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Probable NAFLD, by ALT levels, and Diabetes among Filipino-American Women

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Abstract

BACKGROUND—Studies have shown alanine aminotransferase (ALT), a marker for nonalcoholic fatty liver disease (NAFLD), to predict type 2 diabetes (T2DM).

OBJECTIVE—To examine the association between probable NAFLD and T2DM in non-obese, non-alcoholic consuming Filipino-American women aged 48 – 73 years.

RESEARCH DESIGN AND METHODS—The UCSD Filipino Women's Health Study measured glucose, hepatic enzymes, adiponectin and visceral fat (VAT) during clinical visits (1995 –2002). We defined T2DM by 1999 WHO criteria and probable NAFLD as ALT > 31 U/L.

RESULTS—Prevalence of T2DM was 34.4% and probable NAFLD was 17.2%. Women with T2DM (n = 56) had higher VAT, total:HDL cholesterol, SBP, fasting glucose and insulin, postchallenge glucose, ALT (28.7 vs. 19.1 U/L, p<0.0001), GGT, AST, and probable NAFLD (32.1 vs. 9.35%, p = 0.0002) and lower adiponectin than those without T2DM (n = 107). GGT (p = 0.0008) and ALT (p = 0.002) were associated with increasing VAT levels. Probable NAFLD was independently associated with T2DM (AOR 6.32, 95% CI 2.2–18.0), after adjusting for risk factors.

CONCLUSION—Probable NAFLD was elevated and associated with T2DM, independent of VAT, adiponectin and other risk factors. ALT may serve as a useful marker for NAFLD or diabetes risk in Filipino women.

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Keywords

NAFLD; non-alcoholic fatty liver disease; ALT; alanine aminotransferase; Filipino women; Adiponectin; Diabetes

INTRODUCTION

Type 2 diabetes has become a significant public health problem among Asian-Americans who comprise the second largest ethnic minority in California [1]. Filipinos are the largest Asian-American population in California and the third largest immigrant group in the United States [2]. In 1958–59, before the onset of the American obesity epidemic, Filipino-Americans had higher diabetes prevalence (22%) compared to Caucasians (7%) and Chinese-Americans (15%) [3]. Filipinos, like many Asians, are generally non-obese by western standards yet display obesity-related comorbidities including excess diabetes, metabolic syndrome, and hypertension [4, 5].

Visceral adipose tissue (VAT) has been significantly associated with the prevalence and incidence of diabetes in selected Asian populations [6, 7]. We previously reported that despite similar body mass index (BMI) and waist girth as Caucasian women and lower BMI and waist compared to African-American women, Filipino-American women had significantly higher VAT than either group [5]. Even among women with the least VAT (46 cm³), Filipinas maintained the highest diabetes prevalence (22.8%) compared to Caucasians (1.7%) and African-Americans (7.4%). This elevated prevalence, which is not entirely explained by excess VAT accumulation, requires further elucidation about the etiology of diabetes.

Prospective studies have shown that increasing liver enzyme levels, particularly alanine aminotransferase (ALT), predicts incident diabetes [8 - 11] and likely reflects non-alcoholic fatty liver disease (NAFLD). The liver damage of NAFLD ranges from simple fatty liver to fatty liver with inflammation that may lead to fibrosis or cirrhosis. Its pathology resembles that of alcoholic fatty liver disease and shares a similar characteristic of increased liver enzymes, without the role of excessive alcohol consumption [12]. NAFLD is strongly associated with increasing diabetes prevalence and central obesity among Asians [13, 14] and has been recognized commonly in the Philippines, India, and in aboriginal populations of Australia and Malaysia [13].

Previous studies defining elevated liver enzyme levels [15, 16] have been widely used as surrogate markers for NAFLD [17 - 19]. Though no standard cut-point exists, the National Center for Health Statistics (NCHS) defines elevated ALT >31 U/L for women [16] which was used to suggest NAFLD prevalence [17]. A study of women with diabetes and NAFLD (by computed tomography) had mean ALT levels of 31.9 U/L [20], while a study of women with NAFLD (by ultrasound) in the Philippines had mean ALT levels of 47.7 U/L [21].

Using an ALT >31 U/L, Clark et al. reported women with unexplained aminotransferase elevation (not explained by Hepatitis B, Hepatitis C, normal transferrin saturation, or excessive alcohol consumption) displayed higher BMI, waist girth, triglycerides, fasting

insulin, lower HDL, and higher prevalence of diabetes and hypertension. NAFLD was recognized as the likely causative factor since it has been the most common histological finding among patients with chronically elevated liver enzymes [22] or who were serologically negative for virus-, alcohol-, or drug related diseases [23].

This study used ALT to suggest probable NAFLD rather than GGT or AST because it is specific for both liver injury and fat accumulation and it is the most common liver function test abnormality in individuals with diabetes [24]. Because VAT has positively correlated with fatty liver in non-obese subjects [25], we examined the relationship of liver enzymes with increasing VAT and glucose variables. Further, since hypoadiponectinemia has been associated with NAFLD [26], and Filipinos have low adiponectin levels [5], we assessed the association between adiponectin and probable NAFLD. The objectives of this study were to 1) measure the prevalence of probable NAFLD by ALT levels and 2) determine the association between probable NAFLD and diabetes, independent of known and potential risk factors in non-obese, non-alcohol drinking women.

RESEARCH DESIGN AND METHODS

Filipino-American women, aged 48 – 73 years, were recruited between 1995 and 2002 to a cross-sectional study of several chronic conditions [4]. Convenience-based sampling was necessary since Filipinos were not identified separately in the 1990 census. Recruitment, published previously [27], included tests for various chronic diseases to reduce self-selection bias for participants with known diabetes. All participants spoke functional English and provided written informed consent; a Philippine-born native Tagalog speaker translated when necessary. Approval was obtained from the University of California, San Diego (UCSD) Human Research Protections Program.

