Antecedents of Renal Disease in Aboriginal Children (ARDAC study)

Project Number: 2002/001
Previous approval number: 96051

Investigators

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Research Experience: Clinical research methods with particular reference to urinary tract infection in children, randomised controlled trials, systematic reviews of randomised controlled trials and diagnostic tests.

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Consultant Physician in Paediatric Nephrology, Centre for Kidney Research, NHMRC Centre for Clinical Excellence in Renal Medicine, The Children's Hospital at Westmead
Research Experience: Systematic reviews and meta-analysis for the Cochrane Collaboration. Cross-sectional school based study of urinary abnormalities in Aboriginal and non-Aboriginal children.

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Research Assistant, NHMRC Centre for Kidney Research, Centre for Clinical Excellence in Renal Medicine, The Children's Hospital at Westmead
Tel: (02) 9845 3041 Fax: (02) 9845 3082 *Research Experience: Cohort study of children with symptomatic urinary tract infection (NHMRC funded), Randomised controlled trial in children with vesicoureteric reflux (NHMRC funded), Cross-sectional school based survey of daytime incontinence (Children's Hospital funded), Cohort study of daytime incontinence (PhD).*

Ms Rita Williams BA
Senior Aboriginal Health Education Officer, Centre for Kidney Research, NHMRC Centre for Clinical Excellence in Renal Medicine, The Children's Hospital at Westmead
Research Experience: Cross-sectional school based study of urinary abnormalities in Aboriginal and non-Aboriginal children. Educational workshops for aboriginal health workers.

Associate Professor Paul Roy MB BS, BSc (Med), FRACP
Consultant Physician in Paediatric Nephrology, Centre for Kidney Research, NHMRC Centre for Clinical Excellence in Renal Medicine, The Children's Hospital at Westmead
Research Experience: Over 20 years experience in research, clinical practice, and teaching at both postgraduate and undergraduate levels. Over 50 publications.

Scientific Protocol

Aims

To carry out a prospective cohort study over 5 years of Aboriginal and non-Aboriginal primary school children in NSW in order:-

- To determine the prevalence of urinary sediment abnormalities (haematuria and proteinuria) and monitor their development and progression.
- To determine whether any geographical variation in prevalence exists between urban, rural and remote communities in New South Wales
- To investigate the associations between haematuria and/or proteinuria in primary school children and their height, weight and blood pressure levels

Simple description

The proposed study is a continuation of the study performed in 2002. In 2002 a population-based survey of 1000 Primary School children (500 Aboriginal and 500 non-Aboriginal) aged 5-12 years in selected schools with high proportions of Aboriginal children was carried out in NSW. The aim was to determine the frequency of urinary abnormalities (blood and protein) in Aboriginal and non-Aboriginal children, to determine whether the prevalence of abnormalities varies with geographical location and to investigate the associations of haematuria and proteinuria with blood pressure and growth parameters. During community consultation for the 2002 study, Aboriginal people indicated that they would like an ongoing study of their children. We now propose a further population based survey of 500 Aboriginal and 500 non-Aboriginal primary school children aged 5-12 years in different geographical regions to create a cohort of 2000 children. This cohort will be followed for 5 years to monitor the development and progression of urinary abnormalities in relation to ethnic group and geographical region.

Scientific Background

There are no population-based cross-sectional or cohort studies comparing the prevalences of haematuria and proteinuria in Aboriginal and non-Aboriginal children in Australia. However available data suggest that these abnormalities are found more commonly in Aboriginal compared with non-Aboriginal children. In small studies[1,2] in 3 remote Aboriginal communities in northern Australia, haematuria and proteinuria were detected in 5-13% and 0-8% children respectively. In comparison a South Australian study of 9355 preschool children from all socioeconomic and cultural backgrounds detected haematuria and proteinuria in 2.4% and 0.25% children respectively[3]. No attempt was made to analyse the results according to racial group. Albuminuria is known to be a risk factor in adults for both renal failure and non renal natural death including cardiovascular deaths in remote Aboriginal communities[4]. The increased risk associated with albuminuria is independent of diabetes and hypertension[5]. The northern Aboriginal community with the highest prevalence of proteinuria among children also had the highest prevalence of proteinuria among adults. Therefore haematuria and proteinuria may be early markers for renal disease in these communities. Population-based studies are required to gain more information about the prevalence of haematuria and proteinuria in Aboriginal compared with non-Aboriginal children and to investigate further whether geographical variations exist in prevalence in one or both populations.

