Grand multiparity is associated with type 2 diabetes in Filipino-American women, independent of visceral fat and adiponectin

Running Title: Grand multiparity and type 2 diabetes

Maria Rosario G. Araneta Ph.D. and Elizabeth Barrett-Connor M.D.
Department of Family and Preventive Medicine, University of California San Diego

Corresponding author:
Maria Rosario G. Araneta, Ph.D.
haraneta@ucsd.edu

Submitted 7 August 2009 and accepted 4 November 2009.

This is an uncopyedited electronic version of an article accepted for publication in Diabetes Care. The American Diabetes Association, publisher of Diabetes Care, is not responsible for any errors or omissions in this version of the manuscript or any version derived from it by third parties. The definitive publisher-authenticated version will be available in a future issue of Diabetes Care in print and online at http://care.diabetesjournals.org.
Objective: To determine if multiparity is associated with type 2 diabetes, independent of visceral adipose tissue (VAT) and adipokines.

Research Design and Methods: Participants were from the UCSD Filipino Women’s Health Study with at least one live birth. A two hour 75 gram OGTT was administered; adiponectin, leptin, ghrelin, reproductive history, family history of diabetes, VAT, and lifestyle behaviors were measured between 1995-2002.

Results: Among 152 women, mean age was 59.5 years (range: 48-73), mean parity was 4.3 (range: 1-12 births). Type 2 diabetes prevalence increased by parity group (low:1-2 births,25%; medium: 3-5 births, 30.3%; and grand multiparity: 6-12 births, 50%, p=0.048). Family history of diabetes, exercise, insulin resistance, leptin and ghrelin levels did not differ by parity group. Compared to women in the low parity group, women with ≥6 births were significantly older (62 vs 57 years), had lower college completion (22 vs 58%, p=0.006), more hypertension (72 vs 55%), VAT (74.9 vs 58.4 cm³) and lower adiponectin concentration (5.79 vs 7.61 μg/ml). In multivariate analysis adjusting for adiponectin, VAT, family history of diabetes, age, education, hypertension and estrogen use, grandmultiparous women had a threefold higher odds of type 2 diabetes (Adjusted OR: 3.40, 95% CI: 1.13-10.2) compared to low parity women. No differences were observed in the odds of diabetes between women in the medium (AOR: 1.10, 95% 0.41 - 2.91) compared to the low parity group.

Conclusions: Having ≥6 children was associated with type 2 diabetes, independent of adiponectin, VAT, family history, and other measured diabetes risk factors.
Prior studies have reported elevated type 2 diabetes mellitus (T2DM) prevalence among multiparous women [1-5], however, the elevated risk has been attributed to post-partum weight retention [1,2]. Other studies have shown the excess diabetes risk in multiparous women persisted after adjusting for anthropometric factors [3-5] as well as lifestyle, reproductive and inflammatory factors [3-4].

Visceral adipose tissue (VAT) is an active endocrine organ and is an important determinant of type 2 diabetes. Estimates of obesity including body mass index (BMI), waist girth, waist-to-hip ratio and truncal fat by dual energy xray absorptiometry do not distinguish VAT from subcutaneous adipose tissue (SAT), whereas computed tomography provides a direct estimate of VAT and SAT. Excess VAT accumulation contributes to changes in the production or action of adipocytokines, including adiponectin, resistin, leptin, tumor necrosis factor α and c-reactive protein [6]. Adiponectin, an adipocyte-secreted protein with insulin-sensitizing effects, is inversely associated with VAT, and low levels are predictive of type 2 diabetes even among populations without generalized obesity, such as Japanese and Asian Indians [7-10]. Leptin regulates appetite control and energy metabolism, is strongly correlated with obesity, and may play a major role in islet cell growth and insulin secretion [11, 12]. Ghrelin, a peptide hormone secreted by the stomach, regulates hunger and long-term weight gain or loss, and is thought to play a role in glucose homeostasis and insulin resistance [13]. Plasma ghrelin concentrations are lower in persons with obesity, hypertension and type 2 diabetes [14,15].

