Pediatr Nephrol (2015) 30:1077–1086
DOI 10.1007/s00467-014-2879-3

EDUCATIONAL REVIEW

An overview of disparities and interventions in pediatric kidney transplantation worldwide

Michael A. Freeman · Larissa Myaskovsky

Received: 13 November 2013 / Revised: 3 June 2014 / Accepted: 4 June 2014 / Published online: 15 October 2014

Abstract Despite the stated goals of the transplant community and the majority of organ allocation systems, persistent racial disparities in pediatric kidney transplantation exist throughout the world. These disparities are evident in both living and deceased donor kidney transplantation and are independent of any clinical differences between racial groups. The reasons for these persistent disparities are multifactorial, reflecting both patient and provider barriers to care. In this review, we examine the most current findings regarding disparities in pediatric kidney transplantation and consider interventions which may help reduce those disparities.

Keywords Kidney transplantation · Minority health · Organ allocation · Racial disparities · Socioeconomic status

Introduction

Kidney transplantation is the optimal treatment for patients with kidney failure, resulting in improved duration and quality of life [1, 2]. However, despite the availability of living donor allografts and improvements in immunosuppression which allow broader histocompatibility, the supply of organs remains insufficient to meet demand [3]. Further, there exist pervasive racial and ethnic disparities in kidney transplantation in both the adult and pediatric setting [4-7]. While much of the research examining this issue has been conducted in the USA, similar disparities have been identified in Australia [8], Belgium [7], Canada [9], the Netherlands [7], South Africa [10], and the UK [11], among others, indicating the global nature of this situation. Although it is important to note that some of these disparities may be the result of factors that are beyond the control of the medical system (e.g., co-morbidities and hereditary diseases that are associated with certain ethnic groups) [12, 13], studies have repeatedly demonstrated that differences in medical factors alone are not sufficient to explain the disparities in transplantation in their entirety [8, 14],

Given the relatively low rates of pediatric kidney transplantation, collecting data on a sufficiently large population of recipients is technically difficult. As a result, the majority of studies have focused on the analysis of data from pre-existing databases. Although these databases are an invaluable tool for determining nationwide practice patterns, they may not record important clinical or socioeconomic characteristics and may be incomplete due to voluntary reporting standards. Studies designed to examine the underlying causes of racial and ethnic disparities in pediatric kidney transplantation or to evaluate pediatric-specific interventions are rare. Consequently, due to the relative lack of these pediatric studies, we must seek further insight from studies performed in the adult kidney transplant population. Even though it is important to be judicious in applying the results of any adult study to the pediatric population, many of the non-medical factors that affect the transplant evaluation process and procedure (e.g., economic, social, and cultural constraints of the patient's families) affect families as a whole and therefore can be informative for assessing similar disparities in the pediatric population.

In this article, we review some of the most current findings regarding disparities in pediatric and adult kidney transplantation as a means to identify specific economic, cultural, and psychosocial factors that contribute to these disparities. We then review the various interventions which have been designed to address some of these disparities. We purposefully composed this review with a broad focus in order to maximize the utility of this article to clinicians unfamiliar with this field.

M. A. Freeman (✉)
Division of Pediatric Nephrology and Hypertension, Penn State Hershey Children's Hospital, Mail Code H085, 500 University Drive, Hershey, PA 17033, USA
e-mail: MFreeman3@hmc.psu.edu

L. Myaskovsky
Center for Health Equity Research and Promotion, VA Pittsburgh Healthcare System, University Drive (151C), Pittsburgh, PA 15240, USA

Racial disparities in kidney transplantation

Adult data from the United States 2012 Scientific Registries of Transplant Recipients (SRTR) report demonstrated that although African American (AA) patients and other minority groups represent 62.1 % of the kidney transplant waiting list, minority patients received only 47.4 % of all kidneys transplanted [15]. Furthermore, AA patients were significantly less likely to receive a living donor kidney transplant (LDKT) than their white counterparts (17.2 % of all AA transplant recipients vs. 40.9 % of all white transplant recipients), with a commensurate decrease in allograft longevity.

This is not an isolated problem for adult kidney transplant recipients. Cumulative data from 2009 to 2011 indicate that among U.S. pediatric kidney transplant recipients, white children received approximately 50.3 % of all transplants despite representing only 39.4 % of all wait-listed patients during that time [16].[1] The disparities in living donation allografts are even more stark. AA children received only 9.5 % of all living donor allografts transplanted during that period, despite comprising 25.9 % of the transplant waiting list.[2] Furthermore, an analysis of the raw number of transplants performed in each ethnic group does not capture the true extent of the disparity. There is substantial evidence that racial and ethnic minority patients experience longer waiting times for transplantation, lower rates of preemptive transplantation, lower rates of living donor transplantation, and worse post-transplant outcomes than the majority population in many countries. For example, a review of the data in the North American Pediatric Renal Trials and Collaborative Studies (NAPRTCS) database demonstrated that 3- and 5-year graft survival was significantly lower in AA children than white children, which only compounds the effects of health disparities engendered during the allocation and transplant process [17]. Although the racial disparities in pediatric transplantation in the USA are particularly well documented, these disparities have been noted in other countries as well [8, 9].

Disparities in initiating transplant evaluation

Pediatric patients with significant kidney disease are commonly managed by, or in conjunction with, pediatric nephrologists associated with an academic medical center. As a result, pediatric nephrologists frequently serve as the initial referring physician for transplantation. Therefore, disparities in access to nephrological care can have a significant effect on the transplant evaluation process. The implications of delays in initiation of care are twofold. First, if patients are referred to specialty care only when there are obvious signs of advanced kidney disease, they may not receive the preventive care necessary to optimize their native kidney function. As a result, these patients may require renal replacement therapy at a higher rate or at an earlier time during their disease course than those patients referred more promptly. Second, following the initiation of nephrological care there is generally a period of time during which a patient's clinical status is being assessed and optimized. If patients do not access nephrological care until they have had significant progression of their kidney disease, the need for this initial assessment may mean that evaluation for kidney transplantation will be deferred.

