



# Immunologic Characteristics of Mongolian Patients Receiving Kidney Transplantation in a Single Center in Korea

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## ABSTRACT

**Background.** Among foreigners undergoing kidney transplantation (KT) in Korea, Mongolians are the most common, and most of these cases are conducted at our center. We report the immunologic characteristics and clinical outcomes of these patients.

**Methods.** Consecutive Mongolian patients who underwent KT from September 2009 to August 2017 in our center were retrospectively analyzed. Pre- and post-transplant HLA antibody status and clinical data of the Mongolian patients were collected and compared with the Korean patients who underwent living donor KT during the same period.

**Results.** Sixty-two Mongolian and 85 Korean patients received KT and were followed up for 20.9 and 50.8 months ( $P = .01$ ), respectively. Before transplantation, 17.7% of the Mongolian patients and 7.1% of the Korean patients were highly sensitized ( $P = .05$ ). The patients were monitored consistently throughout the entire post-transplant period. Follow-up loss occurred in some cases. Of the patients, 32 Mongolian patients and 79 Korean patients were monitored for post-transplant HLA antibodies at any time point. Estimated glomerular filtration rates were comparable between Mongolian and Korean patients at 1 month (77.1 vs 71.5 mL/min/1.73m<sup>2</sup>,  $P = .21$ ) and 1 year (64.6 vs 68.7 mL/min/1.73m<sup>2</sup>,  $P = .25$ ) after transplantation but tended to be different at 3 years (57.2 vs 67.3 mL/min/1.73m<sup>2</sup>,  $P = .06$ ) and 5 years (56.9 vs 73.1 mL/min/1.73m<sup>2</sup>,  $P = .04$ ) post transplant.

**Conclusions.** Mongolian patients undergoing KT in Korea were often highly sensitized. Mean follow-up time was short and follow-up loss was common in Mongolian patients compared with Korean patients. Cautious follow-up is needed for foreigner transplant recipients, especially for those at high-risk immunologically, to achieve better outcomes.

**C**HRONIC kidney disease (CKD) is common in Northeast Asia, but the strategies to manage the disease are diverse among countries. A recent paper reports that the prevalence of CKD among the general adult population is 13.9% in Mongolia, which is the highest among Northeast Asian countries [1]. The incidence of treated end-stage renal disease (ESRD) is reported to be 226.6 per million population per year, but the prevalence of ESRD is not even known for this country [2]. It is speculated that the prevalence of renal replacement therapy will double in 10 years, but the coverage and quality of the dialysis registries still need to be improved in Mongolia [3].

Although patients with ESRD can be maintained on dialysis, kidney transplantation (KT) is the best treatment

option to enhance the quality of life of the patients. The need for KT is especially high in Mongolia since CKD is common, but functioning dialysis units are limited. However, global inequalities in access to transplant surgery exist, and the number of KT cases conducted in Mongolia are reported to be limited [4]. Transfer systems among

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neighboring countries can be an alternative for patients with a living donor.

Among foreigners undergoing KT in Korea, Mongolians are the most common, and most of these cases are conducted at our center [5]. We report the immunologic characteristics and clinical outcomes of Mongolian patients receiving KT in a single center in Korea.

## METHODS

Medical records of consecutive Mongolian patients who underwent KT from September 2009 to August 2017 in Korea University Anam Hospital were retrospectively analyzed. All patients received transplants from living donors, which were all approved by the Korea Network for Organ Sharing. The Korea Network for Organ Sharing strictly evaluates the relationship between the donor and the recipient to prevent any kind of organ trafficking.

Pre- and post-transplant anti-HLA antibody status, post-transplant estimated glomerular filtration rates (eGFRs), biopsy results for rejection, and graft survival status for each patients were collected. Anti-HLA antibody testing was performed with Luminex assays (Immucor Transplant Diagnostics, Norcross, GA, United States) using class I and class II panel reactive antibody identification kits, and highly sensitized patients were defined as having a maximal mean fluorescent intensity of higher than 10,000. eGFR was calculated according to the chronic kidney disease epidemiology collaboration equation [6]. Rejection was diagnosed according to the Banff 2009, 2011, and 2013 classifications [7–9]. Last follow-up was defined as the last visit to the center or patient death at the center. Medical records were analyzed 1 year after the last KT was conducted. Data were compared with those of the Korean patients who underwent living donor KT during the same period.

