

THE ROLE OF MATERNAL DIET IN PROGRAMMING OBESITY, HYPERTENSION AND METABOLIC DISEASE AND ITS RELEVANCE TO THE WESTERN PACIFIC POPULATION

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Abstract

The increasing prevalence of non-communicable diseases reflects an escalating cost and burden to society. Metabolic diseases such as hypertension, diabetes, insulin resistance, renal diseases and cardiovascular disease are a few of the interrelated diseases that are traditionally attributed to lifestyle factors such as obesity. However these diseases may also be programmed *in-utero*, as a result of exposure to a sub-optimal *in-utero* environment. Maternal factors such as dietary intake, central adiposity and general health during gestation may significantly contribute to the programming of an offspring disease phenotype. Ethnicity is an identified independent risk factor as indigenous societies appear to have a greater risk of expressing cardiovascular and metabolic disease phenotypes compared with their Western counterparts. This together with the shift towards Western diets and an increasingly sedentary lifestyle caused by changing work habits increases the propensity for diabetes and hypertension in indigenous populations.

This review discusses the developmental origins of obesity and related diseases and the impact of obesity and related cardiovascular and metabolic disease. We discuss these implications in reference to the global community as well as the Western Pacific.

Introduction

Previously associated with Western populations, obesity is now widespread and is prevalent in regions such as China, India, South America and the South Pacific. Globally, approximately 1.6 billion adults are obese creating a crucial public health issue throughout the world¹. In developing nations worldwide, societies are undergoing rapid transition from agrarian to urban lifestyles and the

variety and availability of food is rapidly changing. This situation is relevant to many nations throughout the Western Pacific and may also contribute to the obesity epidemic that is seen in this geographic region.

Type 2 diabetes mellitus (T2DM) and obesity-related hypertension are also at epidemic levels in developing nations, especially among indigenous and ethnic groups. Although there are adult risk factors for the development of obesity and related disease, emerging evidence suggests that the environment encountered during foetal development can also play a major role in the determination of these diseases. This review discusses the developmental origins of health and disease with regard to the development of obesity and associated metabolic and cardiovascular disease. Wherever possible we present these data in context of the Western Pacific Region.

Obesity

Body mass index (BMI) is used to identify obesity in individuals. Adults with a BMI (kg/m^2) between 25 - 29.9 kg/m^2 are classed as overweight, whereas obesity is defined as having a BMI $\geq 30\text{kg}/\text{m}^2$. This index has, no doubt, gained popularity because of its ease of measurement. However, BMI is not the best estimate of obesity; waist measurements (a measure of abdominal obesity) may be more representative of an unhealthy accumulation of body fat, as opposed to BMI which is an index of overall body heaviness³. Moreover when assessing metabolic disease, BMI measures require ethnic-specific cut-off points. BMI markers are based on European populations and may underestimate the true prevalence of diabetes among those who may be considered as non-obese according to western standards⁴. Across the Western Pacific, ethnic groups demonstrate varied body composition in terms of muscle mass and height.

Estimating the Prevalence of Obesity

Obesity is of particular importance for Australasia and the Western Pacific region. Table 1 shows recent obesity estimates for a selection of countries in the WHO Western Pacific region. Australia and New Zealand show high incidences of obesity but disparity between obesity rates exists in individuals of Caucasian, Maori and Island descent, suggesting that genetic determinants of body size and obesity interact with the environment. Indeed, Island states throughout the Pacific have obesity prevalences that are amongst the highest in the world. The discrepancy between obesity prevalence in urban and rural populations highlights the fact that the environment is an important modulator of bodyweight and similar ethnic groups in differing environments have different disease profiles.

Childhood obesity is associated with dyslipidaemia, hyperinsulinaemia, endothelial dysfunction and hypertension⁵. Although the long term consequences of the rise in childhood obesity are still unknown, 22 million chil-

dren under the age of 5 are overweight⁶ and early onset of T2DM and cardiovascular disease may shift in the prevalence of metabolic diseases to a younger generation.

Obesity and Type 2 Diabetes Mellitus

Longstanding obesity is one of the greatest risk factors for the development of T2DM and globally it is estimated that the prevalence of diabetes will increase from 171 million individuals in the year 2000 to 366 million in 2030, even if obesity rates remain constant⁷. Indigenous peoples and ethnic minorities within developed nations, show an increased susceptibility to T2DM when compared with their Caucasian and European counterparts^{4, 8, 9, 10, 11, 12}. The Pacific Islanders are one such group of people who show an increased incidence and prevalence of T2DM (see Table 2)⁷.

