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Obesity, albuminuria, and gamma-glutamyl transferase predict incidence of hypertension in indigenous Australians in rural and remote communities in northern Australia

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Objective: To describe the incidence of hypertension in a cohort of Australian Aboriginal and Torres Strait Islanders.

Method: A follow-up study conducted among 1831 indigenous population aged 15 years and over without hypertension at baseline from 19 communities in North Queensland during 1997–2008. Main measurements included baseline and follow-up weight, waist circumference, blood pressure, fasting glucose, lipids (triglycerides and cholesterol), gamma-glutamyl transferase, urinary albumin creatinine ratio, self-reported tobacco smoking, alcohol intake and physical activity.

Results: Hundred cases of hypertension developed over 2633.4 person-years giving a crude incidence of hypertension of 22.6 (16.2–31.4) per 1000 person-years in females and 60.0 (47.1–76.6) per 1000 person-years for males. Age standardized overall incidence was 51.9 per 1000 person-years. Aboriginal participants were twice as likely as Torres Strait Islanders to develop hypertension, which increased with age. Obesity (BMI >30) strongly predicted incident hypertension independently of age or sex (adjusted hazard ratio 2.9, 95% confidence interval 1.9–4.8). Albuminuria and elevated gamma-glutamyl transferase increased the risk of hypertension (adjusted hazard ratio 1.4–1.7) in this population.

Conclusion: Incidence of hypertension in indigenous Australian adults is nearly double than that of the general Australian population. High background prevalence of obesity, diabetes and albuminuria contributes to this excess. As well as early detection and management of high blood pressure, albuminuria and diabetes in primary care settings, attention should be equally focused on community-level prevention and management of obesity.

Keywords: albuminuria, Australian indigenous population, gamma-glutamyl transferase, incidence of hypertension, overweight and obesity

Abbreviations: AusDiab, The Australian Diabetes, Obesity and Lifestyle Study; BP, blood pressure; GGT, gamma-glutamyl transferase; TSIs, Torres Strait Islanders; UACR, urinary albumin creatinine ratio

INTRODUCTION

High blood pressure (BP) is a major risk factor for death, stroke, and renal and coronary heart disease. The estimated global prevalence of hypertension in 2000 was 26% of adults, and by 2025, it was estimated that this would rise by 24% in developed countries and 80% in developing countries [1]. In Australia, high BP is the most common of all the conditions of the circulatory system. In 2011–2012, it was estimated that 32% Australians aged 18 years and over had high BP (SBP or DBP was $\geq$140/90 mmHg or taking medication). Of these, more than two-thirds (68%) had uncontrolled or unmanaged high BP [2]. High BP was the greatest contributor to the burden of cardiovascular disease (CVD), accounting for 42.1% of CVD's total burden in Australian population as reported in 2003 [3]. Most of the studies reporting hypertension incidence and its risk predictors are from the United States [4]. Demographic, anthropometric and dietary factors have been associated with hypertension [4]. Diabetes or fasting insulin concentrations also predict hypertension incidence [5,6]. The Australian indigenous population has higher prevalence of risk factors including poor diet, smoking and features of the metabolic syndrome [7]. A survey of central Australian Aboriginal adults in the 1990s found that the prevalence of hypertension was three times higher than in non-indigenous Australians, and was associated with overweight, higher albumin creatinine ratio (ACR) and diabetes [8]. The incidence of hypertension in Australian population, especially among indigenous populations, has

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not been reported to date. We have previously found that overweight and obesity predict diabetes incidence [9], whereas hyperglycaemia or diabetes and hypertension, in turn, predict coronary heart disease and act conjointly with albuminuria [10]. This study aimed to document hypertension incidence and to find the predictive metabolic and lifestyle factors.

RESEARCH DESIGN AND METHODS

Study population

Baseline data were collected from 2152 adults in 19 rural indigenous communities across three health districts in far North Queensland, who participated in the 'Well Person's Health Check' between 1999 and 2000. Methods for this cross-sectional study have been reported in detail elsewhere [11]. Briefly, all indigenous residents of the communities aged 13 years and over were invited to attend a health check through printed media, local radio and word of mouth via local health services, community councils and community groups. On the basis of the local census data, the study achieved a participation rate of 44.5%, with greater participation noted in smaller communities. The follow-up data were collected during 2005–2007. On the basis of the census data, participants overall were not different demographically from the age and sex distribution of the Australian indigenous population as a whole. The study protocols were approved by the Cairns Base Hospital Human Research Ethics Committee with support from the peak Indigenous Health Organizations, Apunipima Cape York Health Council, and the Torres Strait and Northern Peninsula Area Health Council.

