Nephrol Dial Transplant (2012) 27: 2588–2593
doi: 10.1093/ndt/gfr628
Advance Access publication 9 February 2012

Fewer pre-emptive renal transplantations and more rejections in immigrant children compared to native Dutch and Belgian children

Wilma F. Tromp[1], Karlien Cransberg[2], Johanna H. van der Lee[3], Antonia H. Bouts[1], Laure Collard[4], Rita Van Damme-Lombaerts[5], Nathalie Godefroid[6], Koenraad J. Van Hoeck[7], Linda Koster-Kamphuis[8], Marc R. Lilien[9], Ann Raes[10], Nadejda Ranguelov[11] and Jaap W. Groothoff[1]

[1]Department of Paediatric Nephrology, Emma Children's Hospital Academic Medical Centre, Amsterdam, The Netherlands, [2]Department of Paediatric Nephrology, Sophia Children's Hospital Erasmus Medical Centre, Rotterdam, The Netherlands, [3]Department of Paediatric Clinical Epidemiology, Emma Children's Hospital Academic Medical Centre, Amsterdam, The Netherlands, [4]Department of Paediatric Nephrology, University Hospital Liege, Liege, Belgium, [5]Department of Paediatric Nephrology, University Hospital Leuven, Leuven, Belgium, [6]Department of Paediatric Nephrology, University Louvain, Brussels, Belgium, [7]Department of Paediatric Nephrology, University Hospital Antwerp, Antwerp, Belgium, [8]Department of Paediatric Nephrology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands, [9]Department of Paediatric Nephrology, Wilhelmina Children's Hospital University Medical Centre Utrecht, Utrecht, The Netherlands, [10]Department of Paediatric Nephrology, University Hospital Ghent, Ghent, Belgium and [11]Department of Paediatric Nephrology, Hospital Universitaire des Enfants Reine Fabiola, Brussels, Belgium

Correspondence and offprint requests to: Wilma F. Tromp; E-mail: W.F.Tromp@amc.uva.nl

Abstract

Background. In the Netherlands and Belgium, an increasing number of children who have end-stage renal disease (ESRD) are of non-Western origin. We analysed renal transplantation practices and outcome for immigrant ESRD children as compared to native children in both countries.

Methods. All Dutch and Belgian children aged <19 years who received their first renal transplantation between 1 September 2007 and 1 January 2011 were included. Therapy characteristics and outcomes were registered prospectively on a 3-monthly basis. Immigrants were defined as children of whom one or both parents had been born outside Western European countries. Multivariable Cox regression analysis was used to quantify the hazard ratio for acute rejection.

Results. One hundred and nineteen first renal transplant recipients were included, of which 41 (34%) were immigrants. Median [range] follow-up time of transplantation was 18 [2–28] months. Compared to native children, immigrants had pre-emptive transplantations (15 versus 32%, $P = 0.040$) and transplantations with a kidney from a living donor less often (24 versus 59%, $P < 0.001$). Survival analysis in 96 children with at least 3 months of follow-up showed an increased risk for acute rejection in immigrants adjusted for donor source, duration of dialysis and number of HLA mismatches on the DR locus [hazard ratio (95% confidence interval) 2.5 (1.1–5.9)].

Conclusions. Immigrant children receive fewer pre-emptive and living donor transplantations compared to native children. After transplantation, immigrant children are at higher risk for acute rejection irrespective of the mode of transplantation.

Keywords: acute rejection episode; children; ethnicity; immigrants; pre-emptive transplantation

Introduction

In the Netherlands and Belgium, a considerable proportion of the children with end-stage renal disease (ESRD) are of non-Western origin. Not much is known about the care and health outcomes for this specific group of patients, despite the fact that the total number of non-Western immigrants in these two small countries is growing [1, 2]. In the Netherlands, the proportion of non-Western immigrants has grown from 9 to 11% of the total population in the last decade, which implies an expansion of this group with >0.5 million people on a total population of 16.6 million people [1]. Therefore, the interest in the specific needs of and care for this group is rising. Immigrants from non-Western origin in the Netherlands are reported to receive less appropriate health care compared to native inhabitants [3]. In a study on asthma in children, ethnicity and insufficient comprehension of the Dutch language appeared to be important risk factors for uncontrolled asthma in these children [4].