End stage renal disease (ESRD) is significantly more common among Aboriginal Australians than in the Australian community as a whole. In 1999, the incidence of ESRD in Aboriginal people was 415 per million population compared with 83 per million population for non-Aboriginal people[6]. The incidence of ESRD is highest in remote regions of the Northern Territory, Western Australia and South Australia (up to 1300 per million per year). The incidence is lowest (less than 100 per million per year) in urban areas of the southern states[7]. In NSW[8] the incidence of ESRD in Aboriginal people was 111 per million in 1997 and was above the incidence of 78 per million among non-Aboriginal people. Within NSW the incidence of ESRD in Aboriginal people is highest in the remote regions of western NSW with lower levels in the rural and coastal areas and the lowest level in the Sydney area[7].

The causes of the increased incidence of ESRD in Aboriginal Australians are poorly understood. The increase in ESRD is accompanying a rise in the rates of hypertension, type 2 diabetes and cardiovascular disease in Aboriginal people in the Northern Territory[9]. High rates of smoking, dyslipidaemia, low birth weights, malnutrition (both obesity and under nutrition) and preventable skin infections (scabies, impetigo) have been found in communities with a high rate of ESRD[10,11]. In a retrospective cohort study in a remote community that experienced two epidemics of post streptococcal glomerulonephritis (PSGN), community members who had had PSGN or "abnormal urine" (haematuria and proteinuria) were at increased risk of persistent albuminuria 10 years later compared with the control group[12]. Studies in Aboriginal communities suggest that a range of social, cultural and medical interventions can reduce the rates of ESRD and death in comparison with historical data[11].

In 2002 a population-based survey of urinalyses and measurements of urinary albumin-creatinine ratios in Aboriginal and comparison groups of non-Aboriginal primary school children was carried out in urban, coastal, rural and remote areas of NSW. Preliminary analysis has shown prevalences of haematuria (10 red cells/μL or more) in Aboriginal children (N=340) of 12.1% (95% confidence intervals 8.6-15.1) and in non-Aboriginal children (N=381) of 6.3% (95% confidence intervals 4.1-9.2). Prevalences of microalbuminuria (urinary albumin/creatinine ratios 3.4-33g/mol) were 11% (95% confidence intervals 7.4-14.5) in Aboriginal children (N=301) and 7.5% (95% confidence intervals 5.0-10.7) in non-Aboriginal children (N=371). With funding from the NHMRC Centre for Clinical Research Excellence grant we plan to extend the cross sectional survey of 1000 children to a prospective cohort study of 2000 children (1000 Aboriginal and 1000 non-Aboriginal children) to clarify whether urinary sediment abnormalities occur more commonly in Aboriginal children compared with non-Aboriginal children. If data from this study indicate that rates of haematuria and proteinuria are increased in comparison with non-Aboriginal children, Aboriginal communities in NSW may wish to introduce programmes for identification, follow up and intervention for renal disease in children and young people as well as adults.

Methods

Organisation of the study

It is proposed that the study in 2003 will be organised in a similar way to the study in 2002. In 2002 after approval was obtained from the local Aboriginal communities and

the NSW Department of Education and Training, individual schools in the areas were approached to invite them to take part in the study. When approval had been given, the teachers and Aboriginal Educational Assistants provided class lists from each school and invited the children to participate in the study. During 2002 children from kindergarten to year 6 in NSW primary schools in Gulargambone, Dubbo, the Armidale area, the Kempsey area, Nowra, Wollongong and the Mt Druitt area were surveyed.

For the proposed study in 2003 consultation with Aboriginal community leaders and Aboriginal health workers is taking place in the Grafton area, Batemans Bay area, Goulburn area, Liverpool and Campbelltown areas and Moree areas. In addition consultation with the Coordinator of Aboriginal Health Services for Macquarie Area Health Service is taking place to determine a suitable remote area in the Far West of NSW for the study. Further approval will be obtained from the Department of Education and Training after approval of the current protocol. Once approval for the study has been obtained from the Department of Education and Training, schools in the study areas with larger numbers of aboriginal children will be preferred for the survey. As in the first survey, the areas to be surveyed have been selected based on the size of the Aboriginal communities in those localities.