Prior studies have reported VAT increases with higher parity, independent of percent body fat among women without diabetes, endocrine disorders or cardiovascular disease [16], but whether VAT or adipocyte-derived proteins mediate the association between multiparity and type 2 diabetes has not been evaluated.

Filipinos in the Philippines, Hawaii, and California have elevated prevalence of type 2 diabetes, despite the absence of general obesity [17-19]. Additionally, Filipino-American women in San Diego had excess VAT despite having similar BMI, waist girth, and percent total body and truncal fat as Caucasian women, and significantly lower anthropometric markers than African-American women [20]. Type 2 diabetes prevalence was 32.1% among Filipinas compared to 5.8% among Caucasian women with similar BMI, waist girth and percentage of truncal fat; when limited to women in the lowest VAT category, the excess diabetes prevalence among Filipinas (22.8%) persisted compared to Caucasians (1.7%) and African-American women (12.1%) [20]. Among normoglycemic women, Filipinas had significantly lower concentrations of adiponectin and ghrelin compared to normoglycemic Caucasian women, even after adjusting for anthropometric markers and insulin resistance [21].

Multiparity has been associated with type 2 diabetes, primarily though post-partum weight retention, however, the association with VAT and adipokines has not been elucidated, particularly in non-obese, highly parous populations. The objective of this study is to determine if multiparity is associated with type 2 diabetes, independent of visceral fat, adipokines and other measured diabetes risk factors.

RESEARCH DESIGN AND METHODS

Study Population: The Rancho Bernardo Study, a San Diego community-based longitudinal study of multiple health outcomes since 1972, includes participants
that are predominantly non-Hispanic Caucasians. Between 1995 and 1999, an ethnic comparison cohort of Filipino women was enrolled [19]. Population-based sampling was not possible because Filipinos were not identified separately from Asians in the 1990 census; consequently, a convenience sample was recruited, as described elsewhere [19]. Clinical evaluations were performed at the UCSD Rancho Bernardo Clinic between 1995 and 1999. Participants without known cardiovascular disease (by history, electrocardiogram abnormalities, angina pectoris by Rose questionnaire) or coronary revascularization surgery were invited between 2001-2002 to measure coronary artery calcium as well as visceral and subcutaneous adipose tissue. The study was approved by the UCSD Human Research Protections Program, and all women provided written informed consent.

Clinical evaluation

Demographic characteristics, lifestyle (cigarette smoking, alcohol use, physical activity), physician diagnosed conditions and menopausal status were determined using structured questionnaires. Reproductive history was assessed by a self-administered questionnaire. Participants who were using prescription or non-prescription medications in the month prior to the clinic visit brought pills and prescriptions to the clinic to be verified and recorded by a nurse. None of the participants were taking thiazolidinediones which have been shown to alter adiponectin concentration.

Height and weight were measured in participants wearing lightweight clothing without shoes. BMI (kg/m\(^2\)) was computed as an estimate of general obesity. Waist circumference was measured at the natural bending point; hip circumference at the iliac crest. VAT and SAT were measured by electron beam computed tomography (GE Imatron C-150 scanner) with three slices between L4 and L5.

A 75-gram oral glucose tolerance test was administered after a minimum 8-hour overnight fast; blood samples were obtained by venipuncture at 0 and 2 hours. Plasma glucose was measured by the glucose-oxidase method and insulin was determined by radioimmunoassay in a diabetes research laboratory. The homeostasis model assessment was used to estimate insulin resistance (HOMA-IR) and β-cell function (HOMA-β). Type 2 diabetes was defined using the 1999 World Health Organization (WHO) criteria: fasting plasma glucose level ≥126 mg/dl, or 2-hour postchallenge glucose level ≥200 mg/dl, or a history of type 2 diabetes diagnosed by a physician, or treatment with an oral hypoglycemic agent or insulin. Two morning blood pressure readings were recorded with a mercury sphygmomanometer using the Hypertension Detection and Follow up Program protocol. Hypertension was defined as systolic blood pressure ≥130 or diastolic blood pressure ≥85 mmHg or use of anti-hypertensive medication. Fasting adiponectin, leptin and ghrelin concentrations were measured by radioimmunoassay (Linco Research, St. Louis, Missouri) in 2004 using archived samples that had been stored frozen at -70°C and not previously thawed.