Renal transplantation (Tx) in children is a complex and intensive therapy. The success of the Tx depends highly on a good mutual understanding between patient and physician and adherence to the therapy. Also, the therapeutic

regimes used are predominantly based on clinical research in Western patients. We hypothesized that cultural as well as biological differences between immigrant and native patients might influence practice and clinical course of renal Tx in non-Western immigrant children.

We therefore investigated the frequency, characteristics and outcome of renal Tx in immigrant children compared to native Dutch and Belgian children.

Materials and methods

Patients

Data were registered prospectively on all children aged <19 years who received their first renal transplantation between 1 September 2007 and 1 January 2011 in the Netherlands and Belgium. These data were collected as part of the RICH-Q project (Renal Insufficiency therapy in Children—Quality assessment and improvement), which aims to improve the quality of care for children with ESRD by collaboration between all four Dutch and five Belgian centres where children with ESRD are cared for [5]. In three Belgian centres, the inclusion period of the RICH-Q project started in January and May 2008, respectively, due to a delay in ethical approval by the local ethical committees. Follow-up data were available until 1 January 2011 or until transition to adult care. Acute rejection episodes (AREs) or graft failures occurring after transition to the adult department are therefore not included in this study. Approval was obtained from the ethical boards of all participating hospitals and written informed consent from all parents of the participants and/or the participants themselves.

Data collection procedures

Data were collected from the medical records of the patients by trained local research nurses or by the participating paediatric nephrologists. The following data were recorded: age, gender, primary cause of ESRD, waiting time on dialysis before the first Tx, country of birth from child and parents, race and Tx date. Primary causes of ESRD were classified retrospectively into five categories; glomerulopathy, haemolytic uraemic syndrome, urinary tract malformation, dysplasia and other. The Tx characteristics we recorded were type of Tx (pre-emptive or after a period of dialysis), type of donor [deceased donor (DD) or living donor (LD)], relationship of LD, donor age, number of HLA mismatches, cold ischaemia time and prophylactic immunosuppressive treatment. The total number of HLA mismatches was calculated by adding up mismatches on A, on B and on DR per Tx. The collected follow-up data included estimated glomerular filtration rate (eGFR), suspected non-compliance, graft failure and ARE with for each episode: biopsy result, type of rejection and treatment. Rejection-free survival was calculated per patient in months from the Tx date until the first ARE or until the end of the follow-up period. As a surrogate outcome for graft failure, we also looked at differences in eGFR between 3 and 12 months after Tx. For the calculation of eGFR, we used the updated version of the Schwartz formula: eGFR (mL/min/1.73m^2) = k (height in cm)/serum creatinine in mg/dL, with k being an age-dependent variable [6]. Children whose eGFR declined >10 mL/min/1.73m^2 between 3 and 12 months after Tx were classified as 'deteriorated'. Non-compliance was recorded in the RICH-Q registry by searching the medical charts for notifications on medication use and by asking the treating paediatric nephrologist. If indicated, we considered that patient as 'suspect for non-compliance'.

Definitions

Immigrants were defined as children of whom one or both parents had been born in non-Western European countries. Natives were defined as children from Western European origin. AREs included biopsy-proven as well as clinically suspected episodes, defined by the use of high-dose steroids or antibody treatment. However, if rejection treatment was started but the biopsy result showed no sign of rejection, we did not count that episode as ARE. Graft failure was defined as a situation of failure of the transplanted kidney, which necessitated the use of another mode of chronic renal replacement therapy.

Statistical analysis

For comparisons of categorical variables between immigrant and native patients, we used the chi-square test or, in the case of small expected cell counts, Fisher's exact test. Student's T-test or Mann–Whitney U-test was used for continuous variables when appropriate. Kaplan–Meier survival analysis was used to analyse rejection-free survival. Cox regression was used to investigate possible confounding factors. If addition of a possible confounder to the model resulted in a change of >10% in the regression coefficient β of the primary determinant (immigrant status), this variable was kept in the model. All analyses were performed using SPSS 18.0 for Windows statistical software.