Secondary Consequences of Obesity and Diabetes Mellitus

The International Diabetes Federation reports that diabetes is the fastest growing contributing factor of kidney failure and the leading cause of end stage renal disease (ESRD) where approximately 30 percent of diabetics develop kidney disease. This trend is

especially on the rise among the Aboriginal population in the Northern Territory of Australia; this population is five times more likely to develop renal impairment and complications compared with their non-Aboriginal counterparts¹⁴ that may be associated with low birth weight¹⁵ and low nephron number¹⁶ characteristic to the population.

Obesity and Hypertension

Blood pressure positively correlates with body weight; the Gaussian distribution that exists between body mass and arterial blood pressure is shifted to the right in obesity¹⁷. Established obesity is associated with a range of interrelated factors such as altered renal structure and function, vascular endothelial dysfunction, cardiac remodelling and systemic inflammation, all of which can contribute to the origins of obesity-related hypertension¹⁸.

Table 1: Recent national adult obesity prevalence rates in from selected countries of the Western Pacific

Country [subset]	Survey year	Percentage BMI \geq 30 kg/m ²		
		Male	Female	Both
Australia	2007-2008	25.6	24	
Cook Islands [Urban]	1996-1996	52	57	
Cook Islands [Urban]	1993-1993.	39.6	38.8	38.8
Fiji [Indigenous]	2004-2004	21.2	41.7	
Fiji [India]	2004-2005	6.5	19.3	
Fijian [Other]	2004-2006	24.5	50	
Kiribati	2004-2006	41.7	58.9	50.6
Micronesia	2002-2002	30	55.8	42.6
Nauru	2004-2004	55.7	60.5	58.1
NZ [Caucasian]	2006-2007			24.3
NZ [Asia]	2006-2007			11
NZ [Maori]	2006-2007			41.7
NZ [Pacific Islands]	2006-2007			63.7
New Zealand [Europeans/Other]	2002-2004	19.4	21	
New Zealand [Asia]	2002-2004	4.5	5.7	
New Zealand [Maori]	2002-2004	38.6	36.6	
New Zealand [Pacific Islands]	2002-2004	50.7	56.1	
Samoa	1995-1995	32.9	60.2	
Tokelau	2007-2007	58.6	67.8	63.4
Vanuatu [Urban]	1998-1998	17.6	28.5	22.98
Vanuatu [Rural]	1998-1998	2.6	4.7	3.69

Abbreviations: BMI, Body Mass Index; NZ, New Zealand; Micronesia, Federated States of Mi-

Table 2: Prevalence of T2DM in selected countries in the Western Pacific region in 2007 and projected incidence for 2025

a. Population number as described in the CIA World Factbook 2000, growth and age distribution adjustment to that of world population growth from 2005 to 2025. b. New Zealand data only self reported; total diabetes calculated as twice that reported.

Selected countries of the Western Pacific Region	Population (Ages 20-79)	Population (Ages 20-79)	DM prevalence (%)			
	2007	2025	National (2007)	National (2025)	Global comparative (2007)	Global Comparative* (2025)
Country/Territory	(000's)	(000's)				
Australia	14,504	17,547	6.4	7.7	5.0	6.0
Cook Islands ^a	13	17	5.5	6.3	5.5	6.4
Fiji	510	626	8.5	10.2	9.2	10.5
French Polynesia	165	220	13.1	16.0	13.5	15.6
Kiribati ^a	67	106	6.4	7.0	6.4	6.9
Marshall Islands	38	61	8.8	10.3	8.8	10.1
Micronesia ^a	55	64	5.2	8.2	5.9	7.3
Nauru ^a	8	12	30.7	33.0	30.7	32.3
New Zealand ^b	2,790	3,244	7.7	8.8	6.4	7.3
Palau ^a	13	18	8.9	10.3	8.9	10.1
Papua New Guinea	3,043	4,901	1.9	2.8	2.9	4.1
Philippines	47,038	70,161	6.5	7.9	7.6	9.3
Samoa	90	114	6.5	8.1	7.5	9.1
Solomon Islands	246	415	2.0	3.0	3.0	4.4
Tokelau ^a	1	1	8.5	9.4	8.5	9.3
Tonga ^a	55	63	11.9	14.4	12.9	15.2
Tuvalu ^a	7	10	13.4	15.8	13.4	15.7
Vanuatu	109	172	2.2	3.2	3.0	4.3

Esler and colleagues¹⁹ show that skeletal muscle and renal sympathetic drive are increased in humans with obesity related hypertension although cardiac sympathetic drive is not augmented. Michaels and colleagues²⁰ show that long-term fat feeding in rabbits is associated with an increase in renal responsiveness to electrical stimulation, resulting in an increase in sodium retention. The mechanisms by which the sympathetic nervous system becomes activated in obesity related hypertension are unclear, however hypertension rates will follow obesity rates and further studies are required.

The Impact of Obesity on Indigenous Populations Ethnicity, Obesity and Diabetes: The Thrifty Genotype Hypothesis

It is suggested that Pacific Islanders, Indians and

other South East Asian populations are genetically more prone to obesity and diabetes when compared with Caucasians^{10, 12, 21, 22, 23}. Neel²⁴ first proposed the “thrifty genotype” hypothesis, suggesting that polymorphisms that conferred survival advantages during times of fluctuating feast and famine are selected by positive evolutionary pressure. This promotes survival in periods of famine but in the face of continuing abundant food, such genes would promote obesity. This evolutionary perspective is consistent with what is known about Polynesian voyagers who settled the island nations²⁵ and perhaps explains the higher prevalence of obesity, hypertension and diabetes in these societies.

Risk Factors for Indigenous Groups

Lifestyle factors that mediate T2DM include increas-

ing obesity^{26, 27}, modernisation, a change to Western diets, environmental risk factors and a sedentary lifestyle. An example of this shift in risk factors is the Island state of Nauru. In 2007, 30.7 percent of the Nauruan population between the ages of 20 - 79 years were diabetic¹³. Obesity rates in this population are also extremely high (see Table 1). Equally, Samoans were found to be increasingly obese or at risk of becoming diabetic following migration from rural to urban areas and also abroad to developed countries^{25, 28, 29}. Reports based on dietary intake among Samoans²⁸, Fijians^{30, 31}, Maori and Pacific Islanders residing in Auckland, New Zealand³² and an extensive study of the dietary patterns of Pacific Islanders³³ show that a significant difference between these ethnic groups and the European population is the relative serving size and frequency of consuming high energy, high fat and high sodium food. Figure 1 shows the macronutrient intake of several Western Pacific states. The overall dietary profile does not directly correlate with obesity rates suggesting the involvement of other factors.

Developmental Programming of Adult Disease

Lifestyle and dietary factors contribute to obesity and related metabolic and cardiovascular disease in Pacific Islanders, however a body of evidence suggests that these diseases may originate in early life^{34,35}. Converging lines of evidence suggest that an adverse *in-utero* environment can predispose or “programme”³⁶ individuals to express these diseases later as adults. In agreement with these hypotheses, the increasing incidence of obese and diabetic cases among ethnic groups over the past two or three decades may involve an interaction between a longstanding thrifty phenotype and genotype and an *in-utero* component that when coupled with a change in maternal diet and an increase in maternal obesity, exacerbates the development of offspring obesity and T2DM³⁷. Maternal dietary manipulation or placental insufficiency may be the principle factors involved in the onset of adult diseases such as obesity, hypertension, T2DM and metabolic syndrome³⁸.

Human Studies

Initial studies, such as that by Barker³⁴ correlated birth weight and the subsequent risk of cardiovascular disease, diabetes and hypertension with an inverse association being observed between birth weight and the incidence of disease. The Dutch Hunger Winter during the Second World War, although a tragic event in human history, provides an opportunity to analyse the effects of calorie restriction in the human. The Hunger Winter occurred over winter/spring of 1944-45 due to a blockade of Holland by occupying forces. The official ration was reduced to between 400-800 calories a day. Following liberation, by the summer of 1945 rations returned to 2000 calories a day³⁹. Individuals exposed to famine early in gestation were, at age 60 years, more likely to be overweight than those not exposed to the famine³⁹. Those exposed in early gestation show dyslipidaemia in adulthood⁴⁰. Those affected by the Dutch Hunger Famine show epigenetic modifications (alterations in gene

methylation) that may underlie the programmed phenotype⁴¹.

