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Framing Disparities Along the Continuum of Care From Chronic Kidney Disease to Transplantation: Barriers and Interventions

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Abstract

Research in renal transplantation continues to document scores of disparities affecting vulnerable populations at various stages along the transplantation process. Given that both biological and environmental determinants contribute significantly to variation, identifying factors underlying an unfairly biased distribution of the disease burden is crucial. Confounded definitions and gaps in understanding causal pathways impede effectiveness of interventions aimed at alleviating disparities. This paper offers an operational definition of disparities in the context of a framework aimed at facilitating interventional research. Utilizing an original framework describing the entire continuum of the transplant process from diagnosis of chronic kidney disease through successful transplant, this paper explores the case of racial disparities, illustrating key factors predicting and perpetuating disparities. Though gaps in current research leave us unable to identify which stages of the transplant pathway adversely affect most people, by identifying key risk factors across the continuum of care, this paper highlights areas suited for targeted interventions and presents recommendations for improvement and future research.

Keywords

inequality; African-Americans; allocation; burden of disease; chronic kidney disease (CKD); kidney transplantation

Introduction

The National Organ Transplant Act (NOTA) that created the Organ Procurement and Transplantation Network (OPTN) emphasized the importance of equitable access for organ transplantation and of equitable allocation of donated organs among medically qualified patients (1). In spite of this ideal, disparities in transplant rates and outcomes in disadvantaged populations have been documented for over thirty years (2). Thus far, research surrounding transplant disparities has been largely descriptive, focused on

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identifying vulnerable populations and isolating specific risk factors along the pathway from end-stage organ disease to transplantation (3-5). Causal pathways remain unclear confounding association and causation, and few studies have presented frameworks useful in designing and implementing successful interventions (6). Concerned over growing disparities, clinicians and health policy leaders have begun to emphasize greater equity. Given that both biological and environmental determinants contribute significantly to variation, it is important to identify factors leading to an unfairly biased distribution of the burden of disease. To this end, the distinction between the terms 'difference' and 'disparity' becomes central.

Definitions: Differences versus disparities

Given observed differences in the incidence of kidney disease, transplantation rates and outcomes, the question becomes: which health differences, if any, constitute health disparities? A myriad of terms has been used to describe variations in health between groups, including: health inequalities, health inequities, health differences, health disparities, social disparities in health, and health gradients, along with many others. While these terms all point to discrepancies, their meanings are distinct.

Numerous inequalities are considered tolerable or acceptable by social standards, underlying the distinction between 'difference' and 'disparity'. Differences can be defined as consistent and measurable variations in health outcomes. Of these differences, disparities can be defined as differences which are “unnecessary and avoidable, but in addition are considered unfair and unjust” (7). Differences stemming from the basic structure of society (gender, class, race, etc.) or resulting from the social division of labor benefiting the advantaged at the expense of the disadvantaged are deemed to be unjust or unfair. Conversely, equity in health can be seen as the unbiased, fair opportunity of all to attain their full health potential.

For example, while poor health outcomes, such as complications from vehicular deaths, are often seen as avoidable differences in health, they become disparities when their underlying cause or statistical pattern suggests involuntary differential risk. If car accident deaths are higher in urban areas due to poorer road infrastructure or fewer police, this difference is in fact a disparity as there is higher involuntary risk associated with living in a certain geographic area. Conversely, sickle cell anemia, which afflicts mostly blacks, results in differences in health outcomes primarily driven by biological determinants and, therefore, is not considered a disparity.

The case of kidney disease and transplantation: differences and disparities in blacks

In this section, we explore disparities in blacks along the transplant continuum as an example, though many disparities (e.g. gender, migration, literacy, geographic, etc.) follow a similar trajectory. In chronic kidney disease (CKD) and transplantation, both differences and disparities exist (Table 1). For example, blacks suffer from a higher prevalence of diabetes and hypertension than whites, which account for 75% of the new cases of ESRD, and are more likely to progress from CKD to end stage renal disease (ESRD) (4,5,8). Although blacks constitute 13% of the general population they make up 37% of the U.S. population receiving dialysis and 35% of those on the transplant waiting list (3), yet they only receive 25% of deceased-donor kidneys and just 15% of live-donor transplants (4,9). Both differences and disparities contribute to these findings.