Measurements

Participants were asked to remove foot wear and heavy clothing, and weighed to the nearest 0.1 kg. Height and waist circumference were recorded to the nearest centimetre, with the latter measured by the same technician at the level of the umbilicus. BMI was calculated as weight (kg) divided by the height squared (m^2). Fruit and vegetable intake, and alcohol consumption were assessed using a methodology derived from that used in the National Nutrition Survey 1995 [12], and categorized using Australian dietary guideline [13]. Physical activity was measured using a 7-day recall method in which participants were asked to report daily physical activities of at least 30 min duration and moderate intensity performed during the week before their health check. Physical activity was categorized using the WHO criteria in which 'enough' means doing moderate to vigorous physical activity for more than 30 min/day for 5 days in the week before the survey [14]. Current smokers were asked how many cigarettes they smoked daily. The self-reported physical activity, smoking and alcohol intake measures are widely used in other studies [15,16].

Gamma-glutamyl transferase (GGT), fasting total cholesterol, high-density lipoprotein cholesterol (HDLC), triglycerides and glucose were measured on blood collected in the early morning after at least an 8 h fast by a medical officer, registered nurse or trained phlebotomist, as described in detail elsewhere [11]. GGT was measured using the kinetic photometric procedure with Cobas Integra 800 (Roche Diagnostics, New York, USA). Blood glucose and blood lipids were measured using photometric enzyme endpoint assay with Cobas Integra 700/400 (Roche Diagnostics).

Blood pressure was the average of three measurements taken sitting after 10 min rest. Participants were seated comfortably with their arms outstretched and supported at chest height. An inflatable cuff appropriate to the participants' arm size was applied just above the elbow centred over the radial artery. BP was measured using a Dinamap model 800 automated blood pressure monitor (Critikon; Tampa, Florida, USA). Three separate measurements were recorded over approximately a 10-min period. Baseline hypertension was ascertained either by detection of high BP at examination (measured BP > 140/90 mmHg) or previous confirmed diagnosis or currently prescribed antihypertensive medication (by medical record review) [11].

Urine specimens provided by participants in sterile 50-ml containers were from the first morning void or a sample at least 2 h from the most recent void. Dipstick urinalysis (Combur-test, Roche) tested the samples for protein, pH, nitrites, leucocytes and blood. ACR was measured by immunoassay in g/mol.

Diabetes was defined as either clinical diagnosis verified by the participants' medical records or a 2-h glucose tolerance test, or fasting blood glucose level at least 7.0 mmol/l [17]. Overweight was defined as BMI 25–30 kg/m^2 and obese as BMI above 30 kg/m^2 using the WHO criteria [14]. Abdominal overweight was defined as waist circumference greater than 80 cm in females and 94 cm in males, and obesity as greater than 88 cm in females and 102 cm in males [13]. Dyslipidaemia was defined as having triglycerides at least 2.0 mmol/l or HDLC below 1.0 mmol/l, as recommended by the National Heart Foundation [18].

Analysis

This analysis excluded participants who were identified as non-indigenous, who were aged less than 15 years or who had hypertension at baseline.

Incident hypertension was defined as the first study visit, subsequent to baseline, at which the participant had SBP at least 140 mmHg, or DBP at least 90 mmHg, or had initiated treatment with antihypertensive medications. The follow-up period for incident hypertension cases was the time from entering the baseline study to diagnosis date. For those who did not develop hypertension, the follow-up period was the interval between the day of baseline survey and the follow-up. The age–sex-specific cumulative incidence rate stratified by ethnicity was calculated by dividing the number of new cases by the total person follow-up years of the corresponding subgroups. Direct standardization was conducted using the 2007 Australian Bureau of Statistics national data as the reference population.

Baseline characteristics including age, sex and ethnicity, self-reported health behaviours including tobacco smoking, alcohol and fruit and vegetable intake, blood pressure, fasting glucose, blood lipids, urinary ACR (UACR) and GGT levels were compared between incident hypertension cases and non-hypertension cases using log-rank tests. The Cox proportional-hazard model was used to identify the significant baseline factors associated with incident hypertension.

The reported crude hazard ratios show the results of a univariate Cox model. The association for each ethnic group was adjusted for age, sex and further adjusted for ethnicity in the combined hazard ratio estimate. The analysis was carried out using STATA 12 (STATAcorp, College Station, Texas, USA) and significance level was set at two-sided P value less than 0.05.

RESULTS

A total of 1831 indigenous population aged 15 years and over without hypertension at baseline from 19 communities in North Queensland during 1997–2008 was included in the analysis. Among them, 401 completed the second survey. Of those lost to follow-up, 83 were dead, 22 were in prison, 344 had moved out of the community and 981 did not attend the follow-up survey. Those lost to follow-up were similar in all baseline characteristics except for a slight excess of younger aboriginal males with a more favourable lipid profile and lower alcohol intake. The baseline characteristics of the 401 participants completing the follow-up were shown in Table 1. Among them, 59% were females, with a mean age of 31.4 years (range 15–78 years). There were 149 aboriginal people (37%) and 190 (47%) Torres Strait Islanders (TSIs). Only 2% met the recommended daily intake for fruits and vegetables, and 23% met the physical activity guidelines, whereas 43% were self-reported 'heavy' drinkers. One hundred and fifty participants (37%) were obese, 37 (9%) were diagnosed with diabetes and 80 (27.1%) had albuminuria. Compared with the aboriginal participants, the TSIs had substantially higher BMI, lower triglycerides and alcohol intake levels, especially in males.