Statistical analysis was performed using IBM SPSS Statistics 20 (SPSS Inc, Chicago, IL, United States). Fisher's exact and Mann-Whitney test were used for comparison of categorical variables and continuous variables between groups, respectively. For all analyses, *P* values < .05 were considered statistically significant.

## RESULTS

Sixty-two Mongolian and 85 Korean patients received living donor KT during the period studied. After transplantation, Mongolians were followed up for a mean time of 20.9 months, which was significantly shorter than that of Koreans, which was 50.8 months (*P* = .01). Twenty of the 62 (32.3%) Mongolian patients were sensitized before transplantation with positive anti-HLA antibodies, and of the sensitized patients, 11 (17.7%) were highly sensitized with a maximal mean fluorescent intensity level of greater than 10,000. For the Korean patients, 22 of the 85 (25.9%) were sensitized, and 6 (7.1%) were highly sensitized pretransplant. The proportion of sensitized patients were similar between the Mongolian and Korean patients (*P* = .40), but Mongolian patients were more often highly sensitized (*P* = .05).

Thirty-two of the 62 Mongolian patients (51.6%) were monitored for post-transplant HLA antibodies at any time point; this proportion was significantly lower than that of the Korean patients (79 of 85, 92.9%, *P* < .01) during the same

period. Seven (21.9%) Mongolian patients developed de novo HLA antibodies, of whom 6 (18.8%) had DQ antibodies, and 14 (17.7%) Korean patients developed de novo HLA antibodies, of whom 9 (11.4%) had DQ antibodies. The proportion of patients who developed de novo HLA antibodies and DQ antibodies were not different between the 2 groups (*P* = .61 and *P* = .30, respectively).

Short-term eGFRs were comparable between Mongolian and Korean patients at 1 month (77.1 mL/min/1.73m<sup>2</sup> vs 71.5 mL/min/1.73m<sup>2</sup>, *P* = .21) and 1 year (64.6 mL/min/1.73m<sup>2</sup> vs 68.7 mL/min/1.73m<sup>2</sup>, *P* = .25) after transplantation, but long-term eGFRs tended to be different at 3 years (57.2 mL/min/1.73m<sup>2</sup> vs 67.3 mL/min/1.73m<sup>2</sup>, *P* = .06) and 5 years (56.9 mL/min/1.73m<sup>2</sup> vs 73.1 mL/min/1.73m<sup>2</sup>, *P* = .04) after transplantation. Antibody-mediated rejection and graft failure occurred in 5 (8.1%) and 4 (6.5%) Mongolian patients and 9 (10.6%) and 2 (2.4%) Korean patients, respectively, which were not significantly different between the 2 groups (*P* = .61 and *P* = .21, respectively) (Table 1).

## DISCUSSION

Despite increasing demands, data on KT conducted in Mongolia is limited. A report of 34 Mongolians who received KT in a single center for 3 years from August 2006 was published [4]. A kidney transplant team that was trained at different international centers was formed in Mongolia,

**Table 1. Characteristics and Outcome of Mongolian Patients Who Underwent Kidney Transplantation in Our Center in Comparison with Korean Patients During the Same Period**

	Mongolians	Koreans	<i>P</i> Value
Patients analyzed			
Number	62	85	
Mean follow-up time, mo	20.9	50.8	.01
Pretransplant immunologic status, No.			
Sensitized	20	22	.40
Highly sensitized (HLA antibody maximal MFI > 10,000)	11	6	.05
Post-transplant immunologic status, No.			
Patients monitored for post-transplant HLA antibodies	32	79	< .01
De novo HLA antibodies	7	14	.61
De novo HLA-DQ antibodies	6	9	.30
Post-transplant eGFR, mean, mL/min/1.73m <sup>2</sup>			
1 mo	77.1	71.5	.21
1 y	64.6	68.7	.25
3 y	57.2	67.3	.06
5 y	56.9	73.1	.04
Transplant outcome			
Antibody-mediated rejection	5	9	.61
Graft failure	4	2	.21