Assessing disparities in access to healthcare can be difficult because many patients excluded from care are concurrently excluded from the common mechanisms of healthcare research. Data from the 2003 National Survey of Children's Heath [18] suggest that patients of Latino and Asian or Pacific Islander descent had difficulty in accessing pediatric specialty care in general, but no data regarding access to pediatric nephrology services specifically were obtained. In 2005, Seikaly et al. [19] published an analysis of United States Renal Data System (USRDS) data which reported that non-white status and lack of insurance were associated with delayed initiation of dialysis in children, although the etiology of this difference could not be explored given the limitations of the USRDS data set. Similarly, a recent analysis by Grace et al.[8] demonstrated that aboriginal and minority children in Australia were significantly more likely to experience a late referral to nephrological care.

Difficulties in accessing appropriate nephrological care are not the only barriers that patients may face before a transplant evaluation is initiated. Because pediatric nephrologists are acutely aware of the limited supply of organs and transplant programs and are assessed based on the outcomes of patients they transplant, there are clear incentives not to initiate the transplant evaluation process for a patient who they do not perceive as "ready" for transplant. In some cases, a patient may be deemed not ready due to clinical instability or the presence of co-morbid conditions, while in other instances, readiness is questioned due to concerns regarding post-transplant social support or patient non-adherence. Although such decisions are entirely appropriate given the limited supply of transplant organs available, they may contribute to disparities in the transplantation process. For example, Furth and colleagues [20] demonstrated that nephrologists caring for pediatric patients were significantly less likely to recommend transplantation in hypothetical patients who demonstrated questionable adherence or frank non-adherence or whose parents had lower levels of education. It is important to remember that racial designations are not simply a description

---

[1] Due to the relatively short wait times for pediatric kidney transplantation, many patients listed receive transplants before the year-end data are compiled. The racial and ethnic composition of patients on the transplant list is based on the composition of the list at the end of the year for each of the years reported.

[2] See 1 above.

of variations of appearance, but rather are frequently associated with significant differences in economic, educational, cultural, and social backgrounds. Therefore, although Furth and colleagues' study did not identify race as an independent factor in the decisions made by the responding pediatric nephrologists, deferring transplant evaluation based on parental education may have a disproportionate effect on minority populations.

Similarly, decisions based on a practitioner's perception of patient adherence may also contribute to disparities in renal transplantation. Non-adherence to treatment is prevalent within the pediatric end-stage renal disease (ESRD) population. However, it remains unclear if most physicians are aware of the extent to which non-adherence is encountered in their routine care. For example, in 2011, Chua and Warady [21] reported on a small retrospective cohort of pediatric patients receiving cyclic automated peritoneal dialysis who had their adherence rate monitored by a recording device within the automated cycler. These authors demonstrated that 45 % of the patients had been non-adherent to some element of their dialysis prescription during a 9-month cycle. A study by Zelikovsky et al. [22] examined a small cohort of 56 adolescents with ESRD who were listed for kidney transplant and found that 38.2 % of the patients missed >10 % of their weekly medication doses and 21.8 missed >20 % of their weekly doses. Despite this fact, only a small segment of this non-adherent population is labeled as such by physicians. Unfortunately, research suggests that physicians possess significant unconscious racial biases in their identification of non-adherence [23]. Prior research has demonstrated that physicians systemically perceive AA and patients with low socioeconomic status (SES) as being less likely to understand and adhere to medical treatment, independent of any history supportive of this fact [24]. A recent study by Sabin et al. [25] demonstrated that while pediatricians demonstrated less implicit race bias than physicians as a whole, there remained significant evidence of an implicit association between perceived patient adherence and race. The decision to refer a patient for transplantation is highly dependent on the opinion of the evaluating physician. Therefore, providers' perceptions, and any accompanying biases that may influence their perceptions, may contribute to disparities in referral for kidney transplantation.

Disparities in the evaluation process

A recent analysis by Patzer et al. [14] of pediatric data obtained from the USRDS for the years 2000–2008 showed that there was a measured, but non-significant difference in the time from diagnosis with ESRD to wait-listing for transplant between AA and white patients between 0 and 17 years of age (hazard ratio 0.94; 95 % confidence interval 0.87–1.02). A significant difference was identified for uninsured Hispanic patients, but this disparity diminished in patients who had any type of insurance. In contrast, the authors demonstrated significant differences for the time to referral for patients aged 18–20 for both AA and non-insured Hispanic patients as compared to white patients, despite adjusting for clinical, demographic, and socioeconomic factors (HR 0.84, 0.70, respectively). Although the authors did not identify the specific reason for disparities in the older age group, [14] they speculated that part of the reason for the disparity in the time required for these patients to be placed on the transplant waiting list may be due to poorer rates of adherence in these groups .

Although the USRDS contains information on the duration of time between being declared ESRD and the time a patient is either wait-listed for a deceased donor kidney transplant (DDKT) or undergoes LDKT, it does not contain specific data regarding the time that a patient's transplant evaluation was initiated. Therefore, studies based on this data lack the sensitivity to distinguish between those patients whose evaluation is delayed and those patients who face barriers which delay completion during the evaluation process itself. Studies performed at adult transplant centers have demonstrated that AA race is associated with a longer time to complete the transplant evaluation process [26]. A prospective study performed by Myaskovsky et al. [27] demonstrated that perceived discrimination within the healthcare system, deficiencies in transplant knowledge, religious objections to LDKT and lower patient income independently predicted a longer time to complete the transplant evaluation process and were sufficient to account for the racial disparities identified.