Hundred hypertension cases developed in a total of 401 participants with 2633.4 person-years of follow-up. The average follow-up period was 6.6 years (ranging from 4.5 to 9 years) among those completing the second survey. Of those, 65 were males with an incidence rate of 60.5/1000 person-years compared to 22.6/1000 person-years in females. The incident rate was 44.4/1000 in aboriginal people compared to 37.3/1000 person-years in TSIs. The overall incidence was 38.3/1000 person-years. The age-standardized hypertension incidence rate in female indigenous participants was 29.8/1000 person-years, and was 74.7/1000 person-years in males, with the total incidence ratio of 51.9/1000 person-years [95% confidence interval (CI) 51.8–52.0]. Males were three times (95% CI 1.9–4.4) more likely to develop hypertension than females. Incidence increased with age. Compared with those aged less than 35 years, those aged 35–54 years had a 2.4 times higher risk of hypertension (95% CI 1.6–3.7), and those aged over

TABLE 1. Baseline characteristics of participants completing follow-up in rural indigenous communities in North Queensland

	Aboriginal	TSI	Joint descendents	All groups
Female	$n = 87$	$n = 110$	$n = 38$	$N = 235$
Age (years)	33.4 (30.5–36.2)	32.0 (30.0–34.1)	31.1 (27.5–34.6)	32.4 (30.9–33.9)
WC (cm)*	91.2 (87.5–94.9)	101.5 (98.4–104.6)	98.5 (92.4–104.5)	97.2 (94.9–99.5)
BMI (kg/m^2)*	25.5 (24.0–27.1)	31.4 (30.0–32.8)	30.3 (27.3–33.2)	29.1 (28.0–30.1)
SBP (mmHg)	114.1 (111.6–116.6)	117.9 (116.0–119.80)	116.6 (113.6–119.6)	116.3 (114.9–117.7)
DBP (mmHg)	64.0 (62.0–66.0)	62.9 (61.2–64.7)	64.2 (61.1–67.3)	63.5 (62.3–64.7)
Fasting glucose (g/l)	5.1 (4.7–5.5)	5.4 (5.0–5.7)	5.1 (4.6–5.6)	5.2 (5.0–5.5)
Cholesterol (mmol/l)	4.6 (4.3–4.8)	4.8 (4.6–4.9)	4.3 (4.1–4.6)	4.6 (4.5–4.8)
HDLC (mmol/l)	1.13 (1.06–1.20)	1.08 (1.03–1.12)	1.09 (1.02–1.17)	1.10 (1.07–1.13)
Triglycerides (mmol/l)	1.6 (1.3–1.9)	1.4 (1.2–1.6)	1.1 (1.0–1.3)	1.4 (1.3–1.6)
GGT (IU)	33.3 (28.1–38.6)	24.4 (21.9–27.0)	23.1 (17.7–28.6)	27.5 (25.0–30.0)
UACR (g/mol)	5.7 (2.4–9.0)	7.6 (2.3–12.9)	12.8 (-2.8–28.4)	8.6 (6.3–11.0)
Smokers (%)	54.7 (44.0–65.3)	51.8 (42.4–61.2)	63.2 (47.5–78.8)	54.7 (48.3–61.1)
Drinkers (%)	52.3 (41.7–63.0)	60.7 (51.4–70.1)	66.7 (51.0–82.4)	58.5 (52.1–64.9)
Risky drinkers (%)	30.2 (20.4–40.0)	29.9 (21.1–38.7)	44.4 (27.9–61.0)	32.3 (26.2–38.4)
PA sufficient (%)	21.8 (13.1–30.6)	26.4 (18.0–34.7)	15.8 (4.0–27.6)	23.0 (17.6–28.4)
Male	$n = 62$	$n = 83$	$n = 24$	$N = 169$
Age (years)	37.5 (34.8–40.3)	35.1 (32.2–38.0)	32.4 (27.4–37.3)	35.6 (33.8–37.5)
WC (cm)*	88.1 (84.5–91.7)	99.3 (95.2–103.5)	100.7 (93.3–108.2)	95.3 (92.6–98.0)
BMI (kg/m^2)*	23.1 (21.9 -24.3)	29.6 (27.9 -31.3)	29.2 (26.2–31.3)	27.1 (26.0–28.2)
SBP (mmHg)	123.0 (120.4–125.5)	126.1 (124.4–127.7)	124.2 (121.1–127.2)	124.6 (123.3–125.9)
DBP (mmHg)	69.9 (67.7–72.0)	66.5 (64.5–68.5)	66.9 (63.8–70.0)	67.8 (66.5–69.2)
Fasting glucose (g/l)	5.4 (4.8–6.0)	5.9 (5.3–6.4)	5.3 (4.2–6.3)	5.6 (5.2–6.0)
Cholesterol (mmol/l)	5.2 (5.0–5.5)	5.1 (4.9–5.4)	4.7 (4.3–5.0)	5.1 (4.9–5.3)
HDLC (mmol/l)	1.16 (1.08–1.24)	1.08 (1.02–1.14)	1.13 (1.03–1.24)	1.11 (1.07–1.16)
Triglycerides (mmol/l)*	2.4 (1.9–2.9)	1.9 (1.6–2.2)	1.3 (1.0–1.6)	2.0 (1.7–2.2)
GGT (IU)	86.8 (66.4–107.2)	40.0 (33.6–46.4)	33.8 (26.9–40.7)	56.0 (47.3–64.6)
UACR (g/mol)	13.9 (5.7–22.2)	6.9 (2.4–11.4)	10.4 (-3.4–24.1)	8.1 (5.5–10.6)
Smokers (%)	71.0 (59.5–82.4)	63.3 (52.5–74.1)	54.2 (33.7–74.7)	64.8 (57.5–72.2)
Drinkers (%)	91.7 (84.6–98.8)	79.7 (70.8–88.7)	95.8 (87.6–104.0)	86.5 (81.2–91.8)
Risky drinkers (%)*	73.3 (62.0–84.7)	48.1 (36.9–59.3)	50.0 (29.4–70.6)	57.7 (50.1–65.3)
PA sufficient (%)	21.0 (10.7–31.3)	41.3 (30.3–52.2)	41.7 (21.4–62.0)	33.7 (26.5–41.0)