Age, education, cigarette smoking, alcohol use, and exercise frequency were determined using structured questionnaires. Prescribed and non-prescribed medications used by participants in the month before their clinic visit were recorded and verified by a nurse.

Clinical evaluations occurred at the UCSD Rancho Bernardo Research Clinic. Two morning blood pressure readings were assessed by a mercury sphygmomanometer using the Hypertension Detection and Follow-up Program protocol [28]. Height and weight were measured with participants wearing lightweight clothing without shoes. Waist circumference was measured at the bending point and at the narrowest point. Hip circumference was measured at the iliac crest and at the largest point. Percent total body fat was determined by dual-energy X-ray absorptiometry (DEXA; model QDR-2000 X-ray bone densitometers; Hologic, Waltham, MA). BMI and waist-to-hip ratio were calculated.

Visceral adiposity was measured in women without known coronary heart disease by electron beam computed tomography [27]. A single-slice CT scan of the abdomen (at the umbilicus) was obtained using an Imatron C-150 ultra-fast CT scanner to measure visceral and subcutaneous adipose tissue volume.

A 75-g oral glucose tolerance test (OGTT) was performed in the morning after a minimum 8-hour fast; blood samples were obtained by venipuncture at 0- and 2- hours. Plasma

glucose was measured by a glucose-oxidase method. Insulin was determined by radioimmunoassay in a diabetes research laboratory; insulin resistance was estimated using the homeostasis-model assessment (HOMA) [29]. Total cholesterol and triglyceride levels were measured using an ABA-2000 biochromatic analyzer (Abbott Laboratories, Irving, TX), a high performance cholesterol reagent (no. 236691; Boehringer-Mannheim Diagnostics, Indianapolis, IN), and a triglyceride agent (no. 6097; Abbott Laboratories). HDL cholesterol was measured using the Lipid Research Clinics Manual. LDL cholesterol was calculated using the Friedewald formula [30]. Total-to-HDL cholesterol was computed. Fasting concentrations of ALT, AST, and GGT were measured by spectrophotometry; fasting total adiponectin was measured by radio-immunoassay (Linco Research, Inc. St. Louis, MO).

Type 2 diabetes was defined by 1999 World Health Organization (WHO) criteria: fasting plasma glucose level ≥ 126 mg/dL, 2-hour post challenge glucose level ≥ 200 mg/dL, diabetes diagnosed by a physician, or treatment with an oral hypoglycemic agent or insulin [31]. Hypertension was defined as antihypertensive medication use, systolic blood pressure ≥ 130 mmHg or diastolic blood pressure ≥ 85 mmHg. Family history of diabetes was defined as a biological mother or father, or sibling diagnosed with diabetes after age forty. Probable NAFLD was defined as ALT > 31 U/L for women based on abnormal aminotransferase levels by the NCHS [16].

STATISTICAL ANALYSIS

Data were analyzed using SAS version 8.1 (SAS, Cary, NC). Student's *t* tests, general linear models, and chi-square tests were used for descriptive statistics. Fasting glucose and insulin, postchallenge insulin, adiponectin, AST, GGT, and ALT were logarithmically transformed before analysis to approximate normal distributions; geometric mean levels were reported. General linear models were used to examine the age-adjusted relationship of liver enzymes, glucose variables, and diabetes with increasing VAT levels.

Univariate analysis was conducted to identify putative predictor variables associated with diabetes. Not all anthropometric and blood pressure variables were included in the regression model due to high collinearity. The log likelihood ratio was used to select the preferred logistic regression model. Multivariable logistic regression was used to evaluate the association between probable NAFLD and diabetes, while adjusting for known and potential confounders including age, exercise, hypertension, education, family history of diabetes, VAT, total-to-HDL cholesterol, adiponectin, GGT, and AST. This association was also examined in a nested sequence of models. The first model contained age only. Next, all known and potential confounders were added. The third sequence included VAT and adiponectin as they are known to influence ALT levels [25, 32]. Finally, AST and GGT were added since both are increased with NAFLD presence. Statistical significance was designated at $P < 0.05$ and 95% confidence intervals excluding one.

RESULTS

A total of 181 Filipino-American women were eligible for this study. After excluding women who drank 3 alcoholic beverages per week ($n = 2$), women who had incomplete OGTT ($n = 5$), and missing ALT or GGT values ($n = 11$), 163 women remained for analysis. Using an ALT > 31 U/L, 28 women (17.2%) had probable NAFLD. One-third of these women had diabetes (34.4%, $n = 56$) and a family history of diabetes (35%, $n = 57$). Filipinas with diabetes ($n = 56$) had significantly larger VAT, waist circumference, BMI, and waist-to-hip ratio and higher fasting glucose and insulin, postchallenge glucose, insulin resistance, total-to-HDL cholesterol, LDL cholesterol, total cholesterol, and systolic blood pressure compared to those without diabetes ($n = 107$) (Table 1).

Levels of GGT (47 vs. 31.9 iU/L, $p = 0.02$), AST (22.2 vs. 19.1 U/L, $p = 0.01$), ALT (28.7 vs. 19.1 U/L, $p = 0.0001$), and adiponectin (5.75 vs. 8.0 ug/ml, $p = 0.0003$) significantly differed by diabetes status. Compared to those without diabetes, Filipinas with diabetes had 3-fold greater prevalence of probable NAFLD (32.1 vs. 9.35%, $p = 0.0002$).

Table 2 presents the age-adjusted anthropometric, