

# Disparities in Care of Patients With End-Stage Renal Disease

## Review of Literature and Action Plan

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Disparities in access to care for patients with end-stage renal disease (ESRD) and particularly to kidney transplantation, as well as discrepancies in follow-up and outcomes have been extensively documented as they relate to race, ethnicity, gender, socioeconomic factors, urban/rural residence, and geographic region. Furthermore, these inequalities seem to be increasing in various parts of the world and it is imperative to develop policies to address them among various population groups, identifying factors that might provide improved care for all patients with kidney disease. Numerous studies from various parts of the world have demonstrated racial, ethnic, and geographic differences regarding the delivery of healthcare to patients with ESRD. To the author's knowledge, although this issue has been studied at transplant centers in Iran on an individual basis, it has not been extensively studied on a national scale. In this paper, the current world literature will be reviewed, with the goal of emphasizing the need to initiate and expand full-scale studies to detect and remedy any existing inequalities in Iran, a vast country with an ethnically, culturally, and economically diverse population. The author proposes the designation, at the national level, of a task force to study disparities and to provide insight into the means of correcting them. As Iran continues to attain a position of regional leadership in the realm of organ transplantation, it seems prudent to invest in research aimed at detecting and remedying any inequalities in the provision of equivalent and just care for patients with ESRD.

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### INTRODUCTION

Advances in surgical techniques, immunology, and pharmacology have led to significant improvements in outcomes of kidney transplantation. However, not all populations have benefited equally from these advances. Disparities in access to the kidney transplant waiting list, waiting times, follow-up, and outcomes have been extensively documented as they relate to race, ethnicity, gender, socioeconomic factors, urban/rural residence, and geographic region. Unfortunately, these inequalities seem to be increasing in various parts of the world.<sup>1,2</sup>

Disparities in healthcare have been labeled as covert *institutionalized racism*,<sup>3</sup> and minimizing

inequality in access to health, particularly in the form of allocation of scarce resources, should be considered an ethical obligation of healthcare planners and the medical profession. It is therefore imperative to develop policies to address the discrepancies in the treatment of end-stage renal disease (ESRD) among various population groups and to identify factors that provide improved care for all patients with kidney disease. A detailed insight into socioeconomic and environmental factors that might contribute to disparities in healthcare delivery to patients with kidney disease will be critical in formulating rational strategies to remedy these inequalities.

Numerous studies from various parts of the world have demonstrated the presence of racial, ethnic, and geographic differences regarding the delivery of healthcare to patients with ESRD. To the author's knowledge, although this issue has been studied at transplant centers in Iran on an individual basis,<sup>4-8</sup> it has not been extensively studied on a national scale. It is the author's conviction that although access to health care is theoretically universal in Iran, there are both a deficit in coverage and disparity in the access to renal replacement therapy, largely as a result of individual socioeconomic limitations and budget constraints, as well as issues such as distance from dialysis units and transplantation facilities.

In this paper, current world literature will be reviewed, with the goal of emphasizing the need to initiate and expand full-scale studies to detect and remedy any existing inequalities in Iran, a vast country with an ethnically, culturally, and economically diverse population.

### TYPES OF DISPARITIES

Inequalities in healthcare delivery to patients with ESRD have been studied in relation to race, ethnicity, gender, economic factors, and geographic location. These disparities take on various forms such as timing of initiation and type of renal replacement therapy, adequacy of dialysis, anemia management, and the use of catheters and grafts rather than fistulas. There have also been documented discrepancies in referral for home dialysis modalities and transplantation, delayed wait-listing for kidney transplantation, and inequalities in access to quality organs. The net effect has translated into disparities in outcomes.