Figures in the table are means or % (95% CI); *$P < 0.05$ with analysis of variance (ANOVA) or Chi-square tests. GGT, gamma-glutamyl transferase; HDLC, high-density lipoprotein cholesterol; IU, international unit; PA, physical activity; UACR, urine albumin creatinine ratio; WC, waist circumference. Risk drinker defined as those more than 4 drinks/day for men and more than 2 drinks/day for women [13]; PA sufficiently defined as having moderate to vigorous physical activity for more than 30 min/day for 5 days in the week before the survey [14].

55 years had 3.1 times the rate of hypertension (95% CI 1.6–5.8). Aboriginal adults were twice as likely as TSIs to develop hypertension (adjusted hazard ratio 1.9, 95% CI 1.2–3.0) (Table 2).

Obesity defined either by BMI or waist circumference strongly associated with hypertension incidence regardless of age and sex (hazard ratio ranging between 2.5 and 2.9). Albuminuria increased the risk of hypertension by 70% (hazard ratio 1.7, 95% CI 1.1–2.8) after adjusted for age, sex, ethnicity and BMI. Blood glucose, lipids and behavioural factors such as smoking and drinking, and physical activity did not appear to predict hypertension incidence. Among the aboriginal subgroup, the hazard ratio for at-risk drinkers (>4 drinks/day for males and >2 drinks/day for females) was 2.2 (95% CI 1.03–4.8) and attenuated to null when adjusted for sex. Higher baseline GGT levels increased the risk by 90% (hazard ratio 1.9, 95% CI 1.01–3.5), independent of age, sex and BMI, and drinking (Table 3).

DISCUSSION

In this cohort of indigenous Australians living in rural and remote communities in North Queensland, we found the standardized hypertension incidence of 51.9 per 1000 person-years with 29.8 in females and 74.7 per 1000 person-years in males. The incidence was approximately twice among a national representative population longitudinal study [The Australian Diabetes (AusDiab) study], which found a 3% annual incidence rate of hypertension using similar methodology and over the same time period [19]. Our findings are similar to those reported in several follow-up studies looking at ethnic differences for African Americans, Hispanics and Asians, which found that incidence varied with age, sex, ethnicity, and year of reporting and the definition of hypertension [4,20]. These make detailed comparisons difficult. Fewer studies were conducted among 'aboriginal people' in other areas of the world, except for the Strong Heart Study, among 4549 American Indians with a 4-year follow-up period [21]. The study shows hypertension incidence increases with age, but does not differ by sex, and is associated with obesity and albuminuria, which is similar to our study [21].

In line with other longitudinal studies among European [22], American [23,24] and Asian [25] populations, we also found that baseline obesity increased the risk of incident hypertension, defined either by BMI and waist circumference. BMI was found to predict the risk of hypertension in a review paper including 15 prospective cohort studies among various populations, although different other factors are added in the risk models in these studies [26]. We found that BMI and waist circumference as measures of obesity were equally predictive of incident hypertension. This is consistent with a recent meta-analysis looking at data from various ethnic groups to evaluate the cross-sectional association between several anthropometric measurements and hypertension [27]. Obesity-related hypertension appears to involve multiple and linked pathways including insulin resistance, inappropriate sympathetic and renal angiotensin system activation, and inflammatory responses leading to endothelial dysfunction, atheroma and arterial wall stiffness. dipeptidyl peptide-4-mediated incretin signalling can affect vascular function, immune responses and natriuresis in obesity states. Oestrogen-mediated insulin sensitivity in premenopausal women who do not have obesity is compromised when they develop obesity. An alteration in the gut microbiome in obesity is another factor that contributes to insulin resistance and dysfunctional immunity [28].