Statistical analysis

Nulliparous women were excluded to exclude those who might have had polycystic ovary disease, a known risk factor for diabetes. Parity, defined as live births, was analyzed as a continuous variable and further classified into: low parity (1-2 births), medium parity (3-5 births) and grand multiparity (6-12 births) groups. Data were analyzed using Statistical Analysis Systems (SAS Version 9.1, Cary, North Carolina). Analysis of variance, general linear models, and chi-square tests were used for descriptive statistics. General linear models were used to compare mean levels of each anthropometric marker, while adjusting for age and diabetes.
The distribution of adiponectin, leptin, and ghrelin were skewed and consequently log-transformed for statistical analysis; geometric mean levels of these proteins are reported. Univariate analysis was performed to identify covariates associated with diabetes. Multivariable logistic regression was performed to identify covariates associated with type 2 diabetes, and to compare the odds of type 2 diabetes by parity category, using the low parity category as the referent group. Covariates included in the multivariable models consisted of variables that differed by parity group and those associated with diabetes in univariate analysis. Statistical significance was designated at p<0.05 and 95% confidence intervals that excluded 1.

RESULTS

The study population included 152 parous Filipino-American women with a mean age of 59.5 years (range: 48 - 73); the majority were immigrants (99%), well educated (44% were college graduates) and engaged in healthy behaviors. Only 14% had ever smoked, 1% had ≥3 alcoholic drinks per week, and 71% reported exercising at least three times per week. Mean BMI was 25.4 kg/m² while mean waist girth was 81.4 cm, and one-third (33.6%) had type 2 diabetes. One fourth (n=39, 25.7%) had at least one biological parent with type 2 diabetes; of these, 18 had both a biological parent and sibling with type 2 diabetes. An additional 14 women (9.2%) had a sibling (diagnosed after age 45) with type 2 diabetes but did not have an affected biological parent, for a total of 34.9% who had a family history of type 2 diabetes. The number of live births ranged from 1 to 12 births (mean: 4.3 live births), and one-fourth had grand multiparity (≥6 live births; mean: 8.1 births).

When stratified by parity group, mean age increased with increasing parity, where women with ≥6 children were significantly older (mean age: 62.4 years compared to 57.1 years for those who bore 1 or 2 children (p<0.001, Table 1). Women with grand multiparity had lower college completion and estrogen use (22.2%; 2.8%) compared to women with medium (47.4% completed college; 26.3% used estrogen) or low parity (57.5%; 32.5%). Grandmultiparous women had significantly higher fasting and 2 hr glucose levels, however, fasting and two hour insulin levels, HOMA-IR and HOMA-β levels, family history of type 2 diabetes and exercise (≥3 times/week) frequency did not vary by parity category (Table 1). The prevalence of hypertension and type 2 diabetes increased significantly by parity category; diabetes prevalence was 25% in the low parity group, 30.3% in the medium birth group and 50% among women with ≥6 births (p=0.048).

Age-adjusted mean BMI, waist girth, and VAT were significantly lower in women in the low parity group compared to either the medium or high parity group, but did not differ between the medium and high parity group (Table 2). Waist-to-hip ratio was significantly smaller in women with 1 to 2 children compared to those with ≥6 children, but did not differ with the medium parity group. Subcutaneous fat was significantly lower in the low parity group compared to women with 3 to 5 children, but did not differ compared to grandmultiparous women. Adiponectin was inversely associated with obesity, and was significantly lower in the medium and high parity groups compared to women with lower parity. Age-adjusted ghrelin and leptin levels did not differ by parity category.

These observations persisted after adjusting for both age and diabetes with the exception of BMI and adiponectin. BMI did not differ by parity group after adjusting for age and diabetes, while adiponectin was significantly lower in the medium parity group, but did not differ between the low and high parity categories. Neither ghrelin nor
leptin levels varied by parity category after adjusting for age and diabetes.