Recruitment and consent procedures

The recruitment and consent procedures will be similar to those in 2002. A parent information sheet explaining the study together with a consent form to participate in the study will be handed out in classrooms to all children by the class teacher and the Aboriginal Education Assistants in the participating schools during the week before the study period at that school. Both Aboriginal Education Assistants and class teachers will assist in ensuring that the consent forms are brought back to the school. Aboriginal children will be matched with non-Aboriginal children of the same age and sex from the same classroom. In 2003 a further 500 Aboriginal and 500 non-Aboriginal children will be recruited with equal numbers of Aboriginal and non-Aboriginal children being recruited from the selected regions to create a total cohort of 2000 children.

The prospective cohort study group will consist of 2000 children. The study group will comprise the 500 Aboriginal children screened in 2002 and the 500 Aboriginal children screened in 2003. The aim is for equal numbers of children to come from each geographical area and from each 12-month age range from 5-12 years (primary school grades kindergarten to Year 6). The comparison group will comprise the 500 non-Aboriginal children randomly selected to match the number of cases from each age range from schools in the same area in 2002 and the 500 non-Aboriginal children matched for age, school class and area to be screened in 2003. All children will be re-screened twice during the five-year period from 2003 to 2007. Children recruited in 2002 will be re-screened in 2004 and 2006 while children recruited in 2003 will be re-screened in 2005 and 2007. The Aboriginal communities and schools where screening took place in 2002 will be re-contacted in 2003 to obtain consent for re-screening. Once this is obtained, the families of children screened in 2002 will be re-contacted to obtain their consent for further screening.

Measurement

An Aboriginal nurse together with the Senior Aboriginal health worker will visit each school to collect data. Together with the Aboriginal Education Assistants and the class teachers, the Senior Aboriginal health worker will perform the matching of Aboriginal to non-Aboriginal children by gender and 'date of birth' from the list of children who have consented to participate.

At each screening, data on urinalysis results, albumin-creatinine ratio, height, weight and blood pressure will be recorded for each child selected using a standard data collection form. Abnormal results will be highlighted on the form, with the suggestion that the child be taken to the parents' doctor of choice for further follow up. All results will be posted to the child's home address and for any child, whose results are abnormal and need immediate action, the parents will be notified via phone. The families will be invited to provide the name and contact details of their doctor of choice or to give permission for abnormal results to be forwarded to the local Aboriginal Medical Service. If this information is provided, abnormal results will also be forwarded to the designated medical contact.

1. Height will be measured with a simple portable stadiometer transported by the team from one site to the next and standardised each day with a one metre measuring stick.

2. Weight will be measured on digital scales, which will also travel with the team from site to site.

3. Blood pressure will be measured on the right arm in duplicate 2 minutes apart with the child seated after 5 minutes rest using a standard aneroid sphygmomanometer and blood pressures cuff with width sufficient to cover 75% of the upper arm. Children with systolic or diastolic blood pressure values above the 95% percentiles for age[13] will have repeat measurements performed after the child sits quietly for a further 10 minutes. The lowest measurement will be recorded.

4. Each child will bring a urine specimen to the school. No urine specimens will be collected at schools unless the child is able to collect the specimen without help. Dipstick analysis of each specimen will be done. In addition for the detection of microalbuminuria ACR will be measured on each specimen using a Bayer machine (Clinitek 50) at the site of survey.
   The following ACR categories in g/mol will be used:
   a) Normal = ACR < 3.4 (95^{th} percentile by laboratory standards)
   b) Microalbuminuria = ACR 3.4 to 33 (30 to 299 mg/g)
   c) Overt albuminuria = ACR $\geq$ 3.4

Data will be entered into an excel spreadsheet.

Statistical Analysis

The 1996 census indicated that there are 386,049 Aboriginal people in Australia and 40% of them are under 15 years of age (154,420). 28.5% live in NSW (109,925 of whom 44,000 are children). The survey of 1000 Aboriginal children in 2002 and 2003

will result in 2.2% of the total population of Aboriginal children in NSW being screened.

1000 children in each group will allow detection at a statistical significance ($p<0.05$) of the following percentage for the prevalence of microalbuminuria between Aboriginal and non-Aboriginal groups with 0.8 power: 2.9 vs 1.05%, 4 vs 1.8%, 5.5 vs 2.9%.

Proportions of urinary sediment abnormalities (proteinuria, haematuria, ACR) will be compared between Aboriginal children and non-Aboriginal children using chi-squared test, with $p < 0.05$ and the measure of associations (blood pressure, height and weight percentiles) will be analysed using OR with 95%CI.

