Natural history of chronic kidney disease in Australian Indigenous and non-Indigenous children: a 4-year population-based follow-up study

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ABSTRACT

Objective: To describe the natural history and risk of early chronic kidney disease (CKD) in Indigenous Australian populations.

Design, setting and participants: A prospective cohort of 2266 Aboriginal and non-Aboriginal children enrolled from primary schools throughout New South Wales from February 2002 to June 2004 and followed for 4 years.

Main outcome measures: Urinalysis, height, weight, blood pressure, birthweight and sociodemographic status at baseline and 2- and 4-year follow-up; CKD risk factors: haematuria, albuminuria, obesity, and systolic and diastolic hypertension.

Results: 2266 children (55% Aboriginal; 51% male; mean age, 8.9 years [SD, 2.0 years]) were enrolled at baseline. 1432 children (63%) were retested at 2-year follow-up, and 1506 children (67%) at 4-year follow-up. Prevalence of baseline CKD risk factors was frequent (2%–7%), but most abnormalities were transient. Besides persistent obesity (5.0%), persistence of CKD risk factors at final follow-up was low: haematuria (1.9%), albuminuria (2.4%), systolic hypertension (1.5%) and diastolic hypertension (0.2%). There was no difference in prevalence of persistent CKD risk factors between Aboriginal and non-Aboriginal children.

Conclusions: Over 4 years of follow-up, Indigenous Australian children had no increased risk for early evidence of CKD. More than 70% of baseline risk factors were transient, and persistent risk factors were uncommon. Our findings suggest the increased risk for end-stage kidney disease seen in Indigenous adults is not yet manifest in these schoolchildren, and may be potentially preventable.

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Chronic and end-stage kidney disease is of epidemic proportions in indigenous populations around the world.[1-4] There are no published studies describing the natural history of early chronic kidney disease (CKD) risk factors in indigenous children compared with non-indigenous children.

The aim of our study was to determine the prevalence of persistent CKD risk factors in Australian Aboriginal and non-Aboriginal children, and whether ethnicity predicts for persistent CKD risk factors after accounting for potential confounders such as geographic remoteness and social disadvantage.

METHODS

Selection of participants

From February 2002 to June 2004, public primary schools in urban, coastal, rural and remote areas of New South Wales where Aboriginal people are known to live were approached regarding testing. NSW has the highest Aboriginal population in Australia. To maximise power, sampling was done to obtain equal numbers of Aboriginal and non-Aboriginal children, and in similar proportions from urban, coastal, rural and remote areas. We aimed to recruit equal numbers of boys and girls, and about equal numbers of children from each 12-month age group. All primary schools in remote communities were approached, and schools in other areas were sampled if more than 20 Aboriginal children in the relevant age range attended. We attempted to enrol all Aboriginal students from participating schools, and to match them by age and sex with a random sample of non-Aboriginal students. Aboriginal status was determined using the Australian Bureau of Statistics best practice recommendations.[5]

Aboriginal community engagement

Consultation with local Aboriginal medical services was undertaken and consent was sought from community leaders before commencement of the study. Approval was obtained from the ethics committees of the Children's Hospital at Westmead, the University of Sydney, NSW area health services, and the NSW Department of Education and Training. Informed consent was obtained for each child and, in accordance with National Health and Medical Research Council (NHMRC) guidelines,[6] data were collected using a standardised form and de-identified for storage and analysis before being returned to each community after the study visit. Permission to publish data was also obtained from each community.