Stepwise logistic regression showed that parity (adjusted odds ratio (OR): 1.27; 95% confidence intervals (CI): 1.09 - 1.49, p-value= 0.0027 was independently associated with type 2 diabetes after adjusting for adiponectin concentration, VAT, family history of type 2 diabetes, hypertension, age, current estrogen use, and education (Table 3, Model 1). Further, family history of diabetes (adjusted OR: 5.03, 95% CI: 2.18 -11.60), hypertension (adjusted OR: 3.16, 95% CI: 1.33 - 7.55) and low adiponectin (log) levels (adjusted OR: 0.45, 95% CI: 0.22 - 0.94) were also independently associated with type 2 diabetes. Neither age, visceral adiposity, education nor estrogen use were associated with type 2 diabetes. These observations persisted when categorized by parity group. Compared to women in the low parity group, women who had > 6 live births had a three-fold higher odds (adjusted OR: 3.40, 95% CI: 1.13 - 10.2) of having type 2 diabetes, independent of adiponectin concentration, VAT, family history of type 2 diabetes, hypertension, age, estrogen use, and education (Table 3, Model 2). Similarly, family history of type 2 diabetes, hypertension and low adiponectin concentration were independently associated with type 2 diabetes. Women in the medium parity group did not have an increased risk of type 2 diabetes (adjusted OR: 1.10, 95% CI: 0.41 - 2.91) compared to the low parity group after adjusting for the above covariates. Neither ghrelin nor leptin were associated with type 2 diabetes in multivariable models that included these proteins (data not shown).

Family history of diabetes was an important correlate of type 2 diabetes, however neither mean adiponectin, BMI, waist, nor VAT differed among those with versus without a family history of diabetes. When limited to the 99 women without a family history of type 2 diabetes, parity remained independently associated with type 2 diabetes (adjusted OR: 1.22, 95% CI: 1.03-1.44, p=0.021) after adjusting for adiponectin, VAT, age, education, estrogen use and hypertension.

CONCLUSIONS

This highly parous cohort of non-obese Filipino-American women with elevated diabetes prevalence offered a unique opportunity to assess the association between multiparity and type 2 diabetes. Prior studies have attributed post-partum weight retention as the primary mechanism for type 2 diabetes in multiparous women [1,2], however, to our knowledge, no studies have included CT-defined VAT measures, adipokines, or ghrelin. Although anthropometric markers, including VAT, increased with parity, visceral adiposity did not explain the excess diabetes prevalence among grandmultiparous women. Low adiponectin concentration and hypertension were independently associated with type 2 diabetes, as was family history of diabetes, reinforcing the important contribution of genetic factors; however, the excess diabetes prevalence in grandmultiparous women persisted when the analysis was limited to those without a family history of type 2 diabetes.

Physical inactivity did not differ by parity group, contrary to other observations. Our observations of decreasing education and estrogen use with increasing parity is consistent with prior studies [3], but neither were independently associated with type 2 diabetes. However, this cohort was highly educated, where almost half were college graduates, including 22% of grandmultiparous women. Consequently, we were unable to observe the confounding effects of education and socioeconomic status on lifestyle behaviors and diabetes risk associated with higher parity in prior studies [5].

Pregnancy is a diabetogenic state characterized by adipose tissue accretion,
hyperinsulinemia, insulin resistance, lipolysis, elevated leptin and resistin levels, and reduced adiponectin secretion [22]. Multiple pregnancies result in longer cumulative exposure to insulin resistance and hypoadiponectinemia. It remains unclear if these conditions are sustained or exacerbated post-partum through middle-age. Low adiponectin was independently associated with type 2 diabetes in this analysis, and levels were significantly lower in multiparous women, but neither insulin resistance (by HOMA-IR) nor leptin concentration differed by parity group.