The prevalence of hypertension and diabetes in American blacks, precursors of ESRD, can partially be attributed to genetic susceptibility in blacks (5,10). Thus, if one considers the

total gap in CKD and ESRD between blacks and whites, the fraction attributed to this biological variation is considered a difference, as it stems from biological factors in which fairness plays no apparent role. Similarly, greater variation in HLA polymorphisms, presensitization, differences in immunosuppression requirements, variability in the pharmacokinetics of immunosuppressive drugs, and in immunologic responsiveness may be important in predicting transplant rates and graft survival (3,5). These are known differences.

Known disparities contributing to uneven distribution of both disease severity and transplantation stem from being less likely to be referred to nephrologists, less likely to be deemed acceptable candidates for transplantation by their physicians, more likely to experience incomplete workups, more likely to wait longer for transplantation, more likely to receive expanded criteria kidneys, less likely to encounter adequate post-operative care, and less likely to enjoy long-term graft survival (6,11). There is recent evidence that disparities in kidney transplantation are getting worse in some regions of the country (12).

Framing disparities in transplantation: The case of racial disparities

Having distinguished between differences and disparities, it becomes clear that a critical role of the transplant community is to reduce disparities stemming from *avoidable, involuntary, and differential* risk. The question then becomes: how can disparities be mitigated and where can and should we intervene?

To better answer this question, we consider disparities along the continuum from CKD to graft survival post-transplantation. While prior models targeting transplant disparities have focused largely on the clinical cascade following initiation of dialysis treatment, there is much evidence indicating that disparities occurring upstream greatly shape whether or not a patient receives dialysis, as well as disparities occurring thereafter (6). Figure 1 presents a framework incorporating both protective and risk factors associated with five main stages in the transplant process: diagnosis of CKD, diagnosis of ESRD, presence on transplant waiting list, eventual receipt of organ transplant, and post-transplant outcomes. Figure 1 illustrates that both risk factors and protective factors impact disparities by influencing progression through the transplantation process.

Development of CKD

Of the 20 million Americans who have CKD, prevalence among blacks is seven times that of whites, and blacks are diagnosed with CKD on average seven years earlier, at 57 versus 64 years of age in whites (4,13). Higher rates and severity of diabetes coupled with a 34% higher prevalence of hypertension contribute to CKD disparities between blacks and whites (4). Risk factors linked to disparities in CKD prevalence and severity include obesity, poorly controlled hypertension and diabetes and infrequent early intervention, literacy limitations, low socioeconomic status (SES), certain ethnic/racial minorities, and unreliable insurance status. These are exacerbated by inconsistent access to health care, exposure to environmental toxins, poor dietary habits, and lack of affordable medications (11). Driven by factors above, this gap cannot be entirely explained by disparities, and genetic predispositions do contribute significantly (3-5). Conversely, protective factors such as low body mass index (BMI), well controlled blood pressure, and continuous access to health care, are strongly correlated with higher SES and non-minority race.

Progression from CKD to ESRD

While for many progression of CKD to ESRD can be prevented or delayed, 700,000 Americans are projected to progress from CKD to ESRD by 2010, with risk of ESRD in blacks 3.89 times that of whites (14). Low SES has been linked to CKD survival, with

adjusted relative risk of death decreasing by three percent per \$1,000 in annual income (15). Blacks experience higher rates of urban poverty, 67% compared to 12% of whites, with 31% non-elderly blacks considered below the poverty line compared to only 11% of whites (14). Insurance also contributes, where blacks face greater hurdles as 45% are either uninsured or publicly insured, versus only 22% of whites (4). Blacks experience increased exposure to environmental toxins leading to higher blood lead concentrations, which have been associated with increased risk of hypertension and impaired renal function (4). Geographic factors and lack of cultural sensitivity also perpetuate these disparities.

Transplant listing

Disparities persist throughout evaluation and wait listing phases. Persons with low SES, minorities and other vulnerable populations who are often uninsured or publicly insured face delayed referrals (11) and higher rates of synthetic graft usage rather than fistula creation for dialysis access, resulting in higher rates of thrombosis and infection, higher rates of complications and longer hospital stays than others (4). Using objective health measures accounting for comorbidities, Epstein et al. (11) found more than twice as many whites as blacks were rated appropriate candidates for transplant (21% vs. 9%), indicating a clear gap in health status late in the transplant pipeline. Racial disparities persisted in patients clinically indicated for transplantation as well as those rated inappropriate through referral for transplant evaluation (98% whites vs. 79% blacks; 52% whites vs. 34% blacks); wait listing (87% whites vs. 71% blacks; 31% whites vs. 17% blacks); and transplantation (52% whites vs. 17% blacks; 10% whites vs. 2% blacks)(11).