Results

Between 1 September 2007 until 1 January 2011, 119 children received their first transplantation, 78 native children and 41 immigrant children. The primary causes of ESRD were comparable between the groups. These and

Table 1. Characteristics of included native and immigrant children[a]

	Total n = 119	Native n = 78 (66)	Immigrant n = 41 (34)
Male	68 (57)	42 (54)	26 (63)
Origin		Netherlands: 58 Belgium: 18 Germany: 1 Luxembourg: 1	Morocco: 8 Turkey: 9 Surinam: 7 Asia: 4 Dutch Antilles/Caribbean: 2 Africa (other): 7 Middle East (other): 4
Race			
Caucasian	97 (82)	77 (99)	20 (49)
Black	13 (11)	0	13 (32)
Asian	3 (2)	0	3 (7)
Mixed	6 (5)	1 (1)	5 (12)
Primary cause of ESRD			
Glomerulopathy	31 (26)	20 (26)	11 (27)
Haemolytic uraemic syndrome	4 (3)	3 (4)	1 (2)
Urinary tract malformation	22 (19)	15 (19)	7 (17)
Dysplasia	39 (33)	28 (36)	11 (27)
Other	23 (19)	12 (15)	11 (27)

[a]Data are presented as n (percentage).

other characteristics of the immigrant and native groups are shown in Table 1. An overview of pre-emptive versus post-dialysis transplantation and donor sources (LD versus DD) is provided in Table 2. From the 119 transplantations, 56 (47%) were performed with a kidney from an LD (24% LD in immigrants versus 59% in natives, P < 0.001, Table 3). LD was mostly performed with a kidney from one of the child's parents (80% of all LD Tx in immigrants versus 83% in natives). Immigrant children had a lower rate of pre-emptive Tx, spent more time on dialysis before Tx, received grafts from younger donors and the median cold ischaemia time was longer (Table 3). A subgroup analysis in children who were transplanted with a kidney from a DD (shown in Table 4) showed no statistically significant differences between months on dialysis before Tx, donor age, median cold ischaemia time and total number of HLA mismatches. Mismatches on the DR locus were significantly more often present in transplantations with a kidney from a DD in the immigrant group (81% in immigrant children versus 56% in native children, chi-square test, P = 0.038, Table 4).

Table 2. Description of types of transplantation (pre-emptive versus post-dialysis transplantation and donor source)

	Total	Immigrant	Native
Pre-emptive transplantation			
LD	29	5	24
DD	2	1	1
Transplantation post-dialysis			
LD	27	5	22
DD	61	30	31
Total	119	41	78

Outcome

Of 99 children, 68 native and 31 immigrant children, follow-up data were available for at least 3 months. In 24 of these patients (24%), one or more ARE occurred after a period of (median [range]) 18 [2–28] months: in 13/68 natives (19%) and in 11/31 immigrants (35%). Five children (one native child and four immigrants) had two AREs. Twenty-two of all 29 AREs (76%) were biopsy-proven, in the other 7 AREs (24%), treatment was given without taking a biopsy. Seventeen AREs were biopsy-proven tubular-interstitial rejections (59%), 4 were biopsy-proven vascular rejections (14%) and in 1, the biopsy showed a combined tubular-interstitial/vascular rejection (3%). The seven AREs for which treatment was given without taking a biopsy, were assumed to be tubular-interstitial rejections, based on the anti-rejection therapy that was given to the patients and the response to that therapy. There were no significant differences in type of rejections between immigrant and native children (P = 0.765).

Kaplan–Meier analysis (Figure 1) showed a significantly longer rejection-free survival for native children (log-rank test P = 0.032). The hazard ratio (95% confidence interval) for immigrant status resulting from the univariable Cox regression analysis was 2.4 (1.1–5.3). Adjustment for potential confounders, such as donor source (DD or LD), duration of dialysis prior to transplantation and one or more

Table 3. Comparison of transplantation characteristics[a]