Abbreviations: eGFR, estimated glomerular filtration rate; MFI, mean fluorescence intensity.

and the first transplant took place in August 2006. One-year patient and graft survival were reported to be 91% and 82%, respectively, which were inferior to results published by main centers. The authors considered that the nomadic lifestyle of Mongolians, which leads to remote geographic location of the patients, was one of the main causes of this result. Also, unavailability of some immunologic tests and treatment strategies could be the reasons, in addition to the learning curve of the transplant team.

A transfer system among neighboring countries has been suggested as an alternative. An extensive study on foreigner transplants in Korea has been performed recently [5]. Between 2006 and 2016, 174 foreign patients underwent KT in Korea, and the Mongolians were the most common group, consisting of 32% of the foreigner KT recipients. Overseas KT program for Mongolian patients has been operated by our center since 2009, and the 3.5-year experience has been published [10]. Thirty-three Mongolian patients underwent KT, and mean post-transplant follow-up time was 12.9 months. Mean eGFR at 1, 6, and 12 months after KT were 88.2 mL/min/1.73 m<sup>2</sup>, 67.5 mL/min/1.73 m<sup>2</sup>, and 63.9 mL/min/1.73 m<sup>2</sup>, respectively, in which the renal function of the Mongolian patients was not significantly different from that of the Korean patients during the same period.

Mongolian patients in this study were more often highly sensitized compared with the Korean patients. HLA is highly polymorphic and is a strong immunogen. In contrast to anti-ABO antibodies of red blood cells, anti-HLA antibodies are not naturally present and are produced by pregnancy, transfusion, or transplantation [11]. This is an obstacle in KT because it can cause a humoral immune reaction, which can lead to rejection [12]. The Luminex assay, which is highly sensitive, was used to detect anti-HLA antibodies in this study [13]. Although the significance of the antibodies with low mean fluorescent intensities has not been clearly defined yet, high mean fluorescent intensities are known to influence clinical outcome [14]. Blood transfusions in CKD patients and the fecundity of the Mongolians may explain the high frequency of highly sensitized patients [15–20].

Short-term eGFRs at 1 month and 1 year post transplant were shown to be comparable among Mongolian and Korean patients in this study. A previous study similarly revealed that eGFRs at 1, 6, and 12 months after KT in Mongolian patients were not significantly different from those of Korean patients [10]. However, long-term eGFRs of Mongolian patients were found to be inferior to those of Korean patients at 3 and 5 years after transplantation. Frequent high-risk patients, inadequate monitoring due to long follow-up intervals, and far distance causing common follow-up loss of the Mongolian patients could have caused the difference in the long-term results between the 2 groups. Also, failure to achieve therapeutic drug levels of immunosuppressive drugs, such as tacrolimus, due to the difficulty of drug monitoring and failure to maintain consistent drug levels due to irregular medications caused by uneven supply

of the immunosuppressants could also be considered as the cause [4]. Thus, periodic, regular follow-up, including renal function monitoring and appropriate instructions for drug administration, should be conducted in the transplanted patients in Mongolia locally. These efforts may also lead to better outcomes in patients transplanted in Mongolia. Until self-sufficiency for organ transplantation is achieved, undergoing KT in neighboring countries with stable environments can still be an alternative.

## CONCLUSIONS

Mongolian patients undergoing KTs in Korea were often highly sensitized. Mean follow-up time was short, and follow-up loss was common in Mongolian patients compared with Korean patients. Cautious follow-up is needed for the transplantation in foreigners, especially for those that are at high-risk immunologically, to achieve better outcomes.

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