We also found that albuminuria predicts incident hypertension in this cohort of Australian indigenous adults independent of age, sex and BMI. This is consistent with other prospective cohort studies in population [29–31] or other

TABLE 2. Hypertension incidence by age, sex and ethnicity among 401 indigenous Australian in North Queensland (cases/1000 person-years)

	Aboriginal ($N = 149$)		TSIs ($N = 193$)		Joint descendents ($N = 62$)		
Sex and age	Case/person year (no.)	Incidence (95% CI)	Case/person year (no.)	Incidence (95% CI)	Case/person year (no.)	Incidence (95% CI)	Total incidence (95% CI)
Female							
15–24	0/174.9 (25)	0	1/194.6 (29)	5.1 (0.7–36.5)	0/46.3 (9)	0	2.4 (0.3–17.1)
25–34	5/ 183.0 (26)	27.3 (11.4–65.7)	7/303.0 (46)	23.1 (11.0–48.5)	0/74.4 (14)	0	21.4 (12.2–37.7)
35–44	7/144.1 (20)	48.6 (23.2–101.9	4/165.5 (24)	24.2 (9.1–64.4)	2/57.7 (11)	34.6 (8.7–138.4)	35.4 (20.5–60.9)
45–54	1/71.4 (9)	14.0 (2.0–99.4)	2/45.7 (8)	43.8 (10.9–175.0)	2/18.4 (4)	108.4 (27.1–433.5)	36.9 (15.4–88.6)
55–64	1/37.6 (5)	26.6 (3.7–188.8)	0/9.0 (1)	0	No observation		21.5 (3.0–152.3)
>=65	1/11.8 (2)	84.7 (11.9–601.2)	2/13.6 (2)	147.1 (36.8–588.0)	No observation		118.1 (38.1–366.0)
Subtotal	15/622.7 (87)	24.1 (14.5–40.0)	16/731.4 (110)	21.9 (13.4–35.7)	4/196.9 (38)	20.3 (7.6–54.1)	22.6 (16.2–31.4)
Male							
15–24	2/54.9 (8)	36.5 (9.1–145.8)	8/158.3 (21)	50.5 (25.3–101.0)	1/42.9 (8)	23.3 (3.3–165.4)	42.9 (23.8–77.5)
25–34	6/115.2 (17)	52.1 (23.4–115.9)	4/138.2 (21)	28.9 (10.9–77.1)	1/45.2 (7)	22.1 (3.1–157.0)	36.8 (20.4–66.5)
35–44	14/144.4 (22)	97.0 (57.4–163.7)	5/99.0 (16)	50.5 (21.0–121.3)	1/30.5 (6)	32.9 (4.6–233.4)	73.0 (47/1–113.2)
45–54	5/73.2 (11)	68.3 (28.4–164.2)	8/89.8 (14)	89.1 (44.6–178.2)	0/5.9 (1)	0	77.0 (44.7–132.5)
55–64	4/30.1 (4)	132.7 (49.8–353.6)	5/38.9 (7)	128.6 (53.5–309.1)	0/11.4 (2)	0	111.9 (58.2–215.0)
≥65	No observation		1/4.6 (1)	217.3 (30.6–1452.3)	No observation		217.3 (30.6–1542.3)
Subtotal	31/417.7 (62)	74.2 (52.2–105.5)	31/528.8 (80)	58.6 (41.2–83.4)	3/135.9 (24)	22.1 (7.1–68.4)	60.0 (47.1–76.6)
Total	46/1040.5 (149)	44.4 (33.1–59.0)	47/1260.2 (193)	37.3 (28.0–49.6)	7/332.8 (62)	21.0 (10.0–44.1)	38.0 (31.2–46.2)

CI, confidence interval; TSIs, Torres Strait Islanders. *N*, total number of observations of three ethnicity backgrounds; no., number of observations in each age group from the designated ethnicity.

TABLE 3. Hazard ratio (95% confidence interval) of risk factors of hypertension incidence by ethnicity among 401 indigenous participants in North Queensland