	Tx total $n = 119$	Tx in native children $n = 78$	Tx in immigrants $n = 41$	P*
Follow-up time, months[b]	18 [2–28]	18 [2–25]	17 [3–28]	0.371[c]
Age at transplantation, years[b]	11.5 [1.6–19.1]	11.7 [2.0–19.1]	11.3 [1.6–17.3]	0.907[c]
Pre-emptive Tx	31 (26)	25 (32)	6 (15)	**0.040**[d]
LD Tx	56 (47)	46 (59)	10 (24)	**0.001**[d]
Relationship of LD				
Parent	46 (82)	38 (83)	8 (80)	
Grandparent	7 (12)	6 (13)	1 (10)	
Uncle/aunt	1 (2)	1 (2)	0	
Second cousin	1 (2)	1 (2)	0	
No relation	1 (2)	0	1 (10)	
Months on dialysis before Tx[b,e]	17 [1–99]	14 [1–67]	26 [3–99]	**0.008**[c]
HLA mismatches (A, B, DR)[f]	2.4 ± 1.1	2.3 ± 1.2	2.7 ± 1.0	0.065[g]
≥1 mismatch on DR	81 (68)	49 (63)	32 (78)	0.090[d]
Donor age, years[b]	43 [2–68]	45 [7–68]	36 [2–60]	**0.001**[c]
Paediatric donor (<10 years)	8 (7)	3 (4)	5 (12)	0.084[c]
Initial immunosuppressive prophylaxis				
Cyclo + Basiliximab + MMF + Cort	81 (68)	50 (64)	31 (76)	
TAC + Basiliximab + MMF + Cort	24 (20)	17 (22)	7 (17)	
Basiliximab + MMF + Cort	7 (6)	4 (5)	3 (7)	
Other combinations	7 (6)	7 (9)	0	

[a]Data are presented as *n* (percentage). Cyclo, cyclosporine; TAC, tacrolimus; Cort, corticosteroids; MMF, mycophenolate mofetil.
[b]Data are presented as median [range].
[c]Mann Whitney *U*-test.
[d]Chi-square test.
[e]Eighty-eight patients were transplanted after a period of Dx; 53 native children and 35 immigrant children.
[f]Data are presented as mean ± SD.
[g]Independent samples *T*-test.
[h]Three native children and one immigrant child had two mismatches on Dr.
*p values < 0.05 are presented in bold.

Table 4. Comparison of transplantation characteristics in 63 transplantations (Tx) with a kidney from a DD[a]

	Tx total $n = 63$	Tx in native children $n = 32$	Tx in immigrants $n = 31$	P
Months on dialysis before Tx[b,c]	18 [1–99]	18 [1–67]	26 [3–99]	0.119[d]
HLA mismatches (A, B, DR)[e]	2.7 ± 1.1	2.7 ± 1.3	2.8 ± 1.0	0.612[f]
≥1 mismatch on DR	43/63 (68)	18/32 (56)	25/31 (81)	**0.038**[g]
Donor age, years[b]	38 [2–62]	40.5 [7–62]	31 [2–58]	0.277[d]
Cold ischaemia time, hours[b]	14 [4–27]	14 [4–26]	15 [5–27]	0.938[d]

[a]Data are presented as *n* (percentage).
[b]Data are presented as median [range]
[c]Two patients were transplanted pre-emptively with a DD and 61 patients were transplanted with a DD after a period of Dx; 31 native children and 30 immigrant children.
[d]Mann–Whitney *U*-test.
[e]Data are presented as mean ± SD.
[f]Independent samples *T*-test.
[g]Chi-square test.