#### Racial Disparities

Racial disparities are among the best-studied examples of inequalities in healthcare delivery. In the United States, it is known that minority groups experience decreased access to kidney transplantation. The majority of the literature regarding racial inequalities has addressed various aspects of the topic as it relates to African-American patients with ESRD. Compared with the white population, African-American patients remain longer on the waiting list, are less likely to undergo transplantation, and are more likely to receive lower-quality organs.<sup>9</sup> In one study,

African-American patients in rural areas were less likely than any other subgroups (African-American urban, white urban, white rural) to be transplanted.<sup>10</sup> Significant racial differences have also been noted among pediatric patients with ESRD in the number of preemptive transplants and type of the graft received.<sup>11</sup> Excluding living donor transplantations, black children were less likely to be wait-listed at any given time during the follow-up.<sup>12</sup>

In addition to black patients, Hispanic, Asian, and native Americans also have higher risks of ESRD, compared to the white population.<sup>13,14</sup> Although Hispanic and native Americans have similar referral rates for kidney transplantation as whites, they are less likely to be placed on a transplant waiting list or receive a transplant.<sup>15</sup> Asian-Americans have a decreased likelihood for transplant referral,<sup>16</sup> and kidney transplantation.<sup>17</sup> They are also more likely to receive lower-quality organs.<sup>9</sup>

Racial disparities in transplantation have also been documented in other parts of the world. In Canada, the adjusted overall transplantation rates are lower in comparison with whites for aboriginals, blacks, and Asians. Race has been found to be at least as a strong predictor of transplantation as other known predictors, such as age, sex, primary renal diagnosis, and comorbidities. Racial inequalities in kidney transplantation rates in Canada have shown an increasing trend from 1990 to 1998 for all racial groups in comparison with whites.<sup>2</sup> In Australia, while there is a higher incidence of ESRD among the indigenous population,<sup>18</sup> they experience a much lower transplantation rate, with both a lower rate of acceptance onto the waiting list and a lower rate of moving from the list to transplantation. These disparities are not explained by differences in age, sex, comorbidities, or cause of the kidney disease and are thought to be secondary to barriers to acceptance onto the waiting list and to moving from the list to transplantation.<sup>19</sup> Nearly, half of these patients are from remote regions with inadequate services for patients with kidney disease.<sup>18</sup> In the United Kingdom, existing data indicates a disparity between the Asian residents and the rest of the population in transplantation rates.<sup>20</sup>

#### Gender Disparities

Inequalities in kidney transplantation rates between the genders have been well studied. Female

sex is associated with a decreased likelihood for transplant referral and women are less likely to be placed on the waiting list than men,<sup>16,21</sup> but similar with regard to quality of the transplanted organ.<sup>9</sup> The most striking component of the gender inequity in kidney transplantation is the disproportionately higher female donation rate, with an overall higher female-to-male and lower male-to-female kidney donations.<sup>22</sup> In a study of 1319 living donations in Norway, the majority of the donors were women, while the majority of the recipients were men. In parental donations, for recipients younger than 30 years of age, both parents were similarly likely to be donors. However, for recipients older than 30 years, mothers were more likely to be donors. In spousal kidney donations, women were more likely to be donors.<sup>23</sup> In another study of 30 258 living donor transplants, women comprised 68% of spousal and 56% of related and unrelated nonspousal donors. There were more often female-to-male donations among all three categories of living related, unrelated nonspousal, and spousal pairs; the most favorable graft survival has been observed among male recipients of male donor kidneys.<sup>24</sup> When spousal pairs are excluded from the analysis, there is a higher proportion of male-to-male donations and a lower proportion of male-to-female and female-to-female transplants in the living unrelated donor group.<sup>25</sup> Interestingly, one study has found a recent decrease in the gender differences in kidney donation, attributed to the introduction of laparoscopic donor nephrectomy.<sup>22</sup> In Iran, in contrast to a previous report,<sup>5</sup> more recent comprehensive studies has concluded that the majority (78% to 81%) of unrelated donors are men.<sup>6,7</sup>