	Aboriginal ($N = 149$)		TSIs ($N = 193$)		Overall ($N = 401$)	
	Crude HR	Adjusted HR[a]	Crude HR	Adjusted HR[a]	Crude HR	Adjusted HR[a]
Abdominal obesity	Reference = <88 cm in women and = <102 in men					
Yes	0.9 (0.5–1.7)	2.0 (0.9–4.2)	1.1 (0.6–2.0)	2.4 (1.2–4.6)	1.1 (0.7–1.6)	2.5 (1.5–3.9)
BMI category	Reference category, BMI <25					
25–29.9	1.3 (0.7–2.7)	1.3 (0.6–2.7)	0.7 (0.3–1.8)	0.8 (0.3–2.1)	0.9 (0.5–1.6)	0.9 (0.5–1.6)
≥30	1.3 (0.6–2.7)	2.5 (1.03–6.2)	1.7 (0.9–3.5)	2.9 ((1.4–6.2)	1.5 (1.0–2.3)	2.9 (1.9–4.8)
Albuminuria	Reference category, UACR <2.5 for males and <3.5 for females					
Yes	1.1 (0.5–2.2)	1.0 (0.5–1.7)	3.5 (1.8–6.7)	2.4 (1.2–4.9)	2.1 (1.4–3.4)	1.7 (1.1–2.8)
GGT categories	Reference category, GGT<50					
≥50	2.8 (1.5–5.0)	1.9 (1.01–3.5)	1.6 (0.7–3.7)	1.1 (0.5–2.5)	2.2 (1.4–3.4)	1.4 (0.9–2.2)
Diabetes	Reference category, No					
Yes	1.0 (0.3–2.7)	0.5 (0.2–1.5)	2.6 (1.2–5.4)	2.1 (0.9–4.7)	2.1 (1.2–3.6)	1.6 (0.9–2.9)
Glucose categories	Reference category, glucose<4.5					
4.5–5.5	1.2 (0.6–2.4)	1.0 (0.5–2.1)	0.9 (0.4–2.0)	0.7 (0.4–1.6)	0.9 (0.6–1.5)	0.8 (0.5–1.3)
≥5.6	1.6 (0.7–3.5)	0.9 (0.4–2.0)	2.0 (0.9–4.6)	1.4 (0.6–3.4)	1.9 (1.1–3.1)	1.3 (0.8–2.4)
Dyslipidaemia	Reference category, No					
Yes	1.3 (0.7–2.3)	1.0 (0.6–1.9)	1.0 (0.5–1.7)	0.9 (0.5–1.7)	1.1 (0.8–1.7)	1.1 (0.7–1.6)
Smoking status	Reference category, No					
Yes	1.6 (0.9–2.9)	1.3 (0.7–2.3)	1.0 (0.5–1.8)	0.8 (0.4–1.4)	0.9 (0.6–1.3)	0.7 (0.5–1.1)
Alcohol drinking	Reference category, No					
Moderate	1.8 (0.7–4.4)	1.8 (0.7–4.5)	0.7 (0.3–1.5)	0.5 (0.2–1.1)	0.9 (0.5–1.6)	0.6 (0.3–1.2)
Risky	2.2 (1.03–4.8)	1.4 (0.6–3.2)	0.8 (0.4–1.5)	0.5 (0.2–1.1)	0.9 (0.6–1.5)	0.6 (0.4–1.0)
PA sufficient	Reference category, No					
Yes	0.7 (0.3–1.5)	1.0 (0.4–2.0)	1.2 (0.7–2.2)	1.1 (0.6–2.1)	0.9 (0.6–1.4)	0.9 (0.6–1.5)

HR, hazard ratio; TSIs, Torres Strait Islanders.
[a]Adjusted for age and sex in each ethnicity subgroup and overall adjusted further for ethnicity; Abdominal obese, and PA sufficient defined by WHO criteria [14]; diabetes defined using WHO criteria [17]; dyslipidaemia defined by National Heart Foundation criteria [18].

ethnic subgroups [32]. Albuminuria is an early marker of endothelial dysfunction and it predicts renal disease progression, cardiovascular and all-cause mortality [33,34]. The mechanisms underlying the link include increased intravascular volume, endothelin secretion, renin–angiotensin and sympathetic nervous system activation, and decreased nitric oxide production and endothelial function [35]. Indeed, the kidney has been proposed as a 'window' for early systemic CVD where glomerular albumin leakage signals widespread the disease [36]. Australian indigenous people have higher rates of albuminuria, but lower estimated glomerular filtration rate (eGFR) than the general population, and this may account for much of the excess CVD risk in this group [37]. We also found that increased GGT significantly predicted incident hypertension independent of age, sex, BMI and self-reported alcohol consumption. This is consistent with a recent meta-analysis including 13 prospective cohort studies during 1991–2012 among males and females from Japan, Korea, China, Turkey, France and USA [38]. Elevated GGT can signal liver injury generally, and non-alcoholic fatty liver disease associated with abdominal obesity and other features of the metabolic syndrome [39]. Increased GGT predicts incident hypertension and diabetes via pro-inflammatory pathways and oxidative stress involving increased fibrinogen, C-reactive protein and free radicals [40,41].

Strengths of this study include a representative community-based sample of indigenous adults and objective clinical measurements. Limitations include a relatively short follow-up period, lack of detailed medical and family history, and some potential confounding factors, and a relatively small follow-up sample. The findings that obesity and other markers of metabolic dysfunction were the strongest predictors of incident hypertension, and that indigenous Australians had excessive risk for both these compared to the general population, were consistent with reports from other ethnic groups in North America and Europe. The challenge going forward is to find effective obesity prevention and treatment measures at a population level which is acceptable and feasible in low-income communities.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of world-wide data. *Lancet* 2005; 365:217–223.
2. Australian Bureau of Statistics. Australian Health Survey 2011/12 (4364.0) October 2012. http://www.abs.gov.au/AUSSTATS/abs@.nsf/Latestproducts/322DB1B539ACCC6CCA257B39000F316C?opendocument. [Accessed 15 May 2014].
3. Begg S, Vos T, Barker B, Stevenson C, Stanley L, Lopez AD. The burden of disease and injury in Australia 2003. PHE82. Canberra: AIHW; 2007.

4. Hajjar I, Kotchen JM, Kotchen TA. Hypertension: trends in prevalence, incidence, and control. *Annu Rev Public Health* 2006; 27:465–490.
5. Ferrannini E, Cushman WC. Diabetes and hypertension: the bad companions. *Lancet* 2012; 380:601–610.
6. Xun P, Wu Y, He Q, He K. Fasting insulin concentrations and incidence of hypertension, stroke, and coronary heart disease: a meta-analysis of prospective cohort studies. *Am J Clin Nutr* 2013; 98:1543–1554.
7. Australian Institute of Health and Welfare. *The health and welfare of Australian's Aboriginal and Torres Strait Islander people, an overview 2011*. Cat. No. IHW 42. Canberra: AIHW; 2011.
8. Wang Z, Sabina K, Wilson A, Rowley KG, Best JD, McDermott R, *et al*. Blood pressure and hypertension for Australian Aboriginal and Torres Strait Islander people. *Eur J Cardiovasc Prev Rehabil* 2006; 13:438–443.
9. McDermott RA, Li M, Campbell SK. Incidence of type 2 diabetes in two indigenous Australian populations: a 6-year follow-up study. *Med J Aust* 2010; 192:562–565.
10. McDermott RA, McCulloch B, Li M. Glycaemia and albuminuria as predictors of coronary heart disease in Aboriginal and Torres Strait Islander adults: a north Queensland cohort. *Med J Aust* 2011; 194:514–518.
11. Miller G, McDermott R, McCulloch B, Leonard D, Arabena K, Muller R. The Well Person's Health Check: a population screening program in indigenous communities in north Queensland. *Aust Health Rev* 2002; 25:136–147.
12. Australian Bureau of Statistics. *National nutrition survey: nutrient intakes and physical measurements, Australia, 1995*. Catalogue no. 4805.0. Canberra: ABS; 1998.
13. National Health and Medical Research Council. Eating for health: Australian Dietary Guidelines. NHMRC: N55a. Canberra. 2013. http://www.nhmrc.gov.au. [Accessed 20 May 2014].
14. World Health Organization. *Obesity: preventing and managing the global epidemic. Report of a WHO Expert Committee*. WHO Technical Report Series no. 894. Geneva: WHO; 1998.
15. Perseghin G, Lattuada G, De Cobelli F, Ragogna F, Ntali G, Esposito A, *et al*. Habitual physical activity is associated with intrahepatic fat content in humans. *Diabetes Care* 2007; 30:683–688.
16. Barr ELM, Magliano DJ, Zimmet PZ, Polkinghorne KR, Atkins RC, Dunstan DW, *et al*. *The Australian diabetes, obesity and lifestyle study: AusDiab 2005*. International Diabetes Institute, Melbourne, Australia; 2006.
17. World Health Organization. *Part 1: diagnosis and classification of diabetes mellitus. In Definition, diagnosis and classification of diabetes mellitus and its complications*. Geneva: Department of Noncommunicable Disease Surveillance, WHO; 1999.
18. National Heart Foundation and Australian Institute of Health and Welfare. *Risk factor prevalence study no. 3 1989*. Canberra: National Heart Foundation and Australian Institute of Health; 1990.
19. Baker IDI – Heart & Diabetes Institute. Key findings from the five year follow-up survey in 2004/2005. https://www.bakeridi.edu.au/ausdiab/keyfindings/. [Accessed 23 May 2014].
20. Carson AP, Howard G, Burke G, Shea S, Levitan EB, Muntner P, *et al*. Ethnic differences in hypertension incidence among middle-aged and older adults. The Multi-Ethnic Study of Atherosclerosis. *Hypertension* 2011; 57:1101–1107.
21. Wang W, Lee ET, Fabsitz RR, Devereux R, Best L, Welty TK, *et al*. A longitudinal study of hypertension risk factors and their relation to cardiovascular disease. The Strong Heart Study. *Hypertension* 2006; 47:403–409.
22. Hu G, Barengo NC, Tuomilehto J, Lakka TA, Nissinen A, Jousilahti P. Relationship of physical activity and body mass index to the risk of hypertension: a prospective study in Finland. *Hypertension* 2004; 43:25–30.
23. Shihab HM, Meoni LA, Chu AY, Wang NY, Ford DE, Liang KY, *et al*. Body mass index and risk of incident hypertension over the life course: the Johns Hopkins Precursors Study. *Circulation* 2012; 126:2983–2989.
24. Gelber RP, Gaziano JM, Manson JE, Buring JE, Sesso HD. A prospective study of body mass index and the risk of developing hypertension in men. *Am J Hypertens* 2007; 20:370–377.
25. Chuang SY, Chou P, Hsu PF, Cheng HM, Tsai ST, Lin IF, Chen CH. Presence and progression of abdominal obesity are predictors of future high blood pressure and hypertension. *Am J Hypertens* 2006; 19:788–795.
26. Echouffo-Tcheugui JB, Batty GD, Kivimäki M, Kengne AP. Risk models to predict hypertension: a systematic review. *PLoS One* 2013; 8:e67370.
27. Huxley R, Barzi F, Lee CMY, Janus E, Lam TH, Caterson I, *et al*. Is central obesity a better discriminator of the risk of hypertension than body mass index in ethnically diverse populations. The Obesity in Asia Collaboration. *J Hypertens* 2008; 26:169–177.
28. DeMarco VG, Aroor AR, Sowers JR. The pathophysiology of hypertension in patients with obesity. *Nature Rev Endocrinol* 2014; 10:364–376.
29. Wang TJ, Evans JC, Meigs JB, Rifai N, Fox CS, D'Agostino RB, *et al*. Low-grade albuminuria and the risks of hypertension and blood pressure progression. *Circulation* 2005; 111:1370–1376.
30. Forman JP, Fisher ND, Schopick EL, Curhan GC. Higher levels of albuminuria within the normal range predict incident hypertension. *J Am Soc Nephrol* 2008; 19:1983–1988.
31. Brantsma AH, Bakker SJ, de Zeeuw D, de Jong PE, Gansevoort RT. Urinary albumin excretion as a predictor of the development of hypertension in the general population. *J Am Soc Nephrol* 2006; 17:331–335.
32. Jessani S, Levey AS, Chaturvedi N, Jafar TH. High normal levels of albuminuria and risk of hypertension in Indo-Asian population. *Nephrol Dial Transplant* 2012; 27 (Supple 3):iii58–iii64.
33. Matsushita K, van Der Velde M, Astor BC, Woodward M, Levey AS, de Jong PE. Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts: a collaborative meta-analysis. *Lancet* 2010; 375:2073–2081.
34. de Zeeuw D, Parving HH, Henning RH. Microalbuminuria as an early marker for cardiovascular disease. *J Am Soc Nephrol* 2006; 17:2100–2105.
35. Campese VM, Mitra N, Sandee D. Hypertension in renal parenchymal disease: why is it so resistant to treatment? *Kidney Int* 2006; 69:967–973.
36. Deckert T, Feldt-Rasmussen BG, Borch-Johnsen K, Jensen T, Kofoed-Enevoldsen A. Albuminuria reflects widespread vascular damage. The Steno hypothesis. *Diabetologia* 1989; 32:219–226.
37. Maple-Brown LJ, Cunningham J, Hodge AM, Weeramanthri T, Dunbar T, Lawton PD, *et al*. High rates of albuminuria but of low eGFR in urban indigenous Australians: the DRUID Study. *BMC Public Health* 2011; 11:346.
38. Liu CF, Gu YT, Wang HY, Fang NY. Gamma-glutamyl transferase level and risk of hypertension: a systematic review and meta-analysis. *PLoS One* 2012; 7:e48878.
39. Li M, Campbell S, McDermott R. γ-Glutamyltransferase, obesity, physical activity, and the metabolic syndrome in indigenous Australian adults. *Obesity* 2009; 17:809–813.
40. Lee DH, Jacobs DR Jr, Gross M, Kiefe CI, Roseman J, Lewis CE, Steffes M. Gamma glutamyl transferase is a predictor of incident diabetes and hypertension: the Coronary Artery Risk Development in Young Adults (CARDIA) Study. *Clin Chem* 2003; 49:1358–1366.
41. Lee DH, Blomhoff R, Jacobs DR Jr. Is serum gamma glutamyltransferase a marker of oxidative stress? *Free Radic Res* 2004; 38:535–539.