Gestational diabetes mellitus (GDM) is a risk factor for future incident type 2 diabetes [23], but GDM history was not ascertained in this study since the majority (88%) gave birth before 1979, when GDM became a clinically recognized entity. Despite the general absence of pre-conceptional obesity, Filipino-American parturients have the 3rd highest GDM prevalence (7.1%) in the United States, following Asian Indians (8.6%) and Pacific Islanders (7.4%), and have higher GDM prevalence compared to Native American, Caucasian, African-American or Hispanic parturients [24]. Women in our cohort might have had similarly elevated prevalence of GDM during multiple pregnancies, consequently exacerbating their risk for type 2 diabetes.

Study limitations included enrollment of a volunteer sample since census data during study enrollment reported Asian-American nationalities collectively, such that population-based sampling of Filipinos was not possible. However, college completion in our cohort was identical to 2000 national census data for all Filipino-American women aged 25 years and older; suggesting that our sample was generalizable to all Filipino-American women with regard to socioeconomic status. Additional considerations include the small sample sizes when stratified into parity categories, as reflected by the wide confidence intervals in multivariable regression analysis. Total adiponectin, rather than the different isomers of adiponectin were measured; the high molecular weight (HMW) form of adiponectin is substantially reduced in GDM [25]; although it remains unclear if HMW adiponectin accounts for the elevated diabetes risk in grandmultiparity. Further, we did not include fetal losses, where long gestations that terminated spontaneously or as stillbirths contributed to the cumulative diabetogenic exposure during pregnancy. Finally, the generalizability of our findings to other highly parous populations is questionable given the elevated prevalence of type 2 diabetes, gestational diabetes, family history of type 2 diabetes, excess VAT accumulation and low adiponectin concentration among Filipino-American women [20, 21, 24].

The strengths of this study include a cohort of highly parous women where one-third had type 2 diabetes and one-fourth of the sample had grandmultiparity. CT-defined VAT allows more precise enumeration of intra-abdominal obesity compared to estimates provided by BMI or waist in prior studies. To our knowledge, this is the first study to assess the role of adiponectin, leptin and ghrelin as mechanisms for the association between multiparity and diabetes. None of the women were using thiazolidinediones, which enabled comparisons by parity group without the confounding effects of medications that can alter adiponectin or ghrelin levels.

In summary, grand multiparity was associated with type 2 diabetes, independent of visceral adiposity and adiponectin concentration. Hypertension, family history of diabetes and low adiponectin levels were also associated with type 2 diabetes, but did not explain the excess diabetes prevalence in grandmultiparous women. Grand multiparity may exacerbate diabetes risk through myriad mechanisms that have yet to be identified.
ACKNOWLEDGEMENTS
This work was supported by American Heart Association Grant 0070088Y, by NIH/NIDDK R01DK31801 and R03 DK60575. Both authors have no conflicts of interest to report.
REFERENCES

1. Manson JE, Rimm EB, Colditz GA, Stampfer MJ, Willett WC, Arky RA, Rosner B, Hennekens CH, Speizer FE. Parity and incidence of non-insulin-dependent diabetes mellitus. *Am J Med* 1992;93:13-18.

2. Collins VR, Dowse GK, Zimmet PZ. Evidence against association between parity and NIDDM from five population groups. *Diabetes Care* 1991;14:975-981.

3. Nicholson WK, Asao K, Brancati F, Coresh J, Pankow JS, Powe NR. Parity and risk of type 2 diabetes: the Atherosclerosis Risk in Communities Study. *Diabetes Care* 2006;29:2349-2354.

4. Kritz-Silverstein D, Barrett-Connor E, Wingard DL. The effect of parity on the later development of non-insulin-dependent diabetes mellitus or impaired glucose tolerance. *N Engl J Med* 1989;321:1214-1219.

5. Simmons D, Shaw J, McKenzie A, Eaton S, Cameron AJ, Zimmet P. Is grand multiparity associated with an increased risk of dysglycaemia? *Diabetologia* 2006;49:1522-1527.

6. Perrini S, Leonardini A, Laviola L, Giorgino F. Biological specificity of visceral adipose tissue and therapeutic intervention. *Arch Physiol Biochem* 2008;114:277-286.