These studies demonstrate that even after the transplant evaluation process has been initiated, substantial barriers to the completion of the evaluation process exist. The evaluation process is complex, frequently requiring multiple clinic visits, laboratory studies, and radiologic tests. This process can provide significant hurdles for patients and families to overcome, particularly for families of lower SES [28]. Patients and families can face difficulties in obtaining the requisite time off work to complete evaluation, as well as financial burdens from having to travel to or stay near pediatric transplant centers.

Disparities in DDKT

Even after listing for DDKT has occurred, minority patients often experience an increased time to transplantation than their majority population counterparts [14]. Data from the Netherlands and Belgium demonstrate that the median time to first transplantation after initiation of dialysis in pediatric patients who received a DDKT was 26 months in immigrant children as opposed to 18 months in native children [7]. These disparities mirror findings in the adult literature [29]. Differences in waiting time have been largely attributed to differential distribution of HLA genotypes in populations of different racial and ethnic backgrounds. Although recent data suggest that on a per capita basis deceased organ donation rates from AAs and Hispanics are equivalent to or exceed those of whites, the rate is insufficient to match the needs of minority CKD patients [16]. Recent estimates of the prevalence of ESRD suggest that AAs are more than twice as likely than whites to develop ESRD during the course of their lifetime [30]. Consequently, AAs would have to donate at twice the rate of whites to supply a sufficient number of deceased donor kidneys if the HLA profile of each of these populations were completely distinct.

There are also clinical characteristics other than HLA matching that can extend the time that minority recipients spend on the waiting list. The recent study by Patzer et al. [14] found that when demographic and clinical factors, such as the underlying etiology of the patient's ESRD, blood type, hemoglobin levels, albumin levels, and peak panel reactive antibodies level were accounted for, racial disparities in the time elapsed between being placed on the waiting list and undergoing a DDKT were eliminated for patients aged 0–17 years. In contrast, a study by Samuels et al. [9] demonstrated that aboriginal children in Canada were 38 % less likely to receive a DDKT than their white counterparts with comparable dialysis time, despite controlling for differences in age, sex, SES, cause of renal failure, and distance from the nearest transplant center. This study, however, did not account for differences in HLA profiles between the recipient and donor populations. These findings suggest that our understanding of the factors which can contribute to delays in transplantation, even after listing for a decreased donor kidney has occurred, remains incomplete and that further investigation to identify the characteristics which place a given individual at risk for these disparities is necessary.

Disparities in LDKT

Compared to DDKT, LDKT has been shown to result in superior graft longevity and subsequently improved mortality [31]. In the USA, both adult and pediatric AA and Hispanic patients undergo LDKT at lower rates than their white counterparts [14, 16, 32]. A recent analysis of SRTR data from 1995–2007 performed by Hall et al. [33] demonstrated that adult AA patients had a 35 % decreased likelihood of receiving a LDKT at centers with the lowest degree of racial disparity and a 76 % decreased likelihood of receiving a LDKT at the centers with the highest degree of racial disparity. Disparities in LDKT have actually increased in the pediatric setting in the USA since the implementation of the "Share-35" protocol in 2005. This protocol is designed to preferentially allocate kidneys from deceased donors under the age of 35 years to pediatric recipients. While this has been very efficacious in reducing waiting times and racial disparities in DDKT, it has increased racial disparities in LDKT [34]. Since its implementation, 31.8 % of all transplants in white recipients have been the result of living donation, as compared to 14.4 % for Hispanic and 10.7 % for AA patients [34]. Similar disparities in LDKT between majority and minority populations have been demonstrated worldwide. Between 2007 and 2011 in Belgium and the Netherlands, 59 % of native children received LDKT, as opposed to 24 % of immigrant children [7]. In Australia, among those patients who did not receive preemptive transplantation, 38 % of white children received LDKT, in comparison to only 23 % of indigenous children [8]. Unfortunately, there have been very few studies in the pediatric population to identify the underlying cause of these disparities beyond population level analysis.

Numerous potential etiologies of this disparity have been proposed, including clinical, demographic, cultural and medical knowledge-related factors [32, 35]. Although clinical factors, such as increased rates of blood group incompatibility within minority populations may play a role, studies in the AA community suggest that these factors are insufficient to explain these disparities [36]. A retrospective review performed by Lunsford et al. [36] of all potential living donors evaluated at the Medical University of South Carolina between 2000 and 2004 showed no significant racial differences in the rate of non-donation due to donor health. Gore et al.[32] reviewed United Network of Organ Sharing (UNOS) data for all adult transplants performed in the USA from 2004 to 2006 and demonstrated that patients with a high school education or less were 38 % less likely to undergo LDKT than their more educated counterparts. These authors also found that patients in the lowest quartile of income were 22 % less likely to receive a LDKT than those in the highest quartile [32]. Finally, cultural factors, such as perceived discrimination in medical care or a religious objection to LDKT, and transplant knowledge have also been shown to predict a decreased likelihood of LDKT [37] [38]. Specifically, those who report experiencing discrimination in the healthcare system, those who perceive religious objections to LDKT, and/or those with less knowledge about kidney transplantation and the advantages of LDKT are significantly less likely to undergo LDKT.