Measurement of chronic kidney disease risk factors

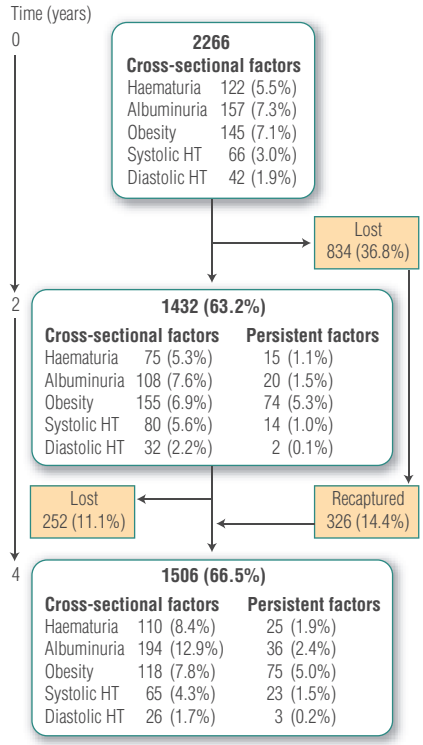
CKD risk factors measured were haematuria, albuminuria, obesity, and systolic and diastolic hypertension. Predictors known and thought to be associated with the development of these risk factors were also recorded, including age, sex, growth parameters, birthweight, and the environmental health determinants of geographic isolation and social disadvantage.

A morning clean-catch urine specimen was collected from each child, with dipstick analysis for haematuria and albuminuria performed on-site on fresh specimens using a Bayer Clinitek 50 analyser (Bayer Healthcare, Sydney, NSW). According to Kidney Disease Outcomes Quality Initiative (KDOQI) definitions, haematuria was defined as ≥ 25 red blood cells/μL (1+), and albuminuria as an albumin–creatinine ratio ≥ 3.4 mg/mmol.[7]

Birthweight was provided by the child's parent or carer by recall or from the child's health record. Body mass index (BMI) standard deviation z scores were calculated using height and weight and an age- and sex-adjusted program.[8] Blood pressure was measured on the right arm with the child sitting, using an aneroid sphygmomanometer and the largest cuff to encircle the arm and cover at least three-quarters of the length of the upper arm.[9]

Follow-up measurements were performed 2 and 4 years after baseline testing at the primary school or new high school on all available children, and the frequency of persistent CKD risk factors (ie, risk factors detected at baseline, 2-year and 4-year follow-up; or, in children

1 Subjects and chronic kidney disease risk factors at baseline, 2-year and 4-year follow-up



HT = hypertension. ◆

with only a baseline and final test, risk factors detected at both) was ascertained.

Standardisation of urban, coastal, rural and remote locality was performed using the Accessibility/Remoteness Index of Australia, with each subject given an index score according to postcode of residence.[10] To determine the level of social and economic wellbeing of areas studied, the Socio-Economic Indexes for Areas 2001[11] Index of Disadvantage was applied to subjects at the level of collection district of residence. This is the smallest geographic area for which the Index is available, and includes about 200 households.

Data analysis

Comparisons between Aboriginal and non-Aboriginal children at final follow-up were made by sex, age groups, birthweight quartiles, BMI SD quartiles, and categories of isolation and disadvantage, using the χ^2 test. Comparisons between children at final follow-up and children with only baseline or baseline and 2-year follow-up results were also made according to these categories using the χ^2 test. Adjusted odds ratios (AORs) for baseline and persistent CKD risk factors in Aboriginal compared with non-Aboriginal children (referent group) were determined using logistic regression, with 95% confidence intervals. AORs for other potential predictors of persistent CKD risk factors (sex, age, birthweight, BMI, geographic isolation and social disadvantage) were determined using logistic regression (with the lowest-risk category for each predictor as the referent group), with 95% confidence intervals. Analyses were adjusted where appropriate for ethnicity, age, sex, BMI SD, birthweight, and categories of isolation and disadvantage. Adjustment was made in all analyses for the effect of cluster sampling by school.

Tests for interactions between ethnicity, sex, age, categories of isolation and disadvantage and other significant variables in the final model were performed. Significance was set at $P<0.05$ for main effects and interactions. Statistical analysis was performed using SAS, version 9 (SAS Institute Inc, Cary, NC, USA) and SPSS, version 15 (SPSS Inc, Chicago, Ill, USA).

We planned to collect data from 1000 Aboriginal and 1000 non-Aboriginal children at baseline — sufficient numbers to detect differences in prevalence of CKD risk factors between the two groups of 2.9% v 1.1% (haematuria), 5.5% v 2.9% (albuminuria), 8.2% v 6.0% (obesity), and 9.4% v 7.2% (systolic hypertension), at 80% power.

RESULTS

Baseline recruitment and follow-up

At baseline, 2266 children were enrolled from 37 primary schools in NSW (Box 1). Partici-

2 Prevalence of chronic kidney disease risk factors at baseline and persistent risk factors at 4-year follow-up in Aboriginal and non-Aboriginal children

	Baseline				Persistent*			
Risk factor	All subjects ($N=2266$)	Non-Aboriginal† ($n=1018$)	Aboriginal ($n=1248$)	P	All subjects ($N=1506$)	Non-Aboriginal† ($n=699$)	Aboriginal ($n=807$)	P
Haematuria (⩾ 25 red blood cells/μL, 1+)								
Number (%)	122 (5.5%)	36 (3.6%)	86 (7.1%)		25 (1.9%)	12 (2.0%)	13 (1.8%)	
AOR‡ (95% CI)		1.00	2.25 (1.37–3.69)	0.001		1.00	0.92 (0.50–2.45)	0.81
Albuminuria (ACR ⩾ 3.4 mg/mmol)								
Number (%)	157 (7.3%)	63 (6.5%)	94 (8.1%)		36 (2.4%)	17 (2.4%)	19 (2.4%)	
AOR‡ (95% CI)		1.00	1.37 (0.93–2.01)	0.11		1.00	0.97 (0.53–2.01)	0.92
Obesity (BMI ⩾ 2 SD)								
Number (%)	145 (7.1%)	63 (6.7%)	82 (7.4%)		75 (5.0%)	30 (4.3%)	45 (5.6%)	
AOR‡ (95% CI)		1.00	1.10 (0.76–1.44)	0.52		1.00	1.32 (0.82–2.11)	0.25
Systolic hypertension (SBP > 95th percentile)								
Number (%)	66 (3.0%)	26 (2.6%)	40 (3.2%)		23 (1.5%)	7 (1.0%)	16 (2.0%)	
AOR‡ (95% CI)		1.00	1.26 (0.77–2.09)	0.36		1.00	2.00 (0.82–5.00)	0.12
Diastolic hypertension (DBP > 95th percentile)								
Number (%)	42 (1.9%)	15 (1.5%)	27 (2.2%)		3 (0.2%)	1 (0.1%)	2 (0.2%)	
AOR‡ (95% CI)		1.00	1.47 (0.78–2.80)	0.23		1.00	1.74 (0.15–19.2)	0.65

AOR = adjusted odds ratio. ACR = albumin–creatinine ratio. BMI = body mass index. SBP = systolic blood pressure. DBP = diastolic blood pressure. * Risk factors found at both baseline and 4-year follow-up. † Referent category. ‡ Adjusted for age, sex, birthweight, BMI SD, SBP, DBP, and isolation and disadvantage categories. ◆

3 Physiological and environmental predictors of persistent chronic kidney disease risk factors in Aboriginal and non-Aboriginal children

