Ethnicity and Renal Replacement Therapy

John Feehally

John Walls Renal Unit, Leicester General Hospital, and Department of Infection, Immunity and Inflammation, University of Leicester, Leicester, UK

Nevertheless, reduction of the varied and substantial inequities faced by ethnic minority populations with kidney disease is an important responsibility for the renal community.

Key Words
Ethnic minorities • Renal replacement therapy • Haemodialysis • Peritoneal dialysis • Renal transplantation

Abstract
There are significant ethnic variations in the incidence of kidney disease. White European populations appear to be uniquely protected compared to increased incidences of end-stage renal disease in indigenous and migrant ethnic minority populations. This increase is partly explained by a high prevalence of diabetic nephropathy, but there is also an increased susceptibility to a range of other renal diseases. The relative contributions of genetic, environmental and fetal environmental factors to this susceptibility are not yet well understood. Strategies for early detection and management of chronic kidney disease to delay progression are particularly critical in countries where access to renal replacement therapy (RRT) is restricted. In developed countries with wide availability of RRT, resources to provide dialysis will need to be increased in regions with substantial minority populations. There is apparently counterintuitive evidence that survival on dialysis is increased in many minority populations. Access to renal transplantation, both from deceased and living donors, is also restricted in many minority populations, and graft survival is often inferior. Analysis of the explanations for these differences is complex because of the many confounding factors (for example cultural, social and economic) which typically cosegregate with ethnicity.

Introduction
People from indigenous or migrant ethnic minority populations have increased susceptibility to chronic kidney disease (CKD). This offers many challenges:

• for researchers in understanding the complex processes which underlie this susceptibility;
• for clinicians seeking to prevent or delay the progression of CKD in an individual patient, and optimising renal replacement therapy (RRT) when it is unavoidable;
• for those responsible for organising, delivering and meeting the cost of the increased demands for RRT in areas serving minority populations.

While it is pragmatically necessary to make broad categories of ethnicity to purposes of epidemiology and clinical research in this field, it is also important to appreciate that within any grouping such as African or South Asian there are populations with enormous variety of culture, religion, education and socio-economic circumstances which makes the interpretation of causal relationships complex.
Epidemiology

Migration of populations across the world continues to increase. This has led to an increasing variety of ethnic minority populations in many countries, some of which also have minority indigenous populations. Minority populations are often geographically localised. For example, ethnic minorities are 9% of the UK population, but in the city of Leicester, the population originating from South Asia has rapidly increased to more than 50% of those living within the city boundary.

Such minority populations present challenges to health care. Even if they had no variations in disease prevalence, substantial language and cultural variations can provide additional demands on the health care system, and these are most difficult in long-term conditions such as CKD. But in fact, there are many disease variations in minority populations, not least an increased incidence of type 2 diabetes and progressive CKD. Furthermore, recent migrant populations typically have a younger age distribution than the indigenous population so that diseases such as CKD, which increase in incidence with increasing age, will at first be underrepresented compared to the eventual population burden as the minority population ages.

The incidence of CKD is increased in many ethnic minority populations. There is a 3- to 4-fold increase in the incidence of end-stage renal disease (ESRD) in South Asian and African Caribbean populations in the UK [1], and there are similar increases in African Americans, Hispanics and Native Americans in the USA [2]. Other populations at increased risk include Aborigines, Maoris and Pacific Islanders in Austraslia. Most studies have used the onset of ESRD and acceptance for RRT as a means of case ascertainment, but this approach might underestimate the true incidence if patients have inequity of access to RRT. It is common to emphasise the increased susceptibility to ESRD in these ethnic minority populations; but perhaps we should instead consider that the white European population seems uniquely at low risk of renal disease. This decreased risk could have a genetic basis or may reflect environmental factors, such as the very gradual urbanisation in most Caucasian European populations compared to the very rapid recent urbanisation in many developing countries.

In more homogeneous populations, the incidence of ESRD is even more strikingly increased. While the Pima Indians have a specific susceptibility to diabetic nephropathy [3], Native Americans of the Zuni Pueblo tribe – with an incidence of ESRD 18 times that of white Americans – have a broader susceptibility to CKD including diabetic nephropathy and glomerulonephritis [4]. The Aborigine population in Tiwi Island, Northern Territory, where obesity and type 2 diabetes are endemic, has an ESRD incidence of more than 2,000/million population/year; comprising only 26% of the population of Northern Territory, Aborigines are 96% of those undergoing RRT [5].

All these ethnic minority populations at increased risk of CKD share a marked increase in susceptibility to type 2 diabetes and an increased susceptibility among diabetics to ESRD. For example, data from Leicester, UK, indicated a 13-fold increase in the risk of a South Asian diabetic developing ESRD compared to a white diabetic [6], the Pima Indians have a risk of ESRD 14 times that of the white US diabetic population [7], and there is also a marked increase in African American type 2 diabetics compared to whites. In many populations severe hypertension adds to the risk for ESRD. Current predictions suggest an increase in the prevalence of type 2 diabetes of at least 30% above current levels by the year 2025 in developed countries, but 2- to 3-fold increases in prevalence in developing countries during the same period [8]. This predicted epidemic of ESRD in people with diabetes will be uncontainable unless effective preventive strategies are developed.

Studies using requirement for RRT for case ascertainment will not distinguish susceptibility to the development of renal disease from an increased risk of progression to ESRD once nephropathy is established. In hypertensive blacks, there is long-established evidence of an increased progression risk despite equivalent blood pressure control [9]. In CKD of other aetiologies, evidence increasingly points to the increased risk of progression as the predominant explanation for increased ESRD. A US birth cohort analysis showed no difference between blacks and whites in the prevalence of CKD, yet 5 years later in the same cohort, a near 5-fold increased risk of ESRD among the blacks was apparent [10]. Recent UK data also show no difference in the prevalence of early CKD between white and South Asian populations despite the marked excess of ESRD in South Asians.

Pathogenesis

Genetic susceptibility to renal diseases and their progression, susceptibility provoked by environmental factors, susceptibility induced by the effects of fetal environment and socio-economic influences all can contribute to susceptibility to CKD in ethnic minority populations [11].

Blood Purif 2010;29:125–129

Feehally
One particular challenge is separating the influence of ethnicity from that of socio-economic disadvantage, two major factors which so often cosegregate. Socio-economic disadvantage is itself associated with an increased risk of ESRD [12], a complex interaction that might directly influence renal damage, be associated with damaging health behaviours or influence the quality of health care of those with kidney disease.

**Preventing Progression to ESRD**

There is much work needed to unravel the contributions of these various pathogenic mechanisms, but in the meantime there are opportunities to prevent CKD in high-risk populations and to detect CKD early, intervening to delay its progression. If such opportunities are grasped, they may not only benefit the individual, but offer significant health system economies if they avoid the cost of RRT, and of course are critically important in health economies where RRT is unavailable or unaffordable.

But such opportunities to turn the tide of ESRD will not be grasped if those at risk are not engaged by the health care system or are unresponsive to our recommendations. Minority populations may lack the awareness or health education to engage, and programmes which approach these problems must be designed with cultural sensitivity.

In the USA, considerable evidence points to blacks having inferior access to health care. Blacks report receiving less information about health care and express more dissatisfaction with their treatment [13]. Fewer black hypertensive patients have their blood pressure checked at least annually. These differences are reported at all income levels, although blood pressure control might be more unsatisfactory among blacks living in inner cities [14]. The only similar study in the UK shows a more reassuring trend for earlier referral of blacks with CKD compared to whites [15].

**Outcome of RRT in Ethnic Minority Populations**

In health care settings where RRT is available, it is important that RRT be delivered with equity in ethnic minority populations. The proper assessment of equity requires evaluation of mortality, morbidity and quality of life, if care is to be optimised.

In the USA, mortality in patients receiving RRT (adjusted for socio-economic factors and comorbidity) is consistently lower in ethnic minorities [16]. The UK Renal Registry reports a significant reduction in 1-year mortality for blacks and South Asians undergoing RRT [17]. In Hong Kong, survival of Chinese patients undergoing peritoneal dialysis (PD) is significantly better than that reported in other large PD studies involving predominantly white populations [18]. The reasons for these discrepant outcomes are likely to be complex; ethnicity itself might not be the explanation, and many other factors might introduce bias. For example, 80% of all dialysis patients in Hong Kong are undergoing PD compared to the predominance of haemodialysis in the USA. A low patient acceptance might also alter the case mix; only 54% of Hong Kong Chinese identified as suitable for PD agreed to receive the treatment [19]. A low transplantation rate, as in Hong Kong, might also lead to younger, fitter patients remaining on PD, thus improving the cohort outcome. The improved survival may also reflect survival advantage, the individuals with the highest risk having not survived to commence RRT.