In order to identify the mechanisms that drive the developmental programming of adult disease, a range of experimental animal models have been used. The maternal diet has frequently been manipulated, including protein and calorie and micronutrient restriction^{42, 43, 43}. Offspring born to these protocols often have low birth weight and those that develop metabolic and cardiovascular disease in later life exhibit characteristic catch-up growth that clearly exacerbates the adverse consequences of developmental programming^{38, 45}.

Maternal nutritional restriction is still a serious health issue in areas of the world. However, perhaps more pertinent to Western societies and many states in the Western Pacific is the issue of maternal obesity and the consumption of fat-rich diets.

Maternal Obesity

Data from the United States estimates that nearly 23 percent of pregnant women are overweight, and 19 percent are obese⁴⁶. There are no data for obesity in pregnancy across the Pacific states, however it is likely high given the overall rates of obesity in women of childbearing ages. Figure 2 shows the rates of obesity for men and women across states in the Pacific. Interestingly, for many of the island nations, female obesity prevalence is greater than that for males.

Gestational Diabetes Mellitus

Obesity in pregnancy is associated with an increased risk of maternal and foetal complications, including preeclampsia and gestational diabetes^{47, 49}. Congenital abnormalities are also associated with maternal obesity⁴⁷. Mothers who develop gestational diabetes mellitus (GDM) during pregnancy exhibit symptoms similar to T2DM such as insulin resistance and glucose intolerance, and foetal glucose exposure is increased^{47, 48}. Offspring tend to be born fatter⁴⁹ even when they are average weight for gestational age.

The onset of T2DM in women during pregnancy may also have an intergenerational effect, as *in-utero* exposure to diabetes has previously been shown to programme obesity and T2DM in offspring⁵⁰. Exposure to hyperglycaemia *in-utero* impairs nephrogenesis resulting in a reduced nephron endowment in the foetus⁵¹ that has been associated with increased risk of developing essential hypertension and chronic renal failure⁵².

Many developed nations, including Australia, USA and Europe derive more than 900 calories per day from fats and sugar⁵³. The caloric intake and macro/micronutrient composition of diets for areas of the Western Pacific have been collated and are shown in Figure 1. Interestingly, the variability in macronutrient intake does not correlate directly with obesity in these nations- for example Fiji has a relatively low obesity rate compared to other Pacific States, however fat intake is still high.

Further studies in this regard would be interesting and maybe important in defining whether island populations are at increased risk of programmed disease as a result of maternal obesity, diabetes, or dietary fat intake.

Experimental Animal Models of Maternal Obesity

Animal models provide valuable insights into the effects of maternal high fat diets on offspring development. Early studies demonstrated that offspring of fat fed rats had altered vascular function, hypertension, endothelial dysfunction, dyslipidaemia, obesity and hyperleptinaemia^{54, 55}, insulin resistance, and mitochondrial dysfunction⁵⁶ - a constellation of signs that are consistent with the metabolic syndrome in humans³⁸. More recent studies⁵⁶ have demonstrated that alterations in aortic structure in offspring of fat fed rats, adult rats exposed to high fat *in-utero*, and during lactation, had low renin hypertension and a reduction in activity and gene expression of the renal Na⁺K⁺-ATPase^{57, 58}.

Mechanisms Underlying Metabolic Programming

Alterations within adult physiology and gene expression are commonly seen in human and animal models of developmental programming. The manner by which the *in-*

utero environment can change foetal development is still unknown, however there are clearly two requisites; the foetus must detect a change in environment and alter gene expression to cope with this altered environment. Cytokines, glucocorticoids, insulin or glucose are thought to act as cues that instigate altered foetal development⁵⁹. Epigenetic modifications such as gene methylation and histone acetylation are, most likely, the mechanism for altering foetal gene expression offspring⁶⁰.