Disparities in preemptive renal transplantation

Numerous studies have demonstrated that preemptive kidney transplantation is associated with increased allograft survival, reduced morbidity and mortality, and increased quality of life in the pediatric population when compared to transplantation after the initiation of dialysis [39, 40]. Unfortunately, significant racial disparities in the rate of preemptive renal transplantation exist. The recent study by Patzer et al. [5] examined the rates of preemptive kidney transplantation among U.S. pediatric patients designated as having ESRD. After excluding patients for whom demographic data was incomplete, these authors determined that from 2000 to 2009, 13.9 % of all pediatric kidney transplantations performed were preemptive. Their results demonstrated that AA patients were 47 % less likely than white patients to be listed for preemptive DDKT, while there was no significant difference in listing between Hispanic and white patients. Of note, however, these differences were no longer significant when the models were adjusted for differences in the etiology of ESRD. In contrast, significant differences persisted in the likelihood of receiving a living donor preemptive transplantation, with AA patients being 76 % and Hispanic patients being 52 % less likely than white patients to receive a living donor allograft, even after controlling for primary diagnosis. Similar disparities can be found worldwide. Data from the UK Renal Registry's 15th Annual report in 2011 [11] demonstrated that minority pediatric patients were significantly less likely to receive preemptive renal transplantation, with black children receiving preemptive transplantation in 12.1 % of all cases as opposed to 33.6 % of white children between 1997–2011. Between 1990 and 2011 in Australia, no indigenous children underwent preemptive transplantation, as opposed to 19 % of white children.[8]

Preemptive transplantation requires that the patients enter into nephrological care promptly to allow completion of the transplant evaluation before other forms of renal replacement therapy are required. Therefore, any disparities in access may be reflected in lower rates of preemptive transplantation. Extending the amount of time necessary to complete the transplant evaluation decreases the likelihood that transplantation can occur before the initiation of dialysis is required. Thus, racial disparities in the time necessary to complete the transplant evaluation will be reflected in the rate of preemptive transplantation as well. In the USA, the majority of preemptive renal transplants performed between 2000 and 2009 were LDKT (66.9 vs. 33.1 % for DDKT); therefore, the known racial disparities in LDKT also influence the rate of preemptive transplantation in minority populations [5]. Given the known advantages in morbidity and mortality from preemptive transplantation, the combined effect of these factors result in significant disparity in health outcomes for minority pediatric patients.

Disparities in transplant outcomes and post-transplant care

Research suggests that racial disparities in renal transplantation extend beyond the evaluation and transplantation period. There are clear disparities in post-transplant outcomes as well [7, 10, 17, 41]. A 2007 analysis of the more than 6,287 pediatric patients who had been registered in the NAPRTCS database demonstrated that 5-year graft survival rates were significantly lower for AA children than for white children (65.6 vs. 83.1 %, respectively) [17]. This increased risk for graft failure persisted in AA children despite correction for demographic and clinical factors, including age, etiology of ESRD, and HLA matching. Data from a single center in South Africa examining pediatric kidney transplant outcomes between 1985 and 2005 demonstrated that black children had a median allograft survival rate of 4.22 years, as compared to 6.29 years for their white counterparts [10]. Disparities in the rates of acute rejection in the post-transplant setting have been described in the Netherlands and Belgium [7]. In addition to being at increased risk for poor graft outcomes, other studies have demonstrated that AA pediatric patients are at increased risk of other health disparities in the post-transplant setting, including increased rates of hypertension [42].

It is likely that several factors contribute to these observed disparities in outcomes. Although all patients are assessed for matching of the major HLA antigens, it is possible that due to differences in the distribution of minor antigen genotypes, minority recipients of DDKT face greater antigen exposure. Studies in adults have demonstrated that lower SES and lower educational achievement are associated with worse outcomes in the post-transplant setting [43]. This is not unexpected, as many minority transplant patients continue to face the same socioeconomic barriers that impeded access to optimal healthcare in the pre-transplant setting. Racial differences in medication adherence in the post-transplant setting are frequently proposed as another contributing factor to disparities in transplant outcome, particularly in the pediatric setting. It is well documented that as children enter adolescence, the risk for medication and treatment non-adherence increases [44]. A recent meta-analysis performed by Dew et al. [45] demonstrated that the non-adherence rates of pediatric solid organ transplant recipients in terms of testing and visits to the clinic were as high as 12.9 events per 100 patient-years. However, race was explicitly not an independent predictive factor of non-adherence, although other socioeconomic markers, such as reliance on public insurance or non-intact families, were. Because minority patients are often more likely to be socioeconomically disadvantaged, they may be at greater risk for non-adherence than the population as a whole.

Interventions to address disparities in kidney transplantation

The preceding sections of this review describe numerous racial and ethnic disparities associated with kidney transplantation, as well as some of the means by which these disparities occur. In this section we examine various interventional approaches which have been used to address these disparities

Disparities in transplant evaluation

Although there is ongoing research to identify modifiable patient characteristics that can contribute to delays in completing the transplant evaluation process [27, 38], few interventions have been developed. One suggested approach has been to streamline the evaluation process. However, although there has been some benefit demonstrated by streamlining the evaluation process in adult populations [46], no similar studies have as yet been performed with pediatric patients.

Disparities in receipt of DDKT

Individual practitioners are limited in their ability to affect disparities in the time necessary to receive a DDKT once listing has occurred. The distribution of allograft organs for patients awaiting a DDKT is controlled by the regional and national organ allocation systems. Therefore, alterations in these allocation systems are the primary means of addressing these disparities. HLA-B matching criteria were removed from the allocation system in the USA in 2003, as HLA-B mismatches were felt to have only a minor effect on the subsequent viability of the allograft [47]. When HLA-B was removed as a matching criteria, racial differences in HLA genotype distribution became less apparent, thereby decreasing the likelihood that a given recipient would require a kidney obtained from a donor of the same racial or ethnic background. Another intervention which has succeeded in reducing racial disparities in pediatric DDKT in the USA is the “Share-35” program. Since instituting this program, disparities in the time elapsed from listing until DDKT have been markedly reduced for minority pediatric patients in the USA [34]. In 2010, the Eurotransplant Kidney Allocation System was changed to give an increased allocation score to patients aged ≤16 years, as well as to preferentially distribute organs from deceased donors under the age of 16 years to this pediatric population [48]. However, it remains unclear if this policy change will offer similar benefits for minority pediatric patients within the Eurotransplant system.