### Geographic Disparities

Geographic differences in the rate of transplantation have been studied in various parts of the world. In the United Kingdom, there is significant geographic variation in median waiting time to transplantation and this has been attributed to regional differences in the prevalence of the underlying kidney disease and donation rates.<sup>26</sup> In France, transplantation rate is highest in the West and lowest in the Paris region.<sup>27</sup> In Switzerland, regional variations in the rate of kidney transplantation have also been reported.<sup>28</sup> In Australia, while the incidence of ESRD in some

regions, inhabited predominantly by the indigenous population, is up to 30 times higher than the incidence for all Australians,<sup>18</sup> the chance of being on the waiting list in these regions is half of the chance in other regions.<sup>29</sup> In the United States, a high degree of variability has been reported among regional allocation networks with regard to donor quality.<sup>9</sup>

Although one-fifth of the United States population is rural, surprisingly little is known about the characteristics and outcomes of rural patients with ESRD. O'Hare and colleagues measured the association of rural residence with survival, and time to transplant among 552 279 patients with ESRD. They found rural patients on dialysis to be older, less racially diverse, and with a higher prevalence of comorbid conditions. They also found that the use of peritoneal dialysis was more frequent in rural areas compared to urban areas, despite the fact that rural facilities are markedly less likely to offer peritoneal dialysis or home hemodialysis training than urban centers. Based on the standard performance measures, rural dialysis facilities tend to perform at least as well as urban facilities.<sup>10</sup>

### STUDIES OF DISPARITIES IN OUTCOME

Disparities in care have been clearly demonstrated to adversely affect outcomes of transplantation. Studying variations in outcomes and understanding the underlying mechanisms will assist in identifying risk factors in various populations for kidney disease and will be helpful in improving predialysis care and kidney transplantation among these populations.

Graft survival in African-American patients is significantly lower than that in all other ethnic groups, independent of genetic matching,<sup>30</sup> and even in a universal access-to-care system such as the Veterans Administration system.<sup>31</sup> In an analysis of 14 617 patients in the United Network for Organ Sharing Registry, Isaacs and coworkers found that blacks were 1.8 times as likely as whites to suffer from graft failure during the 9-year study period.<sup>32</sup> In another study, while the 5-year graft survival was better among whites, there were no racial differences in patient survival and the degree of posttransplant quality of life improvement.<sup>33</sup> The cumulative incidence of graft failure is higher among African-Americans and Hispanics than

that among whites (77% versus 64% versus 60%;  $P < .001$ ) and among transplant recipients living in the poorest areas (70% versus 58% in the richest;  $P < .001$ ). African-American and Hispanic race/ethnicity are independently predictive of graft failure (risk ratios, 1.8 and 1.3, respectively) in multivariate analyses.<sup>34</sup> Among the United States' Asians, mortality on dialysis is lower compared to that in white individuals.<sup>14,17</sup> Of note, despite barriers to access to kidney transplantation, once transplanted, native Americans and Alaskan natives have comparable survival rates to white Americans.<sup>35</sup>

In countries of the European Union, considerable regional disparities in the incidence of ESRD and outcomes have been observed. The incidence of patients with new-onset ESRD follows a clear north to south/west gradient (lowest in Ireland, highest in Italy and Germany). Furthermore, the incidence of ESRD deaths is lowest in Ireland and highest in Germany.<sup>36</sup> In France, posttransplant mortality is highest in the Southeast and lowest in the West.<sup>27</sup>

#### POSSIBLE EXPLANATIONS FOR DISPARITIES

There are multiple complex barriers to timely diagnosis and optimal therapies for kidney disease as well as delayed referral for kidney transplantation among the disadvantages. All of these have led to disparities in the care of the patient with kidney disease. The barriers have been classified into 2 broad categories: patient-related and provider-related barriers. Patient-related barriers include biological factors (genetics/human leukocyte antibody [HLA] typing, differential pharmacokinetics, and underlying disease) and socioeconomic factors (income, educational level, personal and cultural beliefs about transplantation, and geographic location). Barriers which relate to healthcare providers include physician perceptions about posttransplant survival of minorities, inadequate transplant workup, and possible racism.<sup>37</sup>