Improved survival on haemodialysis is found in African Americans despite other factors expected to reduce survival, including non-adherence to treatment regimens, increased use of dialysis catheters and higher requirements for erythropoietin [20].

**Renal Transplantation**

Registry data from several parts of the world including the UK and the USA show lower rates of transplantation in ethnic minorities which may represent inequity of access. Ethnic minorities are overrepresented in dialysis programmes but less likely to be listed for deceased-donor transplantation, wait longer and are less likely actually to be transplanted [21]. Ethnic minority populations are more likely to receive poorly matched kidneys, since they are underrepresented among deceased donors. Graft survival is also reduced in minorities in the USA, and in both blacks and South Asians in the UK [21, 22]. But the most disadvantaged patients of course are eligible patients who are never transplanted, whether with a deceased-donor or living-donor kidney.

Promotion of living-donor transplantation is a key element in strategies for minimizing inequity of access to transplantation. A study from Baltimore, USA, showed that a decade of active encouragement of volunteerism led to the same living-donor transplant rate in blacks as whites, with equivalent patient and graft survival, and median waiting times below the national average [23].
novative approaches to living-donor transplantation, for example strategies aimed at transplanting across AB0 incompatibility barriers, might also assume special importance. US physicians, when asked why ethnic minority patients were referred less frequently for transplantation, most commonly cited the lack of a potential live donor, patient preference, comorbidity or concern that patients did not complete necessary evaluations [24]. While living-donor transplantation is the optimal RRT for many patients, donor selection needs special care in populations which typically have a high incidence of familial renal disease.

The shortage of deceased donors from ethnic minority populations is a continuing concern. In the UK, South Asians and blacks only contribute 1.5% of the total donor pool yet comprise 6% of the general population and 19% of patients on the deceased-donor transplant waiting list. The reasons underlying this shortfall have been extensively explored with these communities, and programmes are in place to improve donor rates by awareness and education, although progress is slow.

An adverse effect of the relative difficulties in identifying appropriate deceased donors for minority populations has been the surge of ‘transplant tourism’ for those with resources to ‘buy’ a living-unrelated-donor kidney, a practice condemned by the international renal community through the Istanbul Declaration [25].

**Public Health Implications**

Although exploration of the mechanisms that underlie susceptibility to renal disease in these populations is of the utmost importance for the future, there is a pressing worldwide health care challenge that will accelerate at a faster pace than fundamental research can head off. In the UK, the overall age-adjusted relative risk remains more than 3-fold in both the South Asian and African Caribbean populations, and this risk might be increasing. The younger age distribution of the ethnic minority population means even larger future increases in the demand for RRT. Estimates of need are based on the presumption that current acceptance rates are a true reflection of demand; this might not be the case if there is inequity of access to health care. Vigorous advocacy must continue if resources sufficient to deliver the required standards of care are to be made available where populations include large ethnic minorities. Indeed it must be recognised that the delivery of high-quality health care that is linguistically and culturally adequate for ethnic minorities will likely require additional resources compared to the resources needed for majority populations. Although intensive efforts at augmenting transplantation rates from both deceased and living donors must continue, a disproportionate requirement for dialysis facilities is unavoidable. In parallel, programmes for screening and early intervention must be introduced if the future RRT burden is to be restrained [29]. Priority must also be given to the long-term goals of understanding genetic and other factors influencing the susceptibility of ethnic populations to CKD if truly effective preventative strategies are to be achieved.
References

1 Lightstone L, Rees AJ, Tomson C, et al: High incidence of end-stage renal disease in Indo-Asians in the UK. Q J Med 1995;88:191–195.

2 US Renal Data System: USRDS 2008 annual data report: atlas of chronic kidney disease and end-stage renal disease in the United States, National Institutes of Health National Institutes of Diabetes and Digestive and Kidney Diseases, Bethesda, MD. 2008. www.usrds.org/adr.htm.

3 Nelson RG: Diabetic renal disease in transitional and disadvantaged populations. Nephrology 2001;6:9–17.

4 Shah VO, Scavini M, Stidley C, et al: Epidemic of diabetic and non-diabetic renal disease among the Zuni Indians: the Zuni Kidney Project. J Am Soc Nephrol 2003;14:1320–1329.

5 Hoy W: Renal disease in Australian Aborigines. Nephrol Dial Transplant 2000;15:1293–1297.

6 Burden AC, McNally PG, Feehally J, Walls J: Increased incidence of end-stage renal failure secondary to diabetes mellitus in Asian ethnic groups in the United Kingdom. Diab Med 1992;9:641–645.

