

**Nutritional status of haemodialysis patients: comparison of Australian cohorts of Aboriginal and European descent**

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**i. Title Page**

**Full Title:** Nutritional status of haemodialysis patients: comparison of Australian cohorts of Aboriginal and European descent

**Short running title:** Australian Indigenous Dialysis Patients

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## ii. Abstract and key words

**Background:** It is not known whether nutritional status of haemodialysis subjects differs between Australian Aboriginal and non-Aboriginal haemodialysis subjects.

**Aim:** To investigate the nutritional status of Australian Aboriginal and non-Aboriginal haemodialysis subjects at satellite dialysis centres.

**Method:** Seventy-six (25 Aboriginal, 51 non-Aboriginal) prevalent haemodialysis patients were enrolled in a three month cross-sectional study. Each month anthropometric and biochemical measurements were collected.. Nutritional status (diet history, patient generated subjective global assessment (PG-SGA), handgrip strength) was assessed by a dietitian.

**Results:** PG-SGA detected mild to moderate malnutrition in 35% of Aboriginal patients and 25% of non-Aboriginal patients. The overall physical rating on the PG-SGA was significantly higher in Aboriginal patients, indicating the presence of a greater deficit in muscle mass in this population. Inter-dialytic weight gain was significantly greater in Aboriginal subjects (median [range] 3.0 [2.1-5.7] vs 2.5 [-0.3-5.0] kilograms,  $p < 0.001$ ). Glucose and HbA1c were significantly higher in Aboriginal subjects with diabetes than in non-Aboriginal patients with diabetes (median [range] 9.4 [4.9-23.4] vs 5.7 [3.1-12.9],  $p = 0.002$ ; 7.0 [5.2-11.0] vs 5.8 [4.6-9.0],  $p < 0.000$ ; respectively). These findings occurred in the setting of each cohort having adequate dialysis parameters (median Kt/V of  $> 1.6$  and median normalized protein catabolic rate 1.5). Difficulties were encountered in obtaining dietary information from Aboriginal subjects using the diet history method.

**Conclusion:** Subjects had acceptable parameters of dialysis adequacy; however 35% had evidence of malnutrition. Further research should focus on establishing a knowledge base for the nutritional management for Aboriginal dialysis subjects, and

the development of a validated individual dietary assessment method for use in this population group.

**Keywords:**

Nutrition Assessment

Population Groups

Renal Dialysis

Serum Albumin

Water-Electrolyte Balance

### **iii. Text**

#### **Background**

Aboriginal patients have an increased incidence of kidney disease and are over-represented in the Australian haemodialysis population(1). In 2010 the number of patients on dialysis in Australia was 10590 including 1208 patients who identified as Aboriginal(2). Considering population demographics in Australia, Aboriginal people are therefore four times more likely to require dialysis. The most predominant dialysis modality for end stage kidney disease in Australia is satellite haemodialysis, and this is often the treatment commenced by Aboriginal patients, who are less likely than non-Aboriginal Australians to utilise home-haemodialysis, peritoneal dialysis or receive a transplant(1).

The survival of Australian Aboriginal patients on dialysis, when corrected for age and comorbidities, is similar to non-Aboriginal patients (mortality rate ratio 0.85) (3), however no published data exists on the nutritional management of this population group. The recommended daily nutritional intake for haemodialysis patients(4) differs to that of the normal population. Patients are known to have a high risk of malnutrition, exacerbated by inflammation, and co-morbidities(5). A favourable nutritional status is reflected by maintenance of BMI within the range 23-26kg/m<sup>2</sup> and preservation of skeletal muscle stores(4). Goals of treatment include optimising nutritional status and managing co-morbidities such as blood glucose in diabetic patients. Anecdotally, renal dietitians report differences in anthropometric, biochemical and functional markers of nutritional status between Aboriginal patients and non-Aboriginal patients; however these have not been quantified. The aim of this study was to investigate the nutritional status of Australian Aboriginal patients undergoing maintenance haemodialysis.