7. Matsuzawa Y, Shimomura I, Kihara S, Funahashi T. Importance of adipocytokines in obesity-related diseases. *Horm Res* 2003;60(Suppl 3):56-59.

8. Chandran M, Phillips SA, Ciaraldi T, Henry RR. Adiponectin: more than just another fat cell hormone? *Diabetes Care* 2003;26:2442-2450.

9. Li S, Shin HJ, Ding EL, van Dam RM. Adiponectin levels and risk of type 2 diabetes: a systematic review and meta-analysis. *JAMA* 2009;302:179-88.

10. Snehalatha C, Mukesh B, Simon M, Viswanathan V, Haffner SM, Ramachandran A. Plasma adiponectin is an independent predictor of type 2 diabetes in Asian Indians. *Diabetes Care* 2003;26:3226-3229.

11. Ruhl CE, Everhart JE. Leptin concentrations in the United States: relations with demographic and anthropometric measures. *Am J Clin Nutr* 2001;74:295-301.

12. Rasouli N, Kern PA. Adipocytokines and the metabolic complications of obesity. *J Clin Endocrinol Metab* 2008;93:S64-73.

13. Shiiya T, Nakazato M, Mizuta M, Date Y, Mondal MS, Tanaka M, Nozoe S, Hosoda H, Kangawa K, Matsukura S. Plasma ghrelin levels in lean and obese humans and the effect of glucose on ghrelin secretion. *J Clin Endocrinol Metab* 2002;87:240-244.

14. Poykko SM, Kellokoski E, Horkko S, Kauma H, Kesaniemi YA, Ukkola O. Low plasma ghrelin is associated with insulin resistance, hypertension, and the prevalence of type 2 diabetes. *Diabetes* 2003;52:2546-2553.

15. Langenberg C, Bergstrom J, Laughlin GA, Barrett-Connor E. Ghrelin and the Metabolic Syndrome in Older Adults. *J Clin Endocrinol Metab* 2005;90:6448-6453.

16. Blaudeau TE, Hunter GR, Sirikul B. Intra-abdominal adipose tissue deposition and parity. *Int J Obes* 2006;30:1119-1124.

17. Grandinetti A, Kabolokula JK, Theriault AG, Mor JM, Chang HK, Waslien C. Prevalence of diabetes and glucose intolerance in an ethnically diverse rural community of Hawaii. *Etnh Dis* 2007;17:250-255.

18. Baltazar JC, Ancheta CA, Aban IB, Fernando RE, Baquild MM. Prevalence and correlates of diabetes mellitus and impaired glucose tolerance among adults in Luzon, Philippines. *Diabetes Res Clin Pract* 2004;64:107-115.
19. Araneta MR, Wingard DL, Barrett-Connor E. Type 2 diabetes and metabolic syndrome in Filipina-American women: a high-risk nonobese population. *Diabetes Care* 2002;25:494-499.
20. Araneta MRG, Barrett-Connor E. Ethnic differences in visceral adipose tissue and type 2 diabetes in Filipino, African-American and White women. *Obes Res.* 2005;13:1458-1465.
21. Araneta MRG and Barrett-Connor E. Adiponectin and ghrelin levels and body size in normoglycemic Filipino, African-American and Caucasian women. *Obesity* 2007;15:2454-2462.
22. Zavalza-Gómez AB, Anaya-Prado R, Rincón-Sánchez AR, Mora-Martínez JM. Adipokines and insulin resistance during pregnancy. *Diabetes Res Clin Pract* 2008;80:8-15.
23. Retnakaran R. Glucose Tolerance Status in Pregnancy: A Window to the Future Risk of Diabetes and Cardiovascular Disease in Young Women. *Diabetes Rev.* 2009 (in press)
24. Chu SY, Abe K, Hall LR, Kim SY, Njoroge T, Qin C. Gestational Diabetes Mellitus: All Asians Are not Alike. *Prev Med.* 2009 (in press)
25. Retnakaran R, Connelly PW, Maguire G, Sermer M, Zinman B, Hanley AJ. Decreased high-molecular-weight adiponectin in gestational diabetes: implications for the pathophysiology of Type 2 diabetes. *Diabet Med.* 2007;24:245-52.