Conclusion

Metabolic diseases are due in part to lifestyle factors, a genetic disposition, and a programming effect during development. Among Pacific Islanders, obesity is one of the commonly identified risk factors that drives these disease states. Although the risk factors for Western populations are well defined, ethnic specific cut off points for obesity, especially central adiposity, may need revision for this population. Furthermore, there is a need for up to date statistics on obesity, diabetes, hypertension and dietary patterns across the region to better inform as to the most pertinent risk factors. What is becoming more apparent is the important role the maternal condition before and during gestation

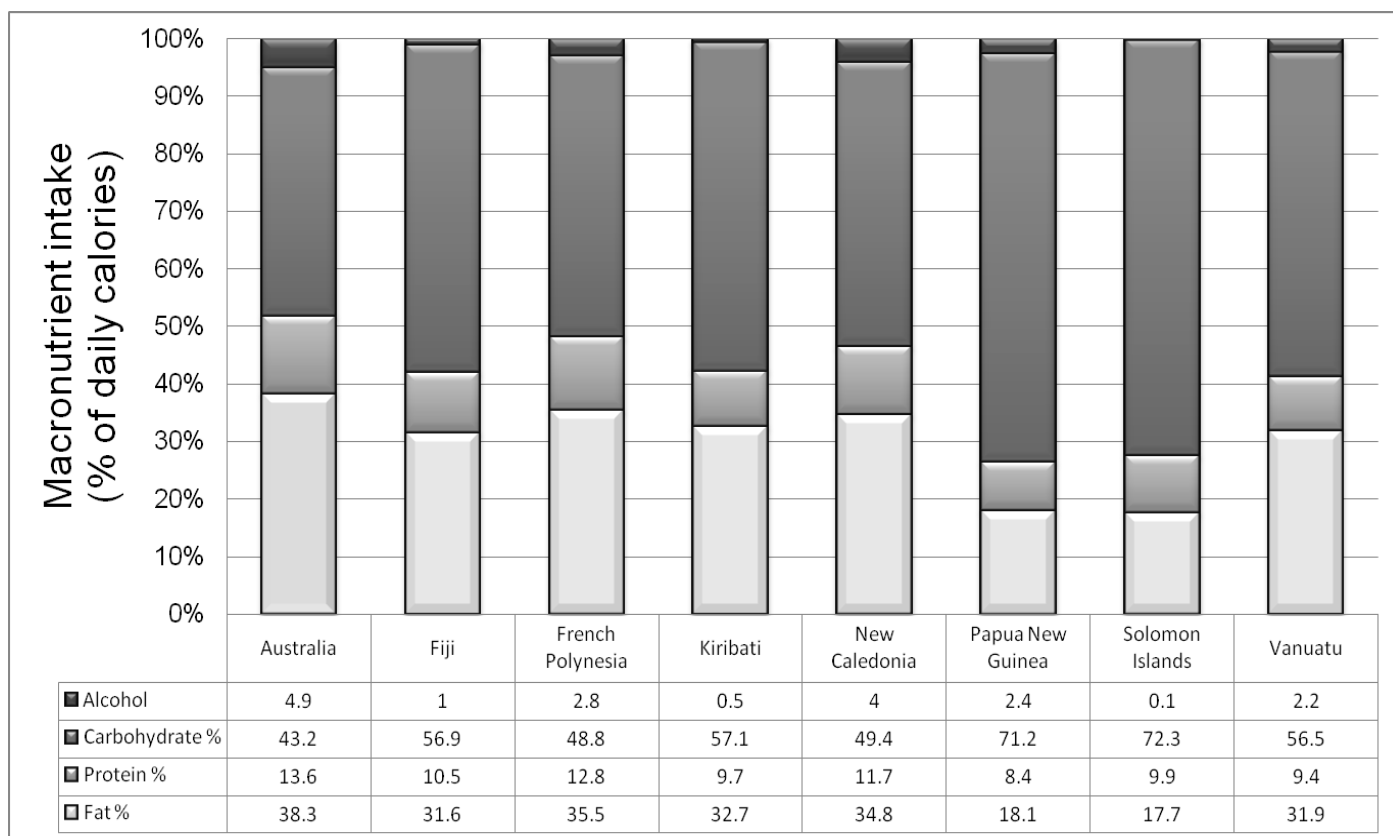


Fig. 1 Macronutrient Intake

The contribution of macronutrient intake to daily caloric load in populations across the Western Pacific. The relative fat, protein and carbohydrate intakes vary between countries, however imbalances in macronutrient intake is not consistently associated with increases in the prevalence of obesity and diabetes in many countries, suggesting that factors other than dietary imbalance are driving the disease process. Data from Hughes 2003³². Unfilled bars indicate % fat intake, light grey fill indicates % protein intake, dark grey represents % carbohydrate intake and black filled bars % alcohol intake.

