% had hypertensive nephropathy, 61.6% had hypertension, 28.5% had chronic glomerulonephritis, and 7.1% had diabetic nephropathy. In a report on first-tier Chinese cities, the distribution of primary ESKD causes assigned was different: compared to Beijing and Guangzhou, Shanghai had more patients with chronic glomerulonephritis and fewer patients with diabetic nephropathy [19]. Our results are somewhat inconsistent with those in other parts of China.

The number of ESKD patients is growing much faster than the number of kidney transplants performed worldwide each year. While kidney transplantation is the best treatment for eligible patients with ESKD, dialysis is the dominant treatment in most countries, with hemodialysis being the most common modality [6]. However, there were approximately 1 million patients with ESKD in China in 2017 and only 52 percent of them received kidney replacement therapy, including peritoneal dialysis, hemodialysis and kidney transplantation [1]. Among our patients, the proportion of dialysis ≥ 3 times a week

was 40.2%, and the proportion of dialysis twice a week was 21.7%. The overall rate for dialysis patients was 61.92 percent.

Kidney anemia is a concern in hemodialysis patients. Data from the Dialysis Outcomes and Practice Patterns Study (DOPPS) indicate a positive association between the standard deviation of facility-level hemoglobin and patient mortality [20]. A substantial proportion of our patients had low hemoglobin concentrations: 47.3% of patients had moderate to severe anemia at a hemoglobin concentration < 90 g/L and 29.9% of patients had mild anemia at a hemoglobin concentration of 90 to 110 g/L. We also found that a considerable proportion of patients had low serum albumin levels: 30.2% of patients had serum albumin < 35 g/L, 29.9% of the patients had serum albumin between 35 to 39 g/L. Serum albumin is considered a nutritional marker and a negative acute phase reactive protein. Previous studies have shown that low serum albumin was an independent predictor of long-term mortality in patients with ESKD [21].

At the same time, we found that serum levels of calcium, phosphorus and parathyroid hormone in ESKD patients were not ideal: 58.4% of patients had calcium below the target range, 23.84% had serum phosphorus below the target range, 32.74% had serum phosphorus above the target range, and 93.6% had parathyroid hormone above the target range. Many studies have shown that increased and decreased serum levels of calcium, phosphorus, and parathyroid hormones were associated with increased all-cause mortality [22,23]. Therefore, we should pay more attention to early integrated treatment and early intervention in ESKD patients to reduce the mortality of patients.

In China, clinical kidney transplantation is facing great challenges due to the largest polymorphism in the HLA genetic system and a shortage of donors [24]. In this retrospective study, a total of 15 HLA-A, 28 HLA-B, 15 HLA-DRB1, and 8 HLA-DQB1 alleles were identified in all kidney transplant candidates with ESKD in Guangxi, southwest China. In this study, we observed that the observed heterozygosity of DQB1 was significantly different from the expected heterozygosity ($p = 0.023$), that is, only DQB1 was not in Hardy-Weinberg equilibrium. This heterozygosity was most likely due to the small sample size. In addition, our sample was composed of ESKD patients, namely non-healthy individuals, and this deviation from Hardy-Weinberg ratio might also be related to the pathological condition itself or to genetic causes [11].

The top three alleles with the highest frequency in each of the four loci were HLA-A*02, -A*11, and -A*24; HLA-B*46, -B*13, and-B*60; HLA-DRB1*15, -DRB 1*14, and -DRB1*16; HLA-DQB1*05, -DQB1*07, and -DQB1*06, respectively. The distribution of HLA genotypes in the present study is generally consistent with that in Hunan Province, Central China. In their study, the top three alleles with the highest frequencies were HLA-A*11, -A*02, and -A*24; HLA-B*60, -B*46, and -B*13, respectively [9]. However, the alleles were different from those of the Han population in Dalian, North China, where the top three alleles with the highest frequency in these three locus were found to be HLA-A*02, -A*11, and -A*24; HLA-B*40, -B*13, and -B*15; and HLA-DRB1*12, -DRB1*09, and -DRB1*04, respectively [14]. Our results were also quite different from those observed in southern Brazil, where the most common allelic genome for each HLA locus were HLA-A*02, HLA-B*44, and HLA-DRB1*13, and the most frequent haplotypes were HLA-A*01-B*08-DRB1*03 [11]. These contradictory results in different areas of China and global populations may be caused by different effects in different ethnic groups, small sample sizes, and so on.

CONCLUSION

In conclusion, data from this study provided some new insights into clinical, treatment and laboratory characteristics data, frequencies of HLA-A, HLA-B, HLA-DRB1, HLA-DQB1 alleles, phenotypes and haplotypes, and PRA results in a population of kidney transplant candidates in southwest China. These allowed us to compare with other populations and aid the process of organ allocation for transplantation in our region and nationally.

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Declaration of Interest:
The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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