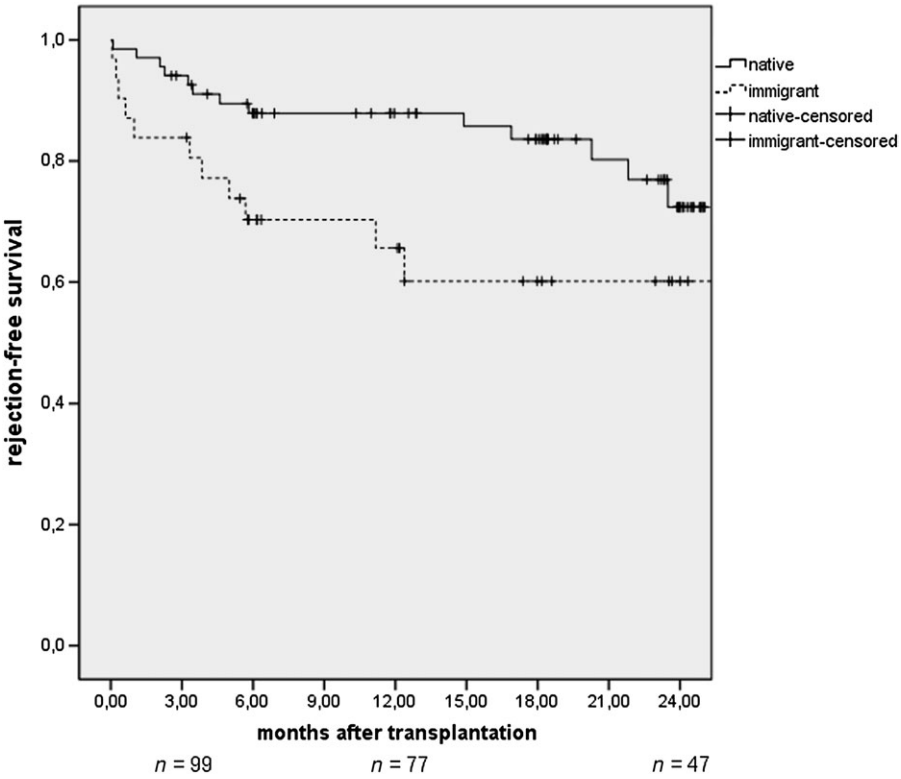

Fig. 1. Kaplan–Meier curve of rejection-free survival in immigrant children compared to native (Western European) children, log-rank test P = 0.032 ($n = 99$ children with >3-month follow-up data on AREs).

HLA mismatches on the DR locus, did not change the effect of immigrant status (Table 5). Graft failures occurred in 2 of 78 Tx (3%) in native children and in 5 of 41 Tx (12%) in immigrants. Five of the seven graft failures occurred within a week after Tx, mainly caused by surgical complications. Only two graft failures, in immigrant children, occurred later during follow-up, after 4 and 24 months, respectively. These two immigrant children with late graft failure had both suffered at least one period of ARE. All other graft failures were not preceded by a period of ARE. Three months after Tx median [range], eGFR was 63 [0–166] mL/min/1.73m^2 in native children ($n = 66$ native children with data to calculate eGFR) and 58 [5–123] mL/min/1.73m^2 in immigrant children ($n = 30$). After 12 months, the median [range] eGFR in both groups was 57 [0–143] mL/min/1.73m^2 ($n = 51$) and 65 [0–134] mL/min/1.73m^2 ($n = 22$), respectively. Deterioration based on eGFR was found in 16 of 49 native children (33%) with data to calculate eGFR at both 3 and 12 months and in 5 of 20 of immigrant children (25%), chi-square test, P = 0.531.

Non-compliance was suspected by the health care providers in 11/68 (16%) of native children and in 9/31 (29%) of immigrants with >3-month follow-up (chi-square test P = 0.122). In general, 9 of the 24 children who had one or more ARE were suspected of non-compliance, but also 11 of the 75 children that did not have any ARE.

Table 5. Results of Cox regression analysis for acute rejection ($n = 99$ children with at least 3-month follow-up)[a]

	Hazard ratio	95% Confidence interval
Univariable model		
Immigrant status	2.4	1.1–5.3
Multivariable model		
Immigrant status	2.5	1.1–5.9
Donor source (LD versus DD)	1.1	0.4–3.0
Months on Dx before first Tx	1.0	0.9–1.0
≥1 mismatch on DR	1.5	0.6–3.3

[a]Dx, dialysis; Tx, transplantation.

Discussion

The most favourable modes of renal transplantation, i.e. pre-emptive and LD transplantation were less often performed in immigrant children than in native children.