#### Patient-related Barriers

**Biological Factors.** There is fairly consistent evidence that the higher prevalence of chronic kidney disease among the underserved and minority populations is largely due to disproportionate prevalence of underlying etiologies of chronic

kidney disease, such as diabetes mellitus and its microvascular complications, hypertension, systemic lupus erythematosus, and human immunodeficiency virus-associated nephropathy. All of these diseases are particularly prevalent among certain races and ethnicities, such as the African-American patients,<sup>13</sup> native Americans, and Alaskan natives.<sup>35</sup> With respect to gender inequities, the higher incidence of ESRD among men and the slight predominance of women in the general population do not adequately explain gender disparities in transplantation.<sup>24</sup> A pervasive explanation for gender differences in kidney transplantation is the higher proportion of wife-to-husband donations and a lower incidence of male-to-female donations among nonspousal living unrelated donor transplants.

It has been proposed that disparities in transplantation rate among minority populations are not totally due to socioeconomic factors, and that they are at least partially due to the fact that these populations are "competing" in HLA matching against the predominant majority pool. In one study, it was shown that regardless of insurance status, disparities in waiting list time and kidney transplant rates exist for blacks and native Americans.<sup>30</sup> It has also been demonstrated that even in a setting of uniform medical care coverage, there is an elevated incidence of ESRD among ethnic minorities, suggesting a possible genetic origin, the contribution of unmeasured environmental factors, or a combination of these factors.<sup>38</sup> In addition, racial differences in pharmacokinetic of immunosuppressive drugs and the predominant independent effect of race and ethnicity on weight gain have been implicated in ethnic disparities in the rates of kidney transplantation and graft outcome.<sup>39,40</sup>

While biological and genetic explanations for disparities are fairly popular in the United States, at least 1 study in France has concluded that the observed racial differences are not totally explained by immunologic and pharmacologic factors. Pallet and colleagues studied the association of race and ethnicity with graft outcomes in a French population of 952 Caucasian patients and 140 African-Europeans who underwent kidney transplantation in a single center. They concluded that ethnic origin does not affect outcome after kidney transplantation in France, as it does in the United States.<sup>41</sup>

**Socioeconomic Factors.** The effects of socioeconomic status and the interaction with race and ethnicity, as related to disparities in transplantation are very complex. The increased risk of graft failure among African-American recipients has been found to be independent of genotypic and phenotypic HLA matching, suggesting that non-HLA mechanisms may contribute to racial differences in transplantation outcomes.<sup>32</sup> It has been clearly demonstrated that providing greater health insurance to low-income patients with ESRD will lead to improved transplantation rates.<sup>42</sup> However, while lack of private insurance and unemployment have been associated with poor graft outcome, the absence of economic barriers has not led to a reduction in disparities in the access to kidney transplantation.<sup>43</sup>

Cultural and sociodemographic differences that lead to racial variation in the choice of ESRD modality have been well-recognized. Various ethnicities and cultures cope with the need for a kidney transplant differently. One study has found the African-American to be more likely to deny the need for a transplant and less likely to be accepting of their chronic illness. This may influence their perception of the need for transplantation and their willingness to ask for live donations.<sup>1</sup> In the United Kingdom, differences in donation rates and particularly the relative reluctance among the Asian community to volunteer as donors have been implicated as potential reasons for racial disparities.<sup>20,26</sup>

Among the reasons for geographic disparities, regional variations in underlying disease have been cited in the United Kingdom and Switzerland.<sup>26,28</sup> In France, regional differences in the background of transplant teams, the extent of activity of the organ procurement organization and severity of comorbidities of the patients on the list are considered as potential explanations for regional disparities in transplantation and outcomes.<sup>27</sup> Rural and isolated locations pose particularly difficult problems for the provision of adequate care to patients with kidney disease. Distance and road conditions make traveling to facilities difficult for the patients and also lead to difficulty in recruiting and retaining staff in remote areas, particularly if there are language and cultural differences, as well.