Disparities in receipt of LDKT

System level changes can also be used to address disparities in LDKT. Live kidney donation may be especially difficult for individuals who are the primary caregivers or income earners in their households, which may restrict availability for donation. A number of countries have instituted programs to compensate living donors for non-medical expenses incurred during the organ donation process [49], but limited data exist regarding the impact of these programs. A recent study examining the impact of changes in organ transplant law in Israel which provide compensation for lost wages, transportation costs, increased insurance costs, and increased social support demonstrated a significant increase in living kidney donation. However, it must be noted that this law also places significant restrictions on patients receiving kidney transplants performed abroad [50].

In some cases, a pediatric patient’s parents may not be an eligible or feasible donor, and it may be difficult for those parents to seek out other potential living donors. Many adult patients have reported difficulty discussing LDKT with family members and other potential donors [51]. This hesitation serves to artificially curtail the donor pool, reducing the likelihood that a potential living donor will be identified. As a result, there have been significant efforts made to identify interventions to ease these conversations. One example of such an intervention is the Talking About Live Kidney Donation (TALK) study [52]. Participants were randomized to receive either (1) routine education regarding LDKT, (2) an educational booklet and video encouraging the patients to talk with their families and providers, or (3) the video and booklet combined with a protocol-directed social work visit. Assessment at the 6-month follow-up indicated superior results for the social work intervention, followed by the video and booklet alone, with routine care being the least effective approach. Subsequent evaluation indicated that patients and families perceived the social work intervention as a positive and helpful experience [53]. Other studies have demonstrated the utility of education as a means to reduce the time to complete transplant evaluation and improve LDKT rates [54, 55]. A recent study by Gordon et al. [56] demonstrated that an educational intervention specifically tailored to address Hispanic cultural concerns was particularly efficacious for that population, which suggests that tailoring educational initiatives to address the specific concerns of a given population may be an effective strategy. Providers should strive to be alert to cultural concerns in their patients and their patient’s families in order to gain the opportunity to tailor the clinical experience and transplant education process to alleviate those concerns. Although longer term follow-ups and larger scale studies are required to determine if such interventions increase the rates of LDKT, these types of intervention may serve as models for similar interventions for pediatric patients and their families.

Disparities in post-transplant adherence

Once transplant has occurred, interventions to improve adherence to treatment recommendations have the potential to both decrease racial disparities in kidney transplantation and improve transplantation outcomes in all racial and ethnic groups [20, 57]. There is extensive research, both recent and ongoing, with the aim to provide electronic reminders for adolescents to take their medications or engage in other aspects of medical care for a variety of chronic pediatric conditions [58–60]. Although these studies have demonstrated varying degrees of efficacy, adolescent patients have been generally positive about the interventions [61, 62]. Increased parental monitoring of medication administration has also been demonstrated to improve the adherence of adolescents with a variety of health conditions [63, 64]. While transition to self-care remains an important goal for adolescent patients, such transitions can be deferred until a pattern of adherence is established. Medication adherence has been shown to be inversely related to dosing frequency and, as a result, long-acting medications should be used whenever adherence is a concern [65]. While initial studies investigating the pharmacokinetics of delayed release tacrolimus formulations were recently performed in pediatric patients, no efficacy trials have as yet been conducted [66]. Dislike for characteristics of the medications themselves, such as pill size or taste, has been associated with poor adherence in children and adolescents, particularly among AA patients [67]. The non-adherence of patients to a particular medication should be investigated.

Conclusions

Significant racial and ethnic disparities in access to kidney transplantation continue to exist for pediatric patients worldwide. Research examining these disparities has been performed in only a relatively low number of countries; however, the widespread nature of these findings suggest that similar disparities likely exist in other countries where such research has not occurred. These disparities arise from a wide array of factors, including the clinical conditions of these patients, the practices of pediatric nephrologists, social, cultural, and economic barriers to LDKT, and the allocation systems for deceased donor kidneys. Although research in adult populations can be beneficial, additional research into the specific barriers faced by pediatric patients and their families is required. While some of these issues require intervention on a regional or national level, others can be influenced by the actions of individual practitioners and healthcare programs. This information will allow us to develop tailored interventions to reduce disparities in pediatric kidney transplantation in the future.

Key points

1. Significant racial disparities in the rates of both DDKT and LDKT continue to exist.
2. These disparities are influenced by a variety of system-level, provider-level, economic, cultural, and psychosocial factors.
3. Disparities persist despite adjustments for clinical differences in patients' presentation.
4. A variety of provider and program-level interventions have the potential to reduce these disparities.

Acknowledgments The data reported in the USRDS 2013 report were supplied by the USRDS. The interpretation and reporting of these data are the responsibility of the author(s) and in no way should be seen as an official policy or interpretation of the U.S. government. The data and analyses reported in the 2011 and 2012 Annual Data Report of the U.S. Organ Procurement and Transplantation Network and the SRTR have been supplied by UNOS and the Minneapolis Medical Research Foundation under contract with the U.S. Department of Health and Human Services/Health Resources and Services Administration. The authors alone are responsible for reporting and interpreting these data; the views expressed herein are those of the authors and not necessarily those of the U.S. government. The contents do not represent the views of the Department of Veterans Affairs or the United States Government. The work of Dr. Freeman on this paper was supported by Grant #T32DKK091202 from the National Institute of Diabetes, Digestive and Kidney Disease and for Dr. Myaskovsky by Grant #R01DK081325 from the National Institute of Diabetes, Digestive and Kidney Disease, and Grants #IIR 06-220 and #CIN 13-405 from the Veterans Affairs Health Services Research and Development Service.