Pre-emptive transplantation with a kidney from a DD was performed only twice in our study population but could be an attractive alternative for LD transplantation. Cransberg *et al.* [7] found that pre-emptive transplantation in children, even with a deceased donor is associated with less ARE than transplantations following dialysis. Unfortunately, the Eurotransplant policy reduces the chances for pre-emptive transplantation with a kidney from a DD, by using time on dialysis as an indicator of urgency on the waiting list. For this reason, the policy of all participating centres in our study is to advocate (pre-emptive) LD transplantation as most advantageous to all patients. This implies that the low number of LD transplantations in immigrants that we found is most likely due to less willingness or ability of non-Western immigrant parents to donate as compared to native parents. Cultural barriers, different beliefs and attitudes towards donation but also misunderstandings and miscommunication between patient or caretakers and physician may have played a role. Unfortunately, in the present study, we had no data on the ability of immigrant parents and patients to communicate adequately in Dutch, English or French. We think that this is an interesting topic for future research. Park *et al.* [8] showed that special attention for these cultural and communicative aspects in an adult multi-ethnic transplantation programme indeed increased the frequency of donation but only at the cost of continuous efforts to overcome educational, language and cultural barriers in motivating potential donors. Another interesting finding that warrants further investigation is the longer time immigrant children spent on dialysis prior to first Tx, in a comparison of children for whom pTx was not possible. It seems that, also for the time spent on dialysis before first Tx, different social or medical factors might play a role. Future research should focus on the identification of these factors that delay Tx in immigrant children.

After transplantation, immigrant children were at higher risk for rejection, irrespective of the mode of transplantation, duration of dialysis before the first Tx and number of HLA mismatches. Whether this results in more adverse outcomes in the long-term in these children, is, as yet, unknown. Due to the short period of follow-up after Tx, long-term outcomes such as graft failure could not be investigated. As a surrogate outcome for graft failure, we looked at differences in eGFR between 3 and 12 months after Tx, but no difference between the two groups of children could be identified. Apparently, as most rejections occurred early after Tx during the period of regular hospital visits with the possibility of immediate treatment, overall median eGFR of both groups was not affected by the number of rejections.

Cultural factors, such as language difficulties, a different awareness of living with a chronic disease or simple misunderstandings between patient and doctor may result in less adherence to the therapy and consequently more rejections [9]. However, in our study, most rejections occurred shortly after transplantation during a period of regular hospital visits according to protocol. Although we had no reliable tools to analyse patient compliance, the occurrence of rejections so soon after transplantation makes non-compliance as an important cause of ARE less likely.

Biological factors may also play a role. We found no differences in primary disease between immigrant and native children. If transplanted with a kidney from a DD, immigrants had significantly more HLA mismatches on the DR locus, but this did not influence the lower rejection-free survival in immigrants. Whether other genetically determined or immunological differences might have influenced the higher rejection frequency in immigrant children remains to be elucidated.

Finally, a different response to anti-rejection prophylactic regimes as a result of a different pharmacokinetic profile of non-western immigrants as compared to native patients might be of importance. Trough levels may be less reliable in these circumstances. Recently, several studies have addressed this topic and suggest that the dosage of immunosuppressive therapy based on area under the concentration time curves could provide a more individualized approach of the immunosuppressive therapy in these patients than based on trough levels, as is the current treatment procedure in the participating centres [10–12]. This warrants more in-depth investigation to inform clinicians about the optimal strategy for the adjustment of dosages of immunosuppressive drugs in individual patients.

At present, more Dutch than Belgian children are included than would be expected based on the demographic numbers of inhabitants of the Netherlands and Belgium (16.7 and 10.8 million people, respectively) [1, 2]. This could be explained by three factors. Firstly, in three of five Belgian centres, the inclusion period of the RICH-Q project started 3–8 months later than in the other four Dutch and two Belgian centres. In those three centres, the RICH-Q project started in January and May 2008, respectively, due to a delay in ethical approval by the local ethical committees. Secondly, we analysed a subgroup of children who received their first transplantation. It might be that coincidentally more Dutch children ($n = 87$) received their first renal transplant during the study period, as compared to the Belgian children ($n = 32$). Lastly, we know that a few Belgian children are not included in the RICH-Q study because they are cared for in France or Germany, but this cannot explain the differences between these numbers of children. Therefore, we are cautious in deriving inferences

when comparing practices and outcomes in the Netherlands and Belgium.