### Provider-related Barriers

Factors relating to provider perceptions and preferences are highly important contributors to disparities in care. Among patients considered to be appropriate candidates for transplantation, black patients have been found to be less likely than whites to be referred for evaluation or to undergo transplantation. At the same time, among patients classified as inappropriate candidates, whites are more likely to be referred for evaluation, to be listed, and to ultimately undergo transplantation.<sup>44</sup> Various explanations have been offered by physicians as important reasons why minority patients are less likely to be evaluated for transplantation. These have included patients' preferences, availability of living donors, failure to complete evaluations, and comorbid illnesses. Other factors that have been cited include differing patient-physician communication and trust, as well as physician bias in identification and referral of transplant candidates.<sup>45</sup> Ironically, improved survival and quality of life for black patients with ESRD on dialysis may also have led to delayed referral for transplantation.

### CONCLUSIONS AND RECOMMENDATIONS

Disparities in access to care, particularly for kidney transplantation, among patients with ESRD and inequities in outcomes are prevalent and unfortunately seem to be increasing in most parts of the world where they have been studied.

Disparities represent a complex interplay of genetic, socioeconomic, cultural, and environmental influences. This has made it difficult to target a single factor. Minimizing these inequalities and developing policies to address these discrepancies should develop into an ethical priority for healthcare planners and the medical profession.

In the realm of organ transplantation, with regard to the quality of surgical and medical care, Iran has assumed a leading role in the region. Considering the national philosophy of healthcare for all, it now seems prudent to invest in research aimed at detecting and remedying any inequalities in provision of equivalent and just care for patients with ESRD. The author proposes the designation, at the national level, of a task force to study disparities. This team will utilize the combined resources of the Ministry of Health and Medical Education, the authorities responsible for planning and budgeting,



the Iranian Academy of Medical Sciences and the Iranian Society of Nephrology, which are all well prepared to conduct basic epidemiologic research as well as economic and outcomes studies. The first step in developing policies to attempt correction of disparities is to collect evidence, with the purpose of improved understanding of the barriers to access. A necessary component of the identification phase will be fulfilled by including as many variables as possible in the dialysis and organ transplant registries (ethnicity, education, socioeconomic factors, and other demographic parameters). Detailed studies are required to identify reasons for poor access to transplantation and to systematically examine each of the steps a new patient on dialysis must navigate in order to receive a transplant. Each of these steps is a potential barrier. Once these disparities have been identified, future work should focus on identifying measures to correct them, some of which have been outlined below:

- Enhanced understanding of physicians' views about differences in access to transplantation and continued development of practice parameters that would preclude or diminish disparities in health care decisions.
- Establishment of non-hospital-based free-standing dialysis units in fairly remote areas, modeled after the native American *reservation-based* dialysis services, may lead to an improvement in the access to renal replacement therapy.<sup>35</sup>
- Resource allocation should have the goal of improving access to care and survival for all individuals at risk for kidney disease, independent of ethnicity, geographic location, or socioeconomic status.
- Gender disparities are highly likely to be identified. If so, it would seem prudent to devise protocols and procedures to promote male organ donation.

The ultimate goal will be to slow progression of kidney disease among all populations, regardless of ethnicity, economic status, and geographic location. This may be achieved by early detection and referral, improved therapeutic alliance between referring nephrologists and the transplant teams, community-based campaigns for promotion of healthy habits and diet, as well as preventive strategies based on pharmacologic interventions,

blood pressure and lipid control, and an increase in the rates of transplantation through improved organ procurement.

#### CONFLICT OF INTEREST

None declared.

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