Questions (answers are provided following the Reference list)

1) For patients in Belgium and the Netherlands, what is the difference between native and immigrant children in the median time from initiating dialysis until receiving a kidney transplantation?

   a) 2 months
   b) 4 months
   c) 6 months
   d) 8 months

2) Changing the organ allocation system is one means of addressing disparities in kidney transplantation. One such change was the "Share-35" system implemented by the USA in 2005. What effect did this change have on racial disparities in pediatric kidney transplantation in the USA?

   a) It had no effect
   b) It reduced disparities in DDKT, but increased disparities in LDKT
   c) It increased disparities in both DDKT and LDKT
   d) It reduced disparities in LDKT, but increased disparities in DDKT

3) Concerns of non-adherence are often cited as a reason to delay kidney transplantation. In the two studies of non-adherence in the pre-transplant ESRD population cited in this review, what was the approximate rate of non-adherence identified?

a) 10 %
b) 20 %
c) 30 %
d) 40 %

4) What percentage of Australian aboriginal children underwent pre-emptive renal transplantation between 1990 and 2011?

a) 0 %
b) 10 %
c) 20 %
d) 30 %

5) One factor associated with poor transplant outcomes is non-adherence. In studies of the U.S. pediatric transplantation population, which of the following has been found to be an independent predictor of non-adherence?

a) Racial or ethnic identification
b) Reliance on public insurance
c) Increased SES
d) Younger age

References

1. Evans RW, Manninen DL, Garrison LP Jr, Hart LG, Blagg CR, Gutman RA, Hull AR, Lowrie EG (1985) The quality of life of patients with end-stage renal disease. N Engl J Med 312:553–559
2. Hunsicker LG (1999) A survival advantage for renal transplantation. N Engl J Med 341:1762–1763
3. U.S. Renal Data System (2013) USRDS 2013 annual data report: atlas of chronic kidney disease and end-stage renal disease in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda
4. Muneeruddin S, Chandar J, Abitbol CL, Seeherunvong W, Freundlich M, Ciancio G, Burke GW, Zilleruelo G (2010) Two decades of pediatric kidney transplantation in a multi-ethnic cohort. Pediatr Transplant 14:667–674
5. Patzer RE, Sayed BA, Kutner N, McClellan WM, Amaral S (2013) Racial and ethnic differences in pediatric access to preemptive kidney transplantation in the United States. Am J Transplant 13:1769–1781
6. Furth SL, Garg PP, Neu AM, Hwang W, Fivush BA, Powe NR (2000) Racial differences in access to the kidney transplant waiting list for children and adolescents with end-stage renal disease. Pediatrics 106:756–761
7. Tromp WF, Cransberg K, van der Lee JH, Bouts AH, Collard L, Van Damme-Lombaerts R, Godefroid N, Van Hoeck KJ, Koster-Kamphuis L, Lilien MR, Raes A, Ranguelov N, Groothoff JW (2012) Fewer pre-emptive renal transplantations and more rejections in immigrant children compared to native Dutch and Belgian children. Nephrol Dial Transplant 27:2588–2593
8. Grace BS, Kennedy SE, Clayton PA, McDonald SP (2014) Racial disparities in paediatric kidney transplantation. Pediatr Nephrol 29:125–132
9. Samuel SM, Foster BJ, Tonelli MA, Nettel-Aguirre A, Soo A, Alexander RT, Crowshoe L, Hemmelgarn BR (2011) Dialysis and transplantation among Aboriginal children with kidney failure. CMAJ 183:E665–E672
10. Pitcher GJ, Beale PG, Bowley DM, Hahn D, Thomson PD (2006) Pediatric renal transplantation in a South African teaching hospital: a 20-year perspective. Pediatr Transplant 10:441–448
11. Pruthi R, O'Brien C, Casula A, Braddon F, Lewis M, Maxwell H, Tse Y, Inward C, Sinha MD (2013) UK renal registry 15th annual report: chapter 4 demography of the UK paediatric renal replacement therapy population in 2011. Nephron Clin Pract 123(suppl 1):81–92
12. Watson L, Leone V, Pilkington C, Tullus K, Rangaraj S, McDonagh JE, Gardner-Medwin J, Wilkinson N, Riley P, Tizard J, Armon K, Sinha MD, Ioannou Y, Archer N, Bailey K, Davidson J, Baildam EM, Cleary G, McCann LJ, Beresford MW (2012) Disease activity, severity, and damage in the UK juvenile-onset systemic lupus erythematosus cohort. Arthritis Rheum 64:2356–2365
13. Hiraki LT, Lu B, Alexander SR, Shaykevich T, Alarcon GS, Solomon DH, Winkelmayer WC, Costenbader KH (2011) End-stage renal disease due to lupus nephritis among children in the US, 1995–2006. Arthritis Rheum 63:1988–1997
14. Patzer RE, Amaral S, Klein M, Kutner N, Perryman JP, Gazmararian JA, McClellan WM (2012) Racial disparities in pediatric access to kidney transplantation: does socioeconomic status play a role? Am J Transplant 12:369–378
15. Matas AJ, Smith JM, Skeans MA, Thompson B, Gustafson SK, Schnitzler MA, Stewart DE, Cherikh WS, Wainright JL, Snyder JJ, Israni AK, Kasiske BL (2014) OPTN/SRTR 2012 annual data report: kidney. Am J Transplant 14:11–44
16. Organ Procurement and Transplantation Network (OPTN), Scientific Registry of Transplant Recipients (SRTR) (2012) OPTN / SRTR 2011 annual data report. Department of Health and Human Services, Health Resources and Services Administration, Healthcare Systems Bureau, Division of Transplantation, Rockville
17. Omoloja A, Mitsnefes M, Talley L, Benfield M, Neu A (2007) Racial differences in graft survival: a report from the North American pediatric renal trials and collaborative studies (NAPRTCS). Clin J Am Soc Nephrol 2:524–528
18. Flores G, Tomany-Korman SC (2008) Racial and ethnic disparities in medical and dental health, access to care, and use of services in US children. Pediatrics 121:e286–e298
19. Seikaly MG, Salhab N, Browne R (2005) Patterns and time of initiation of dialysis in US children. Pediatr Nephrol 20:982–988
20. Furth SL, Hwang W, Neu AM, Fivush BA, Powe NR (2003) Effects of patient compliance, parental education and race on nephrologists' recommendations for kidney transplantation in children. Am J Transplant 3:28–34
21. Chua AN, Warady BA (2011) Adherence of pediatric patients to automated peritoneal dialysis. Pediatr Nephrol 26:789–793
22. Zelikovsky N, Schast AP, Palmer J, Meyers KEC (2008) Perceived barriers to adherence among adolescent renal transplant candidates. Pediatr Transplant 12:300–308
23. van Ryn M (2002) Research on the provider contribution to race/ethnicity disparities in medical care. Med Care 40:I140–I151
24. van Ryn M, Burke J (2000) The effect of patient race and socioeconomic status on physicians' perceptions of patients. Soc Sci Med 50:813–828
25. Sabin JA, Rivara FP, Greenwald AG (2008) Physician implicit attitudes and stereotypes about race and quality of medical care. Med Care 46:678–685
26. Weng FL, Joffe MM, Feldman HI, Mange KC (2005) Rates of completion of the medical evaluation for renal transplantation. Am J Kidney Dis 46:734–745
27. Myaskovsky L, Almario Doebler D, Posluszny DM, Dew MA, Unruh M, Fried LF, Switzer GE, Kim S, Chang CC, Ramkumar M, Shapiro R (2012) Perceived discrimination predicts longer time to be accepted for kidney transplant. Transplantation 93:423–429
28. Kazley AS, Simpson KN, Chavin KD, Baliga P (2012) Barriers facing patients referred for kidney transplant cause loss to follow-up. Kidney Int 82:1018–1023