Receiving a transplant

Though black patients with ESRD comprise over a third of the kidney transplant waiting list, they are 2.7 times less likely to receive a kidney transplant and are more likely to experience kidney failure post-transplantation than whites (16). Risk factors predicting disparities waiting list ascension and progression to transplant include: race and ethnicity, financial status, cultural beliefs, unemployment, lack of commitment to surgery, incomplete workups, and lack of continuous access to care (3,5,11). Another important factor determining transplantation lies in the physician's assessment of the patient's commitment to surgery and likelihood of adherence to the postoperative regimen. While differences such as high prevalence of comorbidities and disparities such as access barriers disproportionately preclude many patients from reaching this stage, patients who do may face additional discrimination. Numerous studies have documented physician bias in decision-making, particularly when evaluating patients of low SES, low literacy rates, higher age, and racial and ethnic minorities (17).

Transplant outcomes

While blacks face higher rates of ESRD and experience lower rates of transplantation, the half-life of renal allografts in blacks is 30% to 40% less than that of whites, and all-cause mortality is higher in blacks compared with whites after renal transplantation (3,10). Data from the Scientific Registry of Transplant Recipients (SRTR) found that black recipients exhibit the worst 5-year unadjusted graft survival rates, 62% compared to 72% in whites, 74% in Hispanics, and 78% in Asians (9). Poorer graft survival is related to immunologic and nonimmunologic factors (3). In a single center report over three eras (1987-1995, 1995-1998, 1998-2004), Eckhoff showed that black recipients had consistently worse graft survival rates, even after normalizing for 20 risk factors. While all groups experienced improvements in graft survival, black patients lagged behind. Improvements in immunosuppression have overcome many immunologic barriers mitigating racial differences in early graft survival rates, but not in long-term graft survival rates (3). While

Eckhoff (3) suggests that SES and compliance underlie late graft loss in black patients, this area is poorly understood and should be explored in depth.

Points of intervention

Although government initiatives (Healthy People 2010) and funding sources (e.g. NIH, National Center on Minority Health and Health Disparities (NCMHD) and HRSA) encourage interventions aimed at reducing disparities in transplantation and its precursors, few studies have been completed (4). Tailoring interventions to critical stages along the transplantation pathway should rely upon causal mechanisms, rather than associations well described in the literature. Interventions grounded in causality are more likely to improve outcomes while alleviating disparities. Though list of interventions below is targeted at critical points in the transplant pathway, they should be addressed in concert, as interventions taken at multiple points on the continuum are likely to have greater impact.

Progression from CKD to ESRD

Disparities in CKD and progression to ESRD stem from disproportionate distribution of disease burden from hypertension and diabetes. Interventions targeted at obesity, improved communication, and compliance with medication regimens show promise in limiting incidence of ESRD (18), and should be more aggressively applied to minority populations. Screening at-risk populations, ensuring timely intervention and referral to nephrologists, better monitoring of the quality (e.g. pay for performance) and universal availability of care are also important. Sequist et al. found that 88 % of surveyed physicians recognized racial disparities in diabetes care within the U.S. health care system, but less than half admitted ongoing disparities within their practice (19). Sequist also revealed that black patients experienced worse outcomes than whites within most physician panels, highlighting the need for increased awareness among individual physicians.

Transplant listing

Blacks were less likely to be listed than whites, even after adjusting for differences in sociodemographic characteristics and health status (4). This racial gap did not narrow over time and was greatest for the youngest and healthiest black patients, who were 50% and 40% less likely to be listed than whites, respectively (20). Interventions should be targeted towards young and healthy blacks who are most likely to benefit from transplantation, while not ignoring other age categories. Vulnerable populations may benefit from aggressive case management to ensure efficient evaluation.

Improving interpersonal communications between physicians and patients may reduce differential listing. Van Ryn and Fu suggest that providers contribute to health disparities by differentially encouraging health promotion and disease prevention and differentially assessing treatment options (21). Evidence suggests that black dialysis patients are less likely than whites to be told about transplantation, complete an evaluation, and discuss the possibility of live donation (22). Ashton et al. examined communication between providers and minority patients and concluded that poor communication is associated with health disparities and requires specific interventions to improve communication patterns (23). The successful impact of interpersonal communication through the use of lay health advisors and community health workers is well documented, suggesting that integrating health communication in both formal to informal contexts could alleviate some disparities (24). Research demonstrates benefit from tailoring culturally-sensitive health messages and targeting vulnerable populations.