#### **Methods**

Ethical approval was obtained from the Royal Adelaide Hospital Ethics Committee (SA Health) and the Human Ethics Committee of the University of South Australia. Potential subjects were provided with information on the study from their treating clinician and the research dietitian managing the study. Subjects were asked for consent to study including investigator access to medical records, nutritional assessment by a dietitian, grip strength measurements, a physical exam to check for wasting of skeletal muscle and fat stores and presence of oedema or ascites. This study was conducted in accordance with the ethical standards laid down in the 2000 Declaration of Helsinki (6<sup>th</sup> revision), and the National Statement on Ethical Conduct in Human Research (Australia, 2007).

A cross-sectional observational study design was utilised. Subjects were included if they were medically stable and receiving thrice weekly haemodialysis at participating satellite dialysis units (one in a regional setting, one in a city location). Subjects were excluded if they became medically unstable or died over the three month data collection period. Data were collected during the winter months (June-August) in 2011 whilst subjects underwent routine haemodialysis treatment, anthropometry and biochemical assays(6). Weight was taken during the first three haemodialysis treatments each month and averaged to obtain the pre-dialysis and post-dialysis weight recorded. Dry weight was determined by clinician assessment. Biochemical specimens were collected pre- and post-dialysis on the first Wednesday or Thursday of each month to obtain an average value over the three month period. Patient generated subjective global assessment (PG-SGA)(7-9) was used to determine the prevalence and severity of malnutrition. PG-SGA is a validated tool which looks at a number of components including recent weight change, physical functioning, nutrition impact symptoms (such as nausea, loss of appetite, or change in bowel motions), and

includes a physical assessment to examine the muscle, fat and fluid stores of a patient to determine current nutritional status (see figure 1 for example). The physical assessment deficit ratings are not based on the initial amount of muscle or fat a patient may have, but rather noticeable signs of wasting, such as sunken areas (temples, thigh and interosseous muscle) or loose skin or very little palpable muscle mass attached to the bones under loose skin (triceps, calf). Grip strength measurements using a Jamar Hydraulic Hand Dynamometer (Model J00105, SI Instruments Pty Ltd) were conducted prior to a routine dialysis session by a trained renal dietitian in the third month of the study. Subjects with diabetes were identified via diagnosis or prescription of insulin or oral hypoglycemic agents in their medical chart. A diet history was collected by a trained renal dietitian.

Data were analysed in SPSS (Version 15). Descriptive statistics were used to determine prevalence of co-morbid conditions and adherence to nutritional management guidelines for patients on haemodialysis(4). Continuous variables were assessed using an independent samples t-test with the fixed factor as ethnicity. A ranked analysis of covariates (Mann Whitney U-test) was undertaken for non-parametric data. Categorical data were assessed by Chi Squared Testing,  $p < 0.05$  was considered statistically significant.

## Results

Participant characteristics are shown in Table 1. Seventy-six subjects undergoing thrice weekly maintenance haemodialysis were recruited (25 Aboriginal and 51 non-Aboriginal), with Aboriginal subjects primarily residing in regional areas.



All patients were haemodialysed against Na<sup>+</sup> 140 baths and other haemodialysis parameters were similar between the groups (see Tables 2 & 3). Dialysis adequacy was acceptable in 97% of subjects ( $Kt/V > 1.2$ ). Aboriginal patients were significantly more acidotic as measured by serum bicarbonate and as such were dialyzed with higher bicarbonate solutions. Inter dialytic weight gain was higher in Aboriginal patients and consequently their dialysis duration per week was higher compared to non-Aboriginal patients (13.5 hours compared to 12 hours;  $p < 0.001$ ). Protein turnover was acceptable in all subjects (normalised protein catabolic rate (nPCR)  $> 0.8\text{g/kg}$ ), and there was no difference between Aboriginal and non-Aboriginal subjects.

Malnutrition was found in both Aboriginal and non-Aboriginal subjects across a range of weights and BMI categories. No significant difference was detected in the total numerical score for PG-SGA, however, Aboriginal subjects were more likely to have an overall physical rating on the PG-SGA that was significantly higher (1 or 2 compared to zero;  $p = 0.043$ ) indicating the presence of a greater deficit in muscle mass than in the non-Aboriginal cohort. When subjects were classified into categories (A-well nourished, B-mild to moderate malnutrition or C-severe malnutrition), 35% of Aboriginal subjects and 25% of non-Aboriginal subjects were classified as B. No subjects in this study were classified into category C. There was no correlation observed between PG-SGA score, body weight or BMI.