29. Roberts JP, Wolfe RA, Bragg-Gresham JL, Rush SH, Wynn JJ, Distant DA, Ashby VB, Held PJ, Port FK (2004) Effect of changing the priority for HLA matching on the rates and outcomes of kidney transplantation in minority groups. N Engl J Med 350:545–551
30. Grams ME, Chow EK, Segev DL, Coresh J (2013) Lifetime incidence of CKD stages 3–5 in the United States. Am J Kidney Dis 62: 245–252
31. Ojo AO, Port FK, Mauger EA, Wolfe RA, Leichtman AB (1995) Relative impact of donor type on renal allograft survival in black and white recipients. Am J Kidney Dis 25:623–628
32. Gore JL, Danovitch GM, Litwin MS, Pham PTT, Singer JS (2009) Disparities in the utilization of live donor renal transplantation. Am J Transplant 9:1124–1133
33. Hall EC, James NT, Garonzik Wang JM, Berger JC, Montgomery RA, Dagher NN, Desai NM, Segev DL (2012) Center-level factors and racial disparities in living donor kidney transplantation. Am J Kidney Dis 59:849–857
34. Amaral S, Patzer RE, Kutner N, McClellan W (2012) Racial disparities in access to pediatric kidney transplantation since share 35. J Am Soc Nephrol 23:1069–1077
35. Myaskovsky L, Switzer GE, Crowley-Matoka M, Unruh M, DiMartini AF, Dew MA (2007) Psychosocial factors associated with ethnic differences in transplantation. Curr Opin Organ Transplant 12: 182–187
36. Lunsford SL, Simpson KS, Chavin KD, Menching KJ, Miles LG, Shilling LM, Smalls GR, Baliga PK (2006) Racial disparities in living kidney donation: is there a lack of willing donors or an excess of medically unsuitable candidates? Transplantation 82:876–881
37. Waterman AD, Rodrigue JR, Purnell TS, Ladin K, Boulware LE (2010) Addressing racial and ethnic disparities in live donor kidney transplantation: priorities for research and intervention. Semin Nephrol 30:90–98
38. Waterman AD, Peipert JD, Hyland SS, McCabe MS, Schenk EA, Liu J (2013) Modifiable patient characteristics and racial disparities in evaluation completion and living donor transplant. Clin J Am Soc Nephrol 8:995–1002
39. Heidotting NA, Ahlenstiel T, Kreuzer M, Franke D, Pape L (2012) The influence of low donor age, living related donation and preemptive transplantation on end-organ damage based on arterial hypertension after paediatric kidney transplantation. Nephrol Dial Transplant 27:1672–1676
40. Kramer A, Stel VS, Geskus RB, Tizard EJ, Verrina E, Schaefer F, Heaf JG, Kramar R, Krischock L, Leivestad T, Palsson R, Ravani P, Jager KJ (2012) The effect of timing of the first kidney transplantation on survival in children initiating renal replacement therapy. Nephrol Dial Transplant 27:1256–1264
41. Matsuda-Abedini M, Al-AlSheikh K, Hurley RM, Matsell DG, Chow J, Carter JE, Lirenman DS (2009) Outcome of kidney transplantation in Canadian Aboriginal children in the province of British Columbia. Pediatr Transplant 13:856–860
42. Sorof JM, Sullivan EK, Tejani A, Portman RJ (1999) Antihypertensive medication and renal allograft failure: a North American pediatric renal transplant cooperative study report. J Am Soc Nephrol 10:1324–1330
43. Goldfarb-Rumyantzev AS, Koford JK, Baird BC, Chelamcharla M, Habib AN, Wang BJ, Lin SJ, Shihab F, Isaacs RB (2006) Role of socioeconomic status in kidney transplant outcome. Clin J Am Soc Nephrol 1:313–322
44. Shellmer DA, Dabbs AD, Dew MA (2011) Medical adherence in pediatric organ transplantation: what are the next steps? Curr Opin Organ Transplant 16:509–514
45. Dew MA, Dabbs AD, Myaskovsky L, Shyu S, Shellmer DA, DiMartini AF, Steel J, Unruh M, Switzer GE, Shapiro R, Greenhouse JB (2009) Meta-analysis of medical regimen adherence outcomes in pediatric solid organ transplantation. Transplantation 88: 736–746
46. Formica RN Jr, Barrantes F, Asch WS, Bia MJ, Coca S, Kalyesubula R, McCloskey B, Leary T, Arvelakis A, Kulkarni S (2012) A one-day centralized work-up for kidney transplant recipient candidates: a quality improvement report. Am J Kidney Dis 60:288–294
47. Hall EC, Massie AB, James NT, Garonzik Wang JM, Montgomery RA, Berger JC, Segev DL (2011) Effect of eliminating priority points for HLA-B matching on racial disparities in kidney transplant rates. Am J Kidney Dis 58:813–816
48. Pape L, Ahlenstiel T, Kanzelmeyer NK (2013) Consequences of the change in Eurotransplant allocation system on kidney allocation in children. Clin Transplant 27:650–651
49. Sickand M, Cuerden MS, Klarenbach SW, Ojo AO, Parikh CR, Boudville N, Garg AX (2009) Reimbursing live organ donors for incurred non-medical expenses: a global perspective on policies and programs. Am J Transplant 9:2825–2836
50. Lavee J, Ashkenazi T, Stoler A, Cohen J, Beyar R (2013) Preliminary marked increase in the national organ donation rate in Israel following implementation of a new organ transplantation law. Am J Transplant 13:780–785
51. Kranenburg LW, Zuidema WC, Weimar W, Hilhorst MT, Ijzermans JN, Passchier J, Busschbach JJ (2007) Psychological barriers for living kidney donation: how to inform the potential donors? Transplantation 84:965–971
52. Boulware LE, Hill-Briggs F, Kraus ES, Melancon JK, Falcone B, Ephraim PL, Jaar BG, Gimenez L, Choi M, Senga M, Kolotos M, Lewis-Boyer L, Cook C, Light L, DePasquale N, Noletto T, Powe NR (2013) Effectiveness of educational and social worker interventions to activate patients' discussion and pursuit of preemptive living donor kidney transplantation: a randomized controlled trial. Am J Kidney Dis 1:476–486
53. DePasquale N, Hill-Briggs F, Darrell L, Boyér LL, Ephraim P, Boulware LE (2012) Feasibility and acceptability of the TALK social worker intervention to improve live kidney transplantation. Health Soc Work 37:234–249
54. Rodrigue JR, Cornell DL, Kaplan B, Howard RJ (2008) A randomized trial of a home-based educational approach to increase live donor kidney transplantation: effects in blacks and whites. Am J Kidney Dis 51:663–670
55. Patzer RE, Perryman JP, Pastan S, Amaral S, Gazmararian JA, Klein M, Kutner N, McClellan WM (2012) Impact of a patient education program on disparities in kidney transplant evaluation. Clin J Am Soc Nephrol 7:648–655
56. Gordon EJ, Reddy E, Gil S, Feinglass J, Rodde J, Abecassis MM, Caicedo JC (2014) Culturally competent transplant program improves Hispanics' knowledge and attitudes about live kidney donation and transplant. Prog Transplant 24:56–68
57. Prendergast MB, Gaston RS (2010) Optimizing medication adherence: an ongoing opportunity to improve outcomes after kidney transplantation. Clin J Am Soc Nephrol 5:1305–1311
58. Miloh T, Annunziato R, Arnon R, Warshaw J, Parkar S, Suchy FJ, Iyer K, Kerkar N (2009) Improved adherence and outcomes for pediatric liver transplant recipients by using text messaging. Pediatrics 124:e844–e850
59. Johnson KB, Culpepper D, Scott P, Gordon JS, Harris C (2011) The utility of providing automated medication dose reminders to young children on chronic medication. J Telemed Telecare 17:387–391
60. Marciel KK, Saiman L, Quittell LM, Dawkins K, Quittner AL (2010) Cell phone intervention to improve adherence: cystic fibrosis care team, patient, and parent perspectives. Pediatr Pulmonol 45:157–164
61. MacDonell K, Gibson-Scipio W, Lam P, Naar-King S, Chen X (2012) Text messaging to measure asthma medication use and symptoms in urban African American emerging adults: a feasibility study. J Asthma 49:1092–1096