**Table 1.** Age adjusted demographic and clinical characteristics, by parity category, Filipino-American women, San Diego, California, 1995-2002

| Number of live births | 1-2 (n=40) | 3-5 (n=76) | 6-12 (n=36) | p-value |
|----------------------|------------|------------|-------------|---------|
| **Age (years)**      | 57.1       | 59.5       | 62.4        | 0.001   |
| College graduate (%) | 57.5       | 47.4       | 22.2        | 0.006   |
| Family history diabetes (%) | 40.0 | 35.5 | 27.8 | 0.528 |
| Exercise (>3 times/wk, %) | 70.0 | 72.4 | 69.4 | 0.940 |
| Estrogen use (current, %) | 32.5 | 26.3 | 2.8 | 0.004 |
| Fasting glucose (mmol/L) | 5.41 | 5.93 | 6.79 | 0.046 |
| 2 hr glucose (mmol/L) | 8.69 | 10.09 | 12.09 | 0.029 |
| Fasting insulin (pmol/L) | 80.94 | 74.59 | 76.24 | 0.947 |
| 2 hr insulin (pmol/L) | 435.63 | 576.36 | 542.39 | 0.157 |
| HOMA-IR | 2.98 | 3.03 | 3.25 | 0.929 |
| HOMA-β index | 119.71 | 113.27 | 96.85 | 0.438 |
| Hypertension (%) | 55.0 | 64.5 | 72.2 | 0.029 |
| Type 2 diabetes (%) | 25.0 | 30.3 | 50.0 | 0.048 |
Table 2. Anthropometric characteristics, adjusted for age and type 2 diabetes, by parity category, Filipino-American women, San Diego, California

| Number of live births | 1-2 (n=40) | 3-5 (n=76) | 6-12 (n=36) |
|-----------------------|------------|------------|-------------|
| BMI (kg/m²)           | 24.55      | 25.71      | 25.85       |
| Waist (cm)            | 78.34      | 82.89*     | 83.04†      |
| Waist:hip             | 0.823      | 0.837      | 0.859†      |
| VAT (cm³)             | 59.39      | 72.12*     | 73.19†      |
| SAT (cm³)             | 140.73     | 163.03*    | 158.94      |
| Adiponectin (μg/ml)   | 7.45       | 5.67*      | 6.02        |
| Ghrelin (pg/ml)       | 1072.0     | 1084.7     | 1039.6      |
| Leptin (ng/ml)        | 12.38      | 14.72      | 13.63       |

*p<0.05, 3-5 vs 1-2 live births; †p<0.05 6-12 vs 1-2 live births

Table 3. Stepwise logistic regression: covariates associated with type 2 diabetes among parous Filipino-American women

| Covariate                           | Adjusted Odds Ratio | 95% CI:          | p-value |
|-------------------------------------|---------------------|------------------|---------|
| **Model 1**                         |                     |                  |         |
| Parity                              | 1.27                | (1.09 - 1.49)    | 0.0027  |
| Adiponectin (log)                   | 0.45                | (0.22 - 0.94)    | 0.0335  |
| Family history of diabetes          | 5.03                | (2.18 - 11.6)    | 0.0001  |
| Hypertension                        | 3.16                | (2.18 - 7.55)    | 0.0095  |
| **Model 2:**                        |                     |                  |         |
| >=6 live births                     | 3.40                | (1.13 - 10.2)    | 0.0295  |
| Adiponectin (log)                   | 0.42                | (0.20 - 0.89)    | 0.0234  |
| Family history of diabetes          | 4.35                | (1.95 - 9.73)    | 0.0003  |
| Hypertension                        | 2.99                | (1.26 - 7.07)    | 0.0128  |

Adjusted for age, education, estrogen use, and VAT
Model 1: parity as a continuous variable;
Model 2: by parity category, with low parity (1-2 births) as the referent group