Subjects identifying as Aboriginal were more likely to have an inter-dialytic weight gain greater than two kilograms (84% vs 41% non-Aboriginal). A similar percentage of Aboriginal and non-Aboriginal subjects (~30%) had low serum albumin ( $< 35\text{g/L}$ ) when measured post haemodialysis. The intra-dialytic difference in serum albumin was  $+4 \pm 3\text{g/L}$  in Aboriginal subjects and  $+1 \pm 2\text{g/L}$  in non-Aboriginal subjects ( $p = 0.007$ ), with post-dialysis serum samples having a greater concentration of albumin than

samples taken pre-dialysis on the same day. One quarter (24%) of patients were misclassified as having low serum albumin levels (<35g/L) when serum albumin was measured from a pre-dialysis serum sample.

Diabetic Nephropathy was the primary renal diagnosis in 35% of Aboriginal subjects and 21% of non-Aboriginal subjects. Diabetes as co-morbidity was prevalent in 92% of the Aboriginal population (45% non-Aboriginal subjects). HbA1c was <7% in 52% of Aboriginal subjects and 82% of non-Aboriginal subjects with diabetes (median [range] 7.0 [5.2-11.0] vs 5.8 [4.6-9.0];  $p<0.000$ ). Pre-dialysis glucose was significantly higher in Aboriginal subjects with diabetes (median [range] 9.4 [4.9-23.4] vs 5.7 [3.1-12.9];  $p=0.002$ ). Lipid lowering medications were more common in Aboriginal subjects, Atorvastatin was the most common lipid lowering agent prescribed, and Gemfibrozil was prescribed to small numbers of patients.

Serum phosphate was >1.78mmol/L in ~30% of subjects, and no differences were noted by descent. Only one subject (non-Aboriginal) had a serum phosphate level less than 0.7mmol/L across the three months of the study.

The method of collecting dietary history using non-leading questions was difficult to administer in Aboriginal subjects, despite only one Aboriginal subject routinely requiring on site interpretation into the Pitjantjatjara language for nephrological review. Overall responses were vague, and dietary details were difficult to obtain from subjects of Aboriginal descent.. For example, for a reported food item the interviewer may ask "How much would you have?", a typical response was "a little" or "it depends (on how much is available)". The interviewer would then ask the subject to look at portion pictures and ask "do any of these pictures looks like the amount you normally eat?" A common response to this question was "it depends, sometimes this amount,

sometimes that amount, it depends” (on how much and how often food was available). Similar problems were encountered when attempting to obtain information regarding frequency of consumption as majority did not have a regular eating pattern.. Entering the information into nutritional analysis software would have required multiple assumptions to be made regarding quantities, frequency of consumption and preparation of food items. Due to the high risk of inaccuracy nutritional analysis was not undertaken. . Diet histories that were obtained from Aboriginal subjects (n=12) showed a reliance on heavily processed low cost carbohydrate based foods such as white bread, white rice, puffed wheat or corn cereal products, and soft drinks. Meat was reported as being consumed “sometimes” or “when we have it”, without being able to further quantify the response.

### Discussion

This is the first study to document dietetic assessment of Australian Aboriginal maintenance haemodialysis subjects. The population of Aboriginal subjects studied in this report had a profile of primary renal disease and co-morbid conditions, consistent with previous reports for this subgroup of haemodialysis subjects (2).

This is also the first documented report of PG-SGA and nPCR in Australian Aboriginal subjects on haemodialysis. Despite being well dialysed a greater percentage of Aboriginal subjects had mild to moderate malnutrition and a significantly higher overall physical rating than observed in the non-Aboriginal cohort. Whilst this rating can aid in determining nutritional status, it is impacted by both longstanding and recent events. Tissue wasting may date back to stage 3 or 4 chronic kidney disease or may be related to recent dietary intake or increased nutritional requirements associated with medical diagnoses(10, 11). It is worth noting the following points when undertaking PG-SGA assessments: 1) a normal reading at an examination site may vary according to

gender; 2) muscle mass will regress with aging (12); 3) muscle atrophy may occur following an injury (12, 13); 4) intentional weight loss will lead to lower fat mass and may affect muscle mass if not combined with resistance exercise (14); and 5) protein malnutrition can occur in the context of an adequate energy intake and may promote the development of sarcopenia (15).