References:

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7. Cass A, Cunningham J, Wang Z, Hoy W. Regional variation in the incidence of end-stage renal disease in Indigenous Australians. Medical Journal of Australia 2001; 175: 24-27
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9. Hoy WE, Rees M, Kile E, et al. Low birthweight and renal disease in Australian Aborigines. *The Lancet* 1998, 352 ;9143:1826-1827.
10. Hoy WE, Norman RJ, Hayhurst BG, Pugsley DJ. A health profile of adults in a Northern Territory Aboriginal community, with an emphasis on preventable morbidities. Australian and New Zealand Journal of Public Health 1997; 21: 2: 121-126.
11. Hoy WE, Baker PR, Kelly AM, Wang Z. Reducing premature death and renal failure in Australian Aboriginals. A community-based cardiovascular and renal protective program. Medical Journal of Australia 2000; 172: 473-478.

12. White AV, Hoy WE, McCredie DA. Childhood post-streptococcal glomerulonephritis as a risk factor for chronic renal disease in later life. Medical Journal of Australia 2001; 174: 492-496.
13. Roy LP, Tiller DJ, Jones DL. The range of blood pressure in Australian children. Medical Journal of Australia 1984:141:9-12.

Ethical Analysis

Potential risks

The study will be carried out only with the approval of the Aboriginal communities. Approval will also be sought for the study from the NSW Department of Education and Training and the individual schools. There will be no potential risks to participants. The research team includes Aboriginal staff members, who are familiar with local cultural practices and sensitivities.

Potential benefits

In preparation for this study, Aboriginal health workers have already taken part in education programmes relating to kidney disease, its detection, treatment and management. An education manual on renal disease has been developed for Aboriginal health workers. Any abnormalities detected will be notified to the child's parent or guardian so that they can seek further investigation and follow up from their physician of choice. If data from this study indicate increased rates of urinary sediment abnormalities in comparison with non-Aboriginal children, Aboriginal communities in NSW may wish to introduce programmes for identification, follow up and intervention for renal disease in children as well as in adults.

Research Plan

Proposed date of commencement

April 2003 (2nd school term)

Estimated duration

5 years

Budget

Funding for the cohort study will come from the NHMRC Centre for Clinical Research Excellence grant to Associate Professor Jonathan Craig. Funding from this source will support the Senior Aboriginal Health Education Officer, the Aboriginal nurse and a research assistant to work on the project. Funding from this source will also be used for the travel and accommodation costs for the Senior Aboriginal Health Education Officer and the Nurse.

Staffing

Three staff will carry out the project. The research assistant will perform data entry, data analysis and prepare the data for publication. The Senior Aboriginal Health Education Officer has organised the education workshops, liaised with Aboriginal communities and organised the recruitment of school children in 2002. In 2003 she will be responsible for obtaining support from Aboriginal communities, contacting the schools to be involved in the project and, with the help of the teachers and Aboriginal Education Assistants, organising the recruitment of children for the study. In addition she will be responsible for contacting the Aboriginal communities and schools

involved in the study in 2002 to gain their consent for the re-screening of children in 2004 and 2006. As in 2002, the nurse will undertake the screening of the children in the schools and will record all the data.

Care of participants & access to data

Confidentiality will be maintained at all times. All data will be collected and entered into an EXCEL database. Data will be accessible only for the staff at Centre for Kidney Research. The results of the study will be fed back to the communities concerned and will not be published without their permission.

Winding up procedures

A report of the findings from this survey will be forwarded to the Aboriginal communities involved, the NSW Department of Health, the NSW Department of Education and Training and principals of all schools involved in the study.

Declaration

We undertake to carry out the research project (*title of project*) as described in this application and to comply with the general and specific conditions laid down by the Ethics Committee.
We do not have a commercial interest in the outcome of the study.
We also undertake to notify the Ethics Committee should any changes to the protocol be necessary, should any unexpected complications or adverse events take place, or should the study be abandoned for any reason.
The results of the study will be reported to the Ethics Committee annually during the course of the study and at its conclusion. A copy of any abstracts or publications resulting from the project will be submitted to the Research & Development Office.

Dr Jonathan Craig	……	Date …….
Dr Elisabeth Hodson	……	Date …….
Ms Premala Sureshkumar	……	Date …….
Ms Rita Williams	……	Date …….
A/Prof Paul Roy	……	Date …….

Head of Department

Dr Elisabeth Hodson	……	Date …….