CHAPTER 12

BEYOND THE BIOMEDICAL PERSPECTIVE: HOW SOCIAL FACTORS DETERMINE RENAL DISEASE

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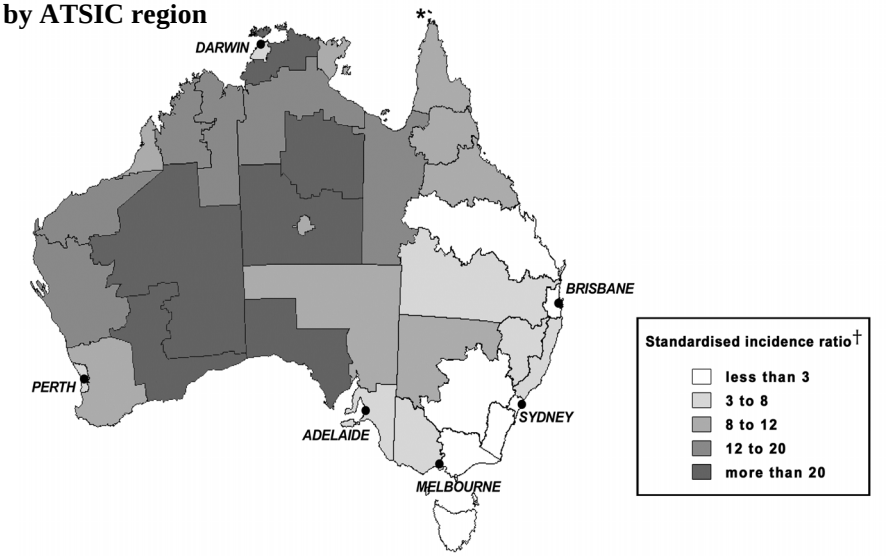
Introduction

Patterns of disease and of the utilisation of health services are significantly influenced by socioeconomic, environmental and cultural factors. Over the past three years, we studied data from the cohort of over 8,000 patients commencing renal replacement therapy (RRT) in Australia during 1993 to 1998. We explored mechanisms by which social factors might determine patterns of renal disease, with a focus on indigenous Australians.

We have explored regional patterns in the incidence of ESRD among indigenous and non-indigenous Australians;[1-3] the relationship between the incidence of ESRD and socioeconomic disadvantage;[1,3,4] the long-term effect of delayed referral to nephrology care on the outcomes of treatment of ESRD;[5] the relationship between delayed referral and socioeconomic disadvantage;[6] and indigenous Australians' access to renal transplantation, compared with that of non-indigenous Australians.[7] We have synthesised this and other research to propose a new explanatory model for the excess burden of renal disease in Australia's indigenous population.

Figure 12.1: Standardised incidence of ESRD in the Indigenous population by ATSIC region



* The standardised incidence ratio for the Torres Strait ATSIC region was 15.0. The region is too small to represent at this level of map resolution.

† The index population for standardisation was the total Australian resident population.

Figure 12.2

Correlation Between Indicators of Socioeconomic Disadvantage and Age, and Sex-standardised Incidence of ESRD For indigenous Australians for the 36 ATSIC Regions [a]

Socioeconomic Indicator (units)	Range	Correlation Coefficient	P Value
Early school leavers [b] (%)	12.5 - 52.4	0.68	<0.001
Unemployment rate [c] (%)	20.2 - 74.8	0.72	<0.001
Household income [d] ($AUS)	80 - 194	-0.71	<0.001
House crowding [e]	1.1 - 3.2	0.84	<0.001
Low birthweight [f] (%)	7.6 - 21.6	0.49	0.003
Summary rank of disadvantage [g]	1 - 36	0.88	<0.001

[a] Aboriginal and Torres Strait Islander Commission regions are legally prescribed administrative areas and are the smallest geographical areas for which accurate indigenous Australian population estimates are available (Australian Bureau of Statistics)
[b] The proportion of adults who left school aged 15 or less, or who did not attend school (Australian Bureau of Statistics)
[c] People employed through the CDEP scheme, a 'work for the dole' scheme targeted at indigenous communities, were classified as unemployed (Australian Bureau of Statistics)
[d] Median household income divided by the average number of persons per household - units are $AUS per household member per week (Australian Bureau of Statistics)
[e] The average number of persons per bedroom (Australian Bureau of Statistics)
[f] The proportion of births less than 2,500 grams (National Perinatal Statistics Unit)
[g] We combined the regional rankings on each indicator, with each indicator given equal weight, to derive a summary rank of disadvantage

ESRD incidence

There is marked regional variation in the incidence of ESRD among indigenous Australians.[2] ESRD occurs most commonly in remote regions, where it is up to 30 times the national incidence for all Australians (fig 12.1). Amongst indigenous Australians, area-based measures of disadvantage are strongly associated with regional incidence (Fig. 12.2).[1]

We have also demonstrated significant variation in incidence in the predominantly *non-indigenous* population of Australian capital cities.[3] There is a significant correlation ($r = -0.41$, $p = 0.003$) between ESRD incidence and the Index of Relative Socio-Economic Disadvantage, an index developed by the Australian Bureau of Statistics to describe the socio-economic characteristics of an area. The more disadvantaged capital city areas have a higher incidence of ESRD.

Delayed referral for nephrology care

Late referral to a nephrologist, defined in this research as needing commencement of dialysis within three months of referral, has been associated with increased early morbidity and with increased early mortality during treatment for ESRD. We examined the predictors of late referral,[8] the relationship between socio-economic disadvantage and late referral[6] and the influence of late referral on the long-term likelihood of either dying while on RRT or of receiving a transplant.[5]

Indigenous ESRD patients were more likely to be referred late (39.9% v. 26.1%, $p<0.001$). The proportion of ESRD patients referred late varied within capital city areas and was significantly higher in areas of greater disadvantage. After adjustment for known predictors of mortality (age, sex, number of co-morbidities, primary renal disease and indigenous status), late referral was associated with increased mortality (adjusted hazard ratio 1.19, 95% CI 1.04—1.35) and with decreased likelihood (adjusted rate ratio 0.78, 95% CI 0.64—0.95) of receiving a transplant beyond the initial year of renal replacement therapy. We believe that this long-term disadvantage might arise from sub-optimally managed chronic renal insufficiency.

Unequal access to renal transplantation

We have compared indigenous Australians' access to renal transplantation with access by non-indigenous Australians.[7] We have investigated whether the disparities we found were associated with a lower rate of acceptance onto the waiting list and/or a lower rate of moving from the waiting list to transplantation. Indigenous patients had a lower transplantation rate (adjusted indigenous:non-indigenous rate ratio 0.32, 95% CI 0.25—0.40). They had both a lower rate of acceptance onto the waiting list and a lower rate of moving from the waiting list to transplantation. The disparities were not explained by differences in age, sex, co-morbidities or cause of renal disease.

Conclusion and new explanatory model for the excess burden of renal disease in indigenous populations

It is generally believed that the excess burden of renal disease in indigenous populations can be explained by an epidemic of type-II diabetes and a yet-to-be-determined genetic predisposition to develop renal disease.[9,10] We have shown that the incidence of ESRD among indigenous Australians is strongly associated with disadvantage. We propose a model which integrates biological and social explanations. We suggest a predisposition to the development of progressive renal disease, arising from intra-uterine and/or genetic influences, although we do not, as yet, have any evidence for genetic factors. Such a predisposition would be compounded by a life-course of renal insults due to recurrent infection and inflammation, a high prevalence of damaging health behaviours (including smoking and poor diet) and inadequate access to effective preventive health care, particularly relating to the control of hypertension and diabetes.

Intrauterine malnutrition has been linked with renal disease.[11] Autopsy studies confirm the wide variation in the number of nephrons in the "normal" kidney.[12] Although their number is fixed at birth, the size of glomeruli can increase in response to a deficit in number,[13] resulting in a restoration of total filtration surface and excretory homeostasis. However, this adaptation might come at a high price. Excessive glomerular enlargement might accelerate the loss of nephrons through glomerular hypertension and hyperfiltration injury.[14] It seems plausible that people born with fewer nephrons might be predisposed to develop hypertension, progressive renal insufficiency and ESRD.[11,15]