Detection of poor nutrition requires a thorough assessment, particularly in an overweight subject. Deconditioning and sarcopenia occurs in both normal and overweight subjects, and inadequate nutrient density is often noted by clinical dietitians despite consumption of adequate energy. It is also important to note that the body composition and body fat distribution of Aboriginal Australians is different to that of a non-Aboriginal person (16), and normal muscle mass in a healthy Aboriginal patient has not been quantified. Consequently, it is difficult to determine if the tissue loss is specifically related to kidney disease or haemodialysis, however, poor muscle quality has been linked to higher mortality in other haemodialysis populations (17). An adequate protein intake and resistance training have been shown to play a role in averting the breakdown of lean body mass in haemodialysis subjects (18).

It was beyond the scope of this study to determine the reasons for the increased inter-dialytic weight gain observed in the Aboriginal population. Specific data on fluid and sodium consumption was not collected; however the authors noted a variety of factors which may have contributed to a higher fluid intake. A small number of Aboriginal subjects were living in rural areas which have a hot dry climate, or in basic dwellings or tented accommodation without air conditioning or access to a refrigerator/freezer to store food and chill fluids and make ice cubes. Alcohol abuse was also noted to be a problem in a few subjects, and could have led to larger inter-dialytic weight gains. In addition, adherence to dialysis regimes was reported by nursing staff to be challenging

for some Aboriginal subjects who had to relocate and live in temporary accommodation to access dialysis services(19); and for whom returning home means missed dialysis sessions and an increased rate of adverse outcomes(20).

The prevalence of diabetic nephropathy in the Aboriginal cohort was consistent with previous observations (2). Aboriginal subjects with diabetes had higher glucose and HbA1c than non-Aboriginal subjects with diabetes. It was beyond the scope of this study to determine the reasons for this finding, however possible explanations include difficulty making suggested dietary changes within traditional eating patterns, inequalities in access to diabetes care, compliance with prescription medicines (21), and ability to manage diabetes in the context of haemodialysis.

Total cholesterol was lower in Aboriginal subjects than non-Aboriginal subjects, which may be related to the increased prescription of cholesterol lowering agents. Total cholesterol concentrations are associated with dietary fatty acid intake, and can reflect dietary intake of saturated and unsaturated fats, however low levels are observed in subjects prescribed statins, consuming inadequate energy intakes or suffering from malnutrition. Triglycerides were elevated in Aboriginal subjects and may reflect fasting status or the fact that Aboriginal subjects have greater genetic predisposition to abdominal obesity, type II diabetes and cardiovascular disease (22, 23).

The impact of increased inter-dialytic weight gain on pre-dialysis measurement of serum albumin, sodium and potassium observed in this study is a cautionary finding with implications for routine clinical practice. Pre-dialysis measurements were significantly lower than post-dialysis measurements in all subjects, but particularly so in Aboriginal subjects. Post dialysis values are likely to be a more accurate reflection of the actual serum concentration, with fluid balance being closer than in the pre-dialysed

state (27). This data suggests measuring serum albumin post-dialysis is important. Serum albumin is strongly correlated with mortality (28), and is known to have a weak relationship with medium-longer term dietary protein intake, however it is often unreliable as a nutritional marker during periods of inflammation and infection, worsening health status and disease progression (29).

A limitation of this study was the inability to obtain detailed diet histories from Aboriginal subjects. Previous reports of the difficulties and limitations of using dietary data collection methods in Australian Aboriginal populations have been published (30), and to date no dietary assessment method has been validated for individual dietary data collection in the Aboriginal population.. As the validity as of diet records and food frequency questionnaires is limited by low levels of literacy and written English in Aboriginal peoples(31, 32), a validated dietary intake assessment method needs to be developed for use in this population group. Use of an interpreter may improve the accuracy of dietary information obtained although difficulties have been documented in translating Aboriginal languages into English (31, 33).