7 Nelson RG, Newman JM, Knowler WC, et al: Incidence of end-stage renal disease in type 2 (non-insulin-dependent) diabetes mellitus in Pima Indians. Diabetologia 1988;31:730–736.

8 King H, Aubert RE, Herman WH: Global burden of diabetes, 1995–2025: prevalence, numerical estimates, and projections. Diabetes Care 1998;21:296–309.

9 Rostand SG, Brown G, Kirk KA, et al: Renal insufficiency in treated essential hypertension. N Engl J Med 1989;38:1696–1699.

10 Hsu CY, Lin F, Vittinghoff E, Shlipak MG: Racial differences in the progression from chronic renal insufficiency to end-stage renal disease in the United States. J Am Soc Nephrol 2003;14:2902–2907.

11 Buck K, Feehally J: Diabetes and renal failure in Indo-Asians in the UK – a paradigm for the study of disease susceptibility. Nephrol Dial Transplant 1997;12:1555–1557.

12 Cass A, Cunningham J, Snelling P, et al: Exploring the pathways leading from disadvantage to end-stage renal disease for indigenous Australians. Soc Sci Med 2004;58:767–785.

13 Powe N: Nephrology forum: to have and have not – health and health disparities in chronic kidney disease. Kidney Int 2003;64:763–772.

14 Kotchen JM, Shakoor-Abdullah B, Walker WE, et al: Hypertension control and access to health care in the inner city. Am J Public Health 1998;88:1696–1699.

15 Steel J, Ellis P: Do demographic variables affect the timing of referral to a nephrologist? EDTNA ERA J 2002;28:185–187.

16 Frankenfield DL, Krishnan SM, Ashby VB, et al: Differences in mortality among Mexican-American, Puerto Rican, and Cuban-American dialysis patients in the United States. Am J Kidney Dis 2009;53:647–657.

17 Roderick P, Byrne C, Casula A, et al: Survival of patients from South Asian and Black populations starting renal replacement therapy in England and Wales. Nephrol Dial Transplant 2009, E-pub ahead of print.

18 Li PTK, Chow KM, Szeto CC: Is there a survival advantage in Asian peritoneal dialysis patients? Int J Artif Org 2003;26:363–372.

19 Lo WK, Li FK, Choy CBY, et al: A retrospective survey of attitudes toward acceptance of peritoneal dialysis in Chinese end-stage renal failure patients in Hong Kong – from a cultural point of view. Perit Dial Int 2001;3:S318–S321.

20 Obrador GT: Anemia of chronic kidney disease and end-stage renal disease: are there unique issues in disadvantaged populations? Ethn Dis 2009;19(suppl 1):S2–55.

21 Rudge C, Johnson RJ, Fuggle SW, et al: Renal transplantation in the United Kingdom for patients from ethnic minorities. Transplantation. 2007;83:1169–1173.

22 Feysa E, Jones-Burton C, Ellison G, Philosophos B, Howell C: Racial/ethnic disparity in kidney transplantation outcomes: influence of donor and recipient characteristics. J Natl Med Assoc 2009;101:111–115.

23 Foster CE, Philosophos B, Schweitzer EJ, et al: A decade of experience with renal transplantation in African Americans. Ann Surg 2002;794–804.

24 Ayanian JZ, Cleary PD, Keogh JH, et al: Physicians’ beliefs about racial differences in referral for renal transplantation. Am J Kidney Dis 2004;43:350–357.

25 The Declaration of Istanbul on organ trafficking and transplant tourism. International Summit on Transplant Tourism and Organ Trafficking. Kidney Int 2008;74:854–859.

26 Bakewell A, Higgins R, Edmunds ME: Does ethnicity influence perceived quality of life of patients on dialysis and following renal transplant? Nephrol Dial Transplant 2001;16:1395–1401.

27 Lopes AA, Bragg-Gresham JL, Satayathum S, et al: Health-related quality of life and associated outcomes among hemodialysis patients of different ethnicities in the United States: the Dialysis Outcomes and Practice Patterns Study. Am J Kidney Dis 2003;41:605–615.

28 Thomas CJ: The context of religiosity, social support and health locus of control: implications for the health-related quality of life of African-American hemodialysis patients. J Health Soc Policy 2002;16:43–54.

29 Lightstone L: Preventing Kidney Disease: The Ethnic Challenge. Peterborough, National Kidney Research Fund, 2001.