Nephron numbers might be determined by intrauterine[13,16] and/or genetic influences.[17,18] Among indigenous Australians, maternal malnutrition, smoking and teenage pregnancy have been established as important causes of intrauterine growth retardation (IUGR).[19] Birthweight data are routinely collected for all Australian births. Low birthweight (less than 2500 grams) is used as a proxy for IUGR. In 1994–1996, 12.4% of indigenous births were low birthweight compared with 6.2% of non-indigenous births.[20] National data on birthweights from 30 to 40 years ago, which would be relevant to the current epidemic of ESRD in indigenous adults, are not available. However, data from selected remote communities suggest a much higher incidence of low birthweight in previous decades.[21]

A few histological studies have explored the association between nephron number and IUGR or birthweight.[16,22,23] A current autopsy study is examining the relationship between nephron number, size and birthweight in indigenous Australians, African Americans and Caucasians.[24] A significant inverse relationship between glomerular number and glomerular size has been demonstrated.[24,25] A preliminary report indicates that children and adults with low birthweight have, on average, 37% fewer nephrons than those with higher birthweights.[26]

Some studies have suggested a relationship between birthweight and clinical or pathological evidence of progressive renal disease.[27-29] In one remote Aboriginal community, after adjustment for age, sex, BMI and blood pressure, the odds ratio for macroalbuminuria in persons of low birthweight, compared with those of higher birthweights, was 2.82 (95% CI 1.26 to 6.31).[21] These findings are consistent with the hypothesis that reduced nephron number at birth might impose an increased susceptibility to renal disease and that the compensatory enlargement of remaining glomeruli might lead to progressive damage through glomerular hyperfiltration and scarring.

We believe that a number of discrete pathways can be outlined, linking the disadvantage experienced by indigenous Australians to their biological processes, culminating in ESRD. These pathways can be direct or indirect, and involve the development and/or progression of renal disease. Here, we present evidence for a *direct* pathway linking house-crowding, *via* endemic and epidemic streptococcal skin infection, to the *development* of renal disease.

A suggested direct pathway

Living conditions, notably overcrowded sleeping arrangements, have been associated with the presence of scabies.[30-32] Scabies and streptococcal skin sores are the predominating skin infections in central and northern Australia.[32] Scabies is endemic in many remote communities, being found in up to 50% of children. The cycles of scabies transmission underlie the high prevalence of skin sores. In some surveys, up to 70% of children have skin sores, with group A streptococcus (GAS) being the major pathogen.[32,33]

In a cross-sectional study in one high-risk remote community, the presence of skin sores and scabies in both children and adults was associated with macroalbuminuria.[34] Adults with persistent antibodies to streptococcal-M protein, markers of past GAS infection, were far more likely to have macroalbuminuria than those lacking such antibodies.[35] GAS is responsible for the continuing outbreaks of acute post-streptococcal glomerulonephritis (APSGN).[32,33,36] A retrospective cohort study showed that, compared with adults lacking a history of APSGN, adults with a documented remote history (on average, 14.6 years earlier) of APSGN had an adjusted odds ratio for macroalbuminuria of 6.1 (95% CI, 2.2—16.9).[37]

Lessons for prevention?

Both primary and secondary prevention strategies, throughout the life-course of indigenous Australians, will be required to reduce their risk of ESRD. Primary preventive initiatives must address the period from before conception to the development of albuminuria. Such initiatives might include improved access to antenatal services to reduce the prevalence of intra-uterine growth retardation and the training of community members to improve housing infrastructure and to maintain the improvements.[38]

Secondary prevention, targeting the period from development of albuminuria through to ESRD, is crucial. Community-based screening and intervention for high-risk groups, aiming for strict control of blood pressure with ACE inhibitors as first-line therapy, and of diabetes with oral hypoglycaemics and insulin, have been demonstrated to be effective in preventing progression to ESRD.[39]

Notwithstanding attempts to improve prevention, the number of indigenous ESRD patients receiving RRT will continue to increase. We face major challenges in delivering a treatment service of high quality to people from remote communities who have a significantly different view of the world from our own. We need to develop more innovative methods of patient education, of training for self-care and of delivery of treatment to allow indigenous patients to remain within their communities whenever possible. We should address the issue of inequitable access to transplantation. An integrated, 'whole of government' approach, beyond the scope of the conventional 'Australian health system', will be required to combat the epidemic of ESRD among indigenous Australians.

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