In the present study, we focussed on immigrants from non-Western European origin. The different composition of the immigrant population in different countries may explain the differences between our findings and others, e.g. those found by Oztek *et al.* [13]. They found equal outcomes in native Austrian children and immigrants, yet the Austrian immigrants were mainly from the Balkan as opposed to the Turkish, North African and Caribbean origins of the Dutch and Belgian immigrants. Our data do show similarities with a previous Dutch study from Roodnat *et al.* [14] on renal graft survival in adults. Overall, the authors found similar graft survival between European and non-European adult recipients but also a higher risk for graft failure for Arab (of which 85% Moroccans) and African recipients (41% Surinam-creoles, 24% Antillians and 35% Cape Verdians). Arab and African origins also constitute a great proportion of the immigrant population in the present study. Within the Netherlands and Belgium, there has been a change over time in the immigrant population in terms of the countries of origin, the reasons for immigration and the number of western-born children, the so-called second generation. This might explain the difference between the results of the present study and a recent Dutch study in adult immigrants, which showed increased survival for adult immigrant patients on dialysis compared to native Dutch dialysis patients [15].

In conclusion, we found that immigrant children receive less pre-emptive and less LD transplantation compared to native children. After transplantation, these children are at higher risk for rejection, irrespective of the donor source. Research should be aimed at identifying the causes of these differences.

Acknowledgements. RICH-Q is funded by the Dutch Kidney Foundation. We are grateful to all patients and the participating centres in the RICH-Q study and to Dr Els Boeschoten, Lucia ten Brinke, Lara Heuveling, Martijn Leegte and Helga Schrijvers from the Hans Mak Institute for their support with data registration and monitoring.

Conflict of interest statement. None declared.

References

1. Centraal Bureau voor de Statistiek. 2011. ; http://www.cbs.nl (1 May 2011, date last accessed)
2. Statistics Belgium. http://statbel.fgov.be (1 August 2010, date last accessed)
3. Stronks K, Ravelli AC, Reijneveld SA. Immigrants in the Netherlands: equal access for equal needs? *J Epidemiol Community Health* 2001; 55: 701–707
4. van Dellen QM, Stronks K, Bindels PJ *et al.* Predictors of asthma control in children from different ethnic origins living in Amsterdam. *Respir Med* 2007; 101: 779–785
5. *Renal Insufficiency therapy in Children—Quality Assessment and Improvement*. 2010. http://www.rich-q.nl/ (13 December 2010, date last accessed)
6. Schwartz GJ, Munoz A, Schneider MF *et al.* New equations to estimate GFR in children with CKD. *J Am Soc Nephrol* 2009; 20: 629–637
7. Cransberg K, Smits JM, Offner G *et al.* Kidney transplantation without prior dialysis in children: the Eurotransplant experience. *Am J Transplant* 2006; 6: 1858–1864
8. Park CW, Limm WM, Wong LL. Improving living renal transplant: lessons from a multi-ethnic transplant program. *Hawaii Med J* 2009; 68: 104–108
9. Chan KS, Keeler E, Schonlau M *et al.* How do ethnicity and primary language spoken at home affect management practices and outcomes in children and adolescents with asthma? *Arch Pediatr Adolesc Med* 2005; 159: 283–289
10. Rong G, Jing L, Deng-Qing L *et al.* Influence of CYP3A5 and MDR1(ABCB1) polymorphisms on the pharmacokinetics of tacrolimus in Chinese renal transplant recipients. *Transplant Proc* 2010; 42: 3455–3458
11. Hesselink DA, van Schaik RH, van der Heiden IP *et al.* Genetic polymorphisms of the CYP3A4, CYP3A5, and MDR-1 genes and pharmacokinetics of the calcineurin inhibitors cyclosporine and tacrolimus. *Clin Pharmacol Ther* 2003; 74: 245–254
12. Emovon OE, Op't HC, Browne BJ. Can a pharmacokinetic approach to immunosuppression eliminate ethnic disparities in renal allograft outcome? *Clin Transplant* 2002; 16 (Suppl 7): 45–48
13. Oztek FZ, Tekin P, Herle M *et al.* Does immigration background influence outcomes after renal transplantation? *Pediatr Nephrol* 2011; 26: 309–315
14. Roodnat JI, Zietse R, Rischen-Vos J *et al.* Renal graft survival in native and non-native European recipients. *Transpl Int* 1999; 12: 135–140
15. van den Beukel TO, Dekker FW, Siegert CE. Increased survival of immigrant compared to native dialysis patients in an urban setting in the Netherlands. *Nephrol Dial Transplant* 2008; 23: 3571–3577

Received for publication: 1.7.11; Accepted in revised form: 26.9.11