Reviewers' Summary Evaluations

Reviewer 1

It is always interesting for epidemiologists to have data about isolated, secluded, primitive or special populations. Although the Aboriginal people living in Northern Queensland described herein probably do not represent a population in the epidemiological meaning of the term, the results add knowledge to the topic of blood pressure trend and risk in particular subjects. We studied in epidemiological setting African (*Lancet* 1996; 348: 784–788; *Arterioscl Thromb Vasc Biol* 1999: 19: 1250–1256) and South-American (*J Hypertens* 1999; 17: 749–756; *J Hypertens* 1997; 15: 1083–1090) primitive people and this remarkable paper represents a new tile in this difficult puzzle.

Reviewer 2

The strength of this study relates to the information about the incidence of hypertension in a so far less well studied population. As reported, the incidence of hypertension in this Aboriginal Australian population is about twice that of the general Australian population and is among the highest world wide. The risk factors for the development of hypertension are interesting, in particular the importance of gamma-glutamyl transferase as a marker for inflammation, which is a strong predictor for hypertension in this population. Another interesting finding in this study is the great difference in the incidence of hypertension between women and men, 22.6 versus 60.0 per 1000 patient years, respectively. The weakness of the study is, as the authors described, the small follow-up sample, but, as the authors mentioned, apart from age, there were no significant differences between the follow-up and the lost to follow-up group of individuals.