	Haematuria ($n = 25$)		Albuminuria ($n = 36$)		Obesity ($n = 75$)		Systolic hypertension ($n = 23$)	
Predictor	No. (%)	AOR* (95% CI)	No. (%)	AOR* (95% CI)	No. (%)	AOR* (95% CI)	No. (%)	AOR* (95% CI)
Sex								
Male†	5 (0.7%)	1.00	14 (1.8%)	1.00	43 (5.5%)	1.00	10 (1.3%)	1.00
Female	20 (3.1%)	4.31 (1.61–11.63)§	22 (3.0%)	1.69 (0.86–3.33)	32 (4.4%)	0.78 (0.49–1.25)	13 (1.8%)	1.39 (0.61–3.18)
Birthweight‡								
> 2500†	15 (1.7%)	1.00	24 (2.4%)	1.00	46 (4.6%)	1.00	19 (1.9%)	1.00
⩽ 2500g	2 (2.4%)	1.39 (0.31–6.16)	2 (2.0%)	0.83 (0.19–3.54)	6 (5.9%)	1.32 (0.55–3.17)	1 (1.0%)	0.52 (0.07–3.92)
BMI SD quartiles								
–4.8 to –0.8†	8 (2.6%)	1.00	10 (2.8%)	1.00	—	—	1 (0.3%)	1.00
–0.7 to 0.1	3 (0.9%)	0.34 (0.09–1.34)	11 (3.0%)	1.07 (0.45–2.54)	—	—	0	0.49 (0.02–14.50)
0.2 to 0.7	8 (2.3%)	0.89 (0.33–2.39)	8 (2.1%)	0.73 (0.28–1.87)	—	—	3 (0.8%)	2.77 (0.29–26.72)
0.8 to 6.9	6 (1.9%)	0.71 (0.24–2.06)	7 (1.9%)	0.66 (0.25–1.75)	—	—	19 (5.1%)	19.05 (2.54–43.09)¶
Isolation								
Least isolation†	9 (2.4%)	1.00	12 (2.9%)	1.00	19 (4.6%)	1.00	7 (1.7%)	1.00
Low-mid isolation	11 (2.6%)	1.07 (0.44–2.61)	7 (1.7%)	0.56 (0.22–1.43)	26 (6.1%)	1.35 (0.73–2.48)	12 (2.8%)	1.67 (0.65–4.28)
High-mid isolation	2 (1.1%)	0.46 (0.10–2.16)	7 (2.1%)	0.72 (0.28–1.86)	9 (2.7%)	0.58 (0.26–1.32)	2 (0.6%)	0.35 (0.07–1.70)
Highest isolation	3 (0.9%)	0.36 (0.10–1.32)	10 (2.9%)	0.99 (0.42–2.33)	21 (6.1%)	1.35 (0.71–2.55)	2 (1.5%)	0.34 (0.07–1.63)
Social disadvantage								
Least disadvantage†	8 (2.3%)	1.00	9 (2.6%)	1.00	19 (5.5%)	1.00	7 (2.0%)	1.00
Low-mid disadvantage	4 (0.9%)	0.40 (0.12–1.33)	11 (2.6%)	0.98 (0.40–2.40)	19 (4.4%)	0.79 (0.41–1.53)	9 (2.1%)	1.04 (0.38–2.81)
High-mid disadvantage	8 (2.7%)	1.17 (0.43–3.16)	6 (1.6%)	0.60 (0.21–1.70)	18 (4.8%)	0.86 (0.44–1.66)	3 (0.8%)	0.39 (0.10–1.51)
Highest disadvantage	5 (2.0%)	0.86 (0.28–2.65)	10 (2.8%)	1.08 (0.43–2.68)	19 (5.4%)	0.97 (0.50–1.86)	4 (1.1%)	0.55 (0.16–1.90)

AOR = adjusted odds ratio. BMI = body mass index. * Adjusted for ethnicity, age, sex, BMI, birthweight, blood pressure, and isolation and disadvantage categories. † Referent category. ‡ Data do not equal column totals because not every child had a birthweight recorded. § $P = 0.001$. ¶ Trend, $P < 0.001$. ◆

pation rates for both Aboriginal and non-Aboriginal children from all schools were 85%–100%. Of the 2266 children, 1248 (55.1%) were Aboriginal, 1156 (51.0%) were male, and the mean age was 8.9 years (SD, 2.0 years). Baseline characteristics have been reported in detail elsewhere.[12]

At 2-year follow-up, from March 2004 to December 2006, 1432 children (63.2%) were available for retesting. Of these, 773 (54.0%) were Aboriginal, 723 (50.4%) were male, and the mean age was 10.5 years (SD, 2.0 years). The 2-year follow-up results have been reported elsewhere.[13] At 4-year follow-up, from February 2006 to December 2007, 1506 children (66.5%) were retested. Of these, 807 (53.6%) were Aboriginal, 768 (51.0%) were male, and the mean age was 13.3 years (SD, 3.2 years).

Characteristics at final follow-up

At final follow-up, there were proportionally more Aboriginal children in the youngest age groups and from the areas of highest isolation and disadvantage (all $P < 0.001$). This was also the case at baseline.[12] There were more Aboriginal children with lower birthweights at final follow-up ($P = 0.001$).

Compared with the overall group who were available for the final follow-up, there were significantly more children in the older age groups who did not have a final follow-up ($P < 0.001$). There were no differences in ethnicity, sex, birthweight, BMI SD, or isolation and disadvantage categories between children who did and did not have a final follow-up.

Prevalence of baseline and persistent chronic kidney disease risk factors

At baseline, CKD risk factors were frequent for the group overall, ranging from 1.9% for diastolic hypertension to 7.3% for albuminuria (Box 2). There was no increased risk of baseline risk factors in Aboriginal children compared with non-Aboriginal children, except for haematuria (7.1% v 3.6%; AOR, 2.25 [95% CI, 1.37–3.69]; $P = 0.001$).

At 4-year follow-up, the overall prevalence of persistent risk factors was lower, ranging from 0.2% for diastolic hypertension to 5.0% for obesity (Box 2). There was no increased risk for any persistent risk factor in Aboriginal children compared with non-Aboriginal children, even after adjusting for geographic remoteness and social disadvantage.

Physiological and environmental predictors of persistent risk factors

Girls had a fourfold increased risk of persistent haematuria compared with boys (AOR, 4.31 [95% CI, 1.61–11.63]; $P = 0.001$) (Box 3). There was an increasing risk of persistent systolic hypertension with increasing BMI SD (trend, $P < 0.001$), and the highest BMI SD quartile had a 19-fold increased risk of persistent systolic hypertension compared with the lowest BMI SD quartile (AOR, 19.05 [95% CI, 2.54–43.09]; $P < 0.001$). There were no other predictors for persistent CKD risk factors in these children; in particular, persistent risk factors were not predicted by lower birthweight, geographic remoteness or social disadvantage.

Association between persistent disease risk factors

All three children with persistent diastolic hypertension had persistent obesity, and two of them also had persistent systolic hypertension. Eleven of the 23 children with persistent systolic hypertension had persistent obesity. There were no interactions found between either environmental health determinant of geographic isolation or social disadvantage and ethnicity, age, sex or other covariates in any model.

DISCUSSION

This 4-year follow-up study has shown that persistent CKD risk factors are infrequent in children in NSW, and there is no increased risk of persistent risk factors in Aboriginal children compared with non-Aboriginal children, even after adjusting for geographic isolation and social disadvantage.

Our cross-sectional survey of this cohort showed that baseline CKD risk factors were frequent in both Aboriginal and non-Aboriginal primary school-aged children, and that, at a single test, Aboriginal children had twice the risk of haematuria as non-Aboriginal children. Our follow-up results suggest that more than 70% of baseline urinary and blood pressure abnormalities in Aboriginal and non-Aboriginal children are transient. Semi-quantitative single estimations of urinary blood and protein in children vary according to posture, illness, exercise and time of day.[14] A higher rate of transient haematuria may reflect the higher incidence of transient disease seen in Indigenous children, such as post-infectious glomerulonephritis.[15]

Obesity was the only frequent persistent CKD risk factor in these children, although no more so in Aboriginal than non-Aboriginal children. The prevalence of persistent obesity found in our study (5%) is similar to the national rate of obesity in Australian primary school-aged children (6%).[16] Increasing BMI and persistent obesity were significantly associated with persistent systolic and diastolic hypertension. These children with clustering of CKD risk factors are also particularly at risk of early-onset diabetes and cardiovascular disease.[17,18]

This study is the first population-based follow-up of chronic disease risk in Indigenous children. Although follow-up was challenging because of high rates of school absenteeism and family mobility, our follow-up rate at 4 years improved on the rate at 2 years due to better community liaison and engagement with Aboriginal area health workers. The group lost to follow-up was not significantly different to those we were able to follow, apart from a higher proportion of older children lost. This may have introduced ascertainment bias, but our follow-up rate of nearly 70% is high. The regression analyses for risk of CKD risk factors in Aboriginal children were adjusted for age to account for these imbalances.

Our finding that there is no increased risk of persistent CKD risk factors in Aboriginal children suggests that the increased risk of CKD experienced by Aboriginal adults in Australia is not yet established in childhood. These results also show that a one-off measurement of CKD risk factors in children is misleading, as most abnormalities are transient. Persistent obesity clusters closely with persistent hypertension, and its frequency suggests it should be addressed from a primary school age. These results provide useful information for primary health care practitioners, paediatricians, nephrologists, policymakers and families.

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COMPETING INTERESTS

None identified.

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