Australian researchers studying communication barriers in this population have recommended the use of educational resources that facilitate discussion on the cultural, social and economic impacts of the illness (34). No separate guidelines currently exist for the dietary management of renal disease in the Aboriginal population and few culturally appropriate resources are available for educating Aboriginal subjects on dietary requirements for dialysis.

### Conclusion

This is the first study to document dietetic assessment of Australian Aboriginal maintenance haemodialysis subjects. Subjects had acceptable parameters of dialysis

adequacy; however 35% had evidence of malnutrition. Further research should focus on establishing a knowledge base for the nutritional management for Aboriginal dialysis subjects, and the development of a validated individual dietary assessment method for use in this population group.

#### **iv. Acknowledgements**

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#### **Author Contributions:**

AT was responsible for study design, ethics clearance, sourcing funding for the project, undertaking data collection, data analysis and manuscript preparation.

AM contributed to study design and manuscript preparation

MG contributed to data collection and manuscript preparation

RC contributed to patient recruitment, data analysis and manuscript preparation.



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## vi. Supporting Information

Nil

**vii. Figure legends**

**Table 1:** Participant characteristics by ethnicity

**Table 2:** Anthropometric and biochemical parameters in a cross-section of Aboriginal and non-Aboriginal Australian haemodialysis subjects

**Table 3:** Clinical and functional parameters in a cross-section of Aboriginal and non-Aboriginal Australian haemodialysis subjects

**Figure 1:** Patient Generated Subjective Global Assessment (adapted version)

## viii. Tables

Table 1

Population Demographics	Non-Aboriginal (n=53)	Aboriginal (n=23)
	Median (range)	
Age (years)	70 (29-83)	51 (34-79)**
Body Mass Index (kg/m <sup>2</sup> )	27 (17-47)	30 (17-46)
Time on Dialysis (years)	3 (0.25-19)	3 (0.25-16)
Dialysis regime (hours/week)	12 (10.5-15.0)	13.5 (10.5-15.0)**
Protein Catabolic Rate (normalised)	1.5 (0.9-2.1)	1.6 (1.0-2.1)
	%	
Male	59	48
Rural / Remote area	10	84***
Current or Previous Smoker	41	68*
Hypertension	98	88
Cardiovascular disease	33	32
Coronary artery disease	27	28
Type I Diabetes	6	8
Type II Diabetes	39	84***
Peripheral vascular disease	14	12
Chronic lung disease	22	28
Prescribed oral hypoglycaemic agent(s)	4	29*
Prescribed insulin regime	34	57
Prescribed lipid lowering agent	50	71
Prescribed antihypertensive agent(s)	88	81
-single agent	20	38
-three or more agents	34	19
Prescribed diuretic	14	14
Prescribed phosphate binder	88	81
Prescribed vitamin D	66	81*
Prescribed B vitamins (including folic acid)	94	95
Prescribed vitamin C	42	90**