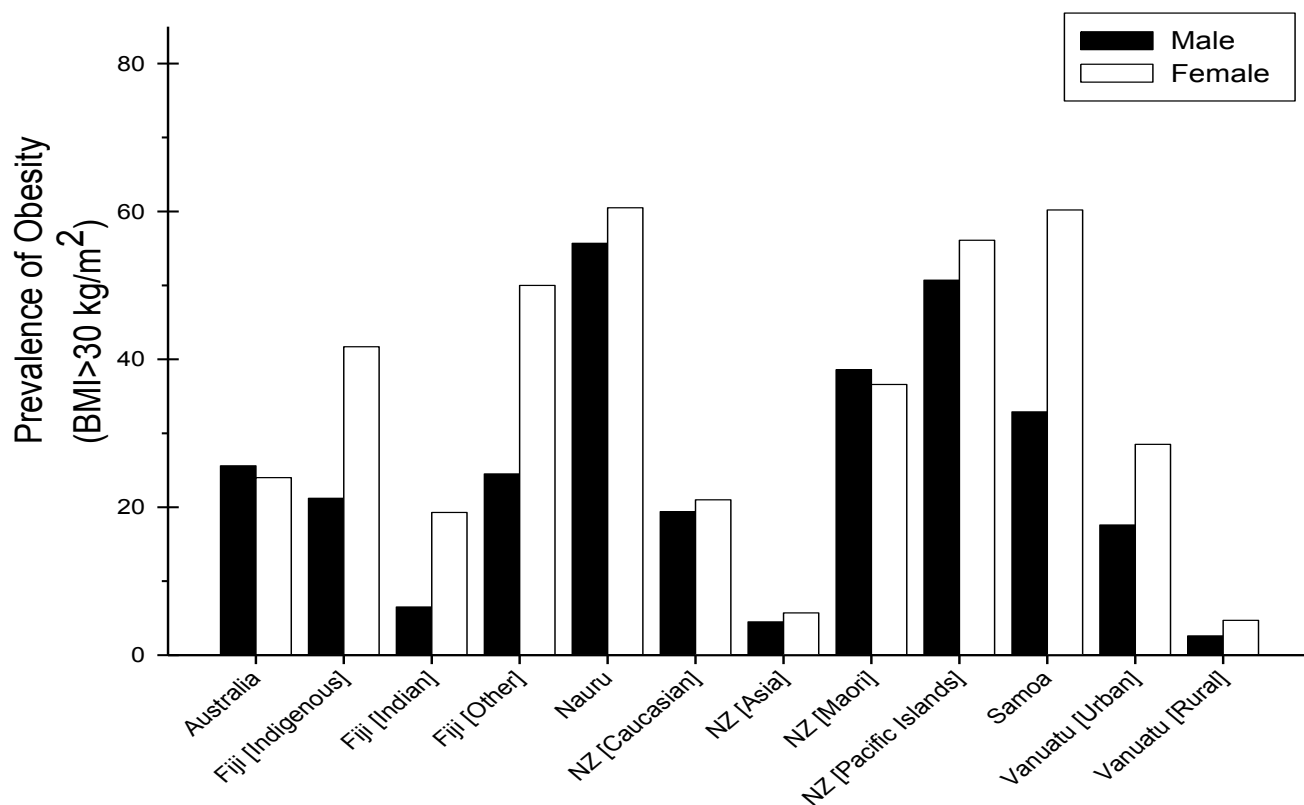


Fig. 2. Prevalence of obesity in adult men and women in areas of the Western Pacific. Adult obesity varies throughout the region and within individual states. Obesity varies significantly with gender and ethnicity. Differences between rural and urban dwellers in the same country are striking as are the differences between rates of obesity for a particular ethnic group that now resides in another country (e.g. New Zealand data). Data are from the WHO Database on Body Mass Index (2006). Male data are shown as black filled bars and female data as unfilled bars. Ethnicity and place of abode are shown in parentheses. NZ=New Zealand.

plays in predisposing their offspring to these phenotypes. Maternal health and well-being including obesity, gestational diabetes, nutritional or dietary intake are just a few of the important parameters which may need to be monitored during pregnancy especially in ethnic communities throughout the Pacific Islands who have a higher predisposition or risk of expressing these phenotypes.

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Funding Source:

Aurora Elisaia is the recipient of an AusAid Australian Development Scholarship.

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