Incomplete pre-transplant evaluations present a greater barrier to renal transplantation for blacks with ESRD than for whites. Patients with instrumental social support networks

(number of friends or family to help with daily activities) are significantly more likely to complete the transplant evaluation (25). Future studies should examine clinical interventions supplementing social support networks thereby improving access to the waiting list.

Receiving a transplant

Live donor kidney transplantation (LDKT) is associated with superior graft and patient survival rates, particularly pre-emptive transplant, and is more cost-effective than long-term dialysis or deceased donor kidney transplantation. However, of patients who received LDKT in 2007, 66% were white and only 15% were black (9). As a result black patients are listed on the deceased donor waiting list where one-third of all deaths are in blacks, in part due to longer waiting times necessitating longer periods of dialysis, poorer QOL, and higher health care costs. Rodrigue et al. demonstrated effectiveness of home-based educational interventions involving the patient's social network, resulting in increased number of living donor inquiries, evaluations, and LDKTs among blacks (22). Increased survival for blacks on dialysis may support subtle biases among physicians that transplantation does not afford as great a benefit to survival in blacks, contributing to low transplant rates (26). More efforts to educate physicians and patients about the benefits of transplantation in black patients are crucial.

Transplant outcomes

Though many immunological barriers to successful transplantation in blacks have been overcome leading to similar short-term graft survival rates, diminished long-term graft survival rates in blacks remain, potentially due to poorer SES and compliance. Interventional research to improve outcomes and reduce disparities post-transplant has been largely neglected. However, as outlined above, likely areas to for improvement include clinician education and increased awareness of disparities in outcomes, increased training in effective clinician-patient communication, engaging social support networks to reduce noncompliance, assuring financial resources for medications, and monitoring compliance as part of quality improvement..

Conclusions

Differences and disparities in the diseases and care of patients with CKD and ESRD have been well documented, as exemplified by the case of racial disparities above. Increased attention to health disparities places the onus on the transplant community to understand distinctions between differences and disparities, and act to identify and mitigate disparities. While a gap in disease burden may persist due to biological variation between various populations, we are compelled to address the portion of the health gap rooted in systemic disparities.

Refocusing future research on understanding the entire transplant process is critical, as many factors most predictive of disparities occur early in the causal pathway and can have downstream impact. Factors consistently correlated with widespread differences and disparities in CKD and ESRD prevalence, kidney transplantation frequency, and post-transplant outcomes include: race and ethnicity, SES, age, gender, insurance status, employment status, geography and disability (12,15). Literacy, language, religion, immigrant status, and housing status present additional factors thought to influence disparities, although research surrounding the role of these factors in transplant disparities is sparse. Currently it is unknown whether navigating the transplant process is similar to a pipeline, in which the chances of getting 'stuck' at each step are approximately equal, or whether the process resembles a funnel, in which large segments of the population get trapped at early stages, and the remaining few travel without much difficulty through the rest

of the process. Better understanding these gaps and the influence of interventions in addressing specific barriers along the pathway will improve our ability to alleviate disparities in CKD, ESRD, and transplantation.

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Figure 1.
Framework for Disparities in Transplantation

Table 1

Examples of Differences and Disparities Along the Continuum of Care from Chronic Kidney Disease to Kidney Transplantation

	Differences	Disparities
CKD prevalence	Higher prevalence due to genetic predisposition	Higher prevalence/ increased severity/ poorly controlled CKD due to environmental factors, e.g. lack of access to care, lack of affordable nutritional options, etc.
Waiting list times	High prevalence of comorbidities precluding suitability for transplant due to genetic predisposition; fewer minority patients opting for surgery due to religious beliefs	Environmental and behavioral components of comorbidities; physician bias in referral and listing; incomplete work-ups; lack of education surrounding transplant; low social and financial support
Low graft survival	Due to poor HLA matching; immunological differences	Poor compliance (due to lack of access, lack of information, lack of social support, financial difficulties); lower rates of live organ transplant; sicker at time of transplant; transplant of poor quality organs