62. Britto MT, Munafo JK, Schoettker PJ, Vockell AL, Wimberg JA, Yi MS (2012) Pilot and feasibility test of adolescent-controlled text messaging reminders. Clin Pediatr 51:114–121
63. Fredericks EM, Dore-Stites D, Well A, Magee JC, Freed GL, Shieck V, James Lopez M (2010) Assessment of transition readiness skills and adherence in pediatric liver transplant recipients. Pediatr Transplant 14:944–953
64. Ellis DA, Templin TN, Podolski CL, Frey MA, Naar-King S, Moltz K (2008) The parental monitoring of diabetes care scale: development, reliability and validity of a scale to evaluate parental supervision of adolescent illness management. J Adolesc Health 42:146–153
65. Claxton AJ, Cramer J, Pierce C (2001) A systematic review of the associations between dose regimens and medication compliance. Clin Ther 23:1296–1310
66. Zhao W, Fakhoury M, Baudouin V, Storme T, Maisin A, Deschenes G, Jacqz-Aigrain E (2013) Population pharmacokinetics and pharmacogenetics of once daily prolonged-release formulation of tacrolimus in pediatric and adolescent kidney transplant recipients. Eur J Clin Pharmacol 69:189–195
67. Tucker CM, Fennell RS, Pedersen T, Higley BP, Wallack CE, Peterson S (2002) Associations with medication adherence among ethnically different pediatric patients with renal transplants. Pediatr Nephrol 17:251–256

Answers to questions

1): e
2): d
3): b
4): a
5): b