Level of significance is denoted by \*p<0.05, \*\*p<0.01. \*\*\*p<0.001

Table 2

Parameter	Non-Aboriginal Median (range)	Aboriginal Median (range)	Non-Aboriginal Mean (SD)	Aboriginal Mean (SD)	Significance
Estimated dry weight (kg)	69.7 (41-134.5)	74.0 (43.5-116.7)	74.8 (20.4)	80.6 (20.2)	
Pre-dialysis weight (kg)	71.5 (42.5-136.7)	76.7 (45.2-119.2)	76.7 (20.6)	83.4 (20.1)	
Post- dialysis weight (kg)	69.8 (40.7-134.2)	73.0 (44.0-116.7)	74.9 (20.4)	80.8 (20.0)	
Serum sodium (mmol/L)	138 (134-143)	136 (130-143)	138 (2)	136 (3)	0.001
Serum bicarbonate(mmol/L)	24.0 (20.3-29.7)	22 (19.3-25.3)	24.2 (2.0)	22.0 (1.6)	<0.001
Serum potassium (mmol/L)	4.83 (4.07-6.55)	4.83 (3.83-5.80)	4.91 (0.55)	4.79 (0.46)	
Serum urea (mmol/L)	20.1 (11.0-35.1)	22.0 (15.2-31.0)	20.3 (4.2)	22.6 (4.6)	0.036
Blood urea nitrogen (mmol/L)	9.4 (5.1-16.3)	10.2 (7.1-14.4)	9.5 (2.0)	10.5 (2.1)	0.036
Serum creatinine (umol/L)	686 (401-1134)	820 (457-1216)	696 (161)	797 (174)	0.014
Haemoglobin (g/L)	118 (100-139)	114 (91-137)	118 (9)	114 (14)	
PTH (pg/ml)	35 (1-136)	41 (1-113)	46 (35)	46 (26)	
Serum calcium (mmol/L)	2.25 (1.91-2.59)	2.13 (1.93-2.37)	2.27 (0.17)	2.15 (0.13)	0.004
Serum phosphate (mmol/L)	1.52 (0.65-2.74)	1.56 (0.88-2.43)	1.60 (0.50)	1.61 (0.42)	
C Reactive protein (mg/L)	8 (0.5-156)	13 (0.3-203)	16 (27)	20 (39)	
Albumin, pre-dialysis (g/L)	35 (25-43)	32 (26-37)	35 (4)	32 (3)	<0.001
Albumin, post dialysis (g/L)	37 (24-49)	36 (28-44)	37 (5)	36 (4)	
Albumin, difference pre-post (g/L)	-0.7 (-0.3-2.0)	-3.3 (-1.0-0.7)	-0.8 (1.6)	-3.8 (3.0)	<0.001
Total cholesterol (mmol//L)	3.75 (2.15-6.65)	3.20 (1.73-5.65)	3.86 (0.88)	3.27 (0.88)	0.007
Triglyceride (mmol//L)	1.45 (0.45-2.90)	1.95 (0.50-6.00)	1.48 (0.60)	2.16 (1.37)	0.024

Table 3

Parameter	Non-Aboriginal Median (range)	Aboriginal Median (range)	Non-Aboriginal Mean (SD)	Aboriginal Mean (SD)
Inter-dialytic weight gain (kg)	1.9 (-0.2-3.5)	2.5 (1.2-3.8)	1.81 (0.76)	2.61 (0.66)***
Inter-dialytic weight gain (%) <sup>^</sup>	2.5 (-0.3-5.0)	3.0 (2.1-5.7)	2.5 (1.1)	3.4 (1.1)**
Systolic blood pressure, pre-dialysis (mmHg)	153 (128-183)	155 (134-174)	153 (13)	157 (12)
Systolic blood pressure, post-dialysis (mmHg)	135 (109-180)	153 (113-207)	138 (18)	148 (21)*
Diastolic blood pressure, pre-dialysis (mmHg)	74 (48-99)	72 (56-96)	71 (13)	73 (11)
Diastolic blood pressure, post-dialysis (mmHg)	64 (46-96)	70 (53-121)	67 (11)	72 (14)
PG-SGA Numerical Score	3 (0-13)	3 (0-12)	4.5 (3.4)	4.2 (3.6)
PG-SGA Overall Physical Rating	1 (0-2)	1 (0-3)*	1.0 (0.6)	1.3 (0.8)**
PG-SGA Fat Stores	0 (0-2)	0 (0-2)	0.6 (0.7)	0.5 (0.7)
PG-SGA Muscle Stores	1 (0-2)	1 (0-3)	1.0 (0.6)	1.3 (0.8)
PG-SGA Fluid Stores	0 (0-2)	0 (0-3)	0.0 (0.3)	0.3 (0.8)
Grip Strength	6 (0-21)	7 (0-24)	7.6 (6.4)	9.0 (9.0)
Urea Reduction Ratio (%)	77 (51-84)	75 (61-83)	76 (6)	74 (6)
Kt/V	1.68 (0.83-2.16)	1.69 (1.19-2.17)	1.67 (0.25)	1.65 (0.25)

<sup>^</sup> Calculated as percentage of estimated dry weight. Level of significance is denoted by \*p<0.05, \*\*p<0.01. \*\*\*p<0.001

**ix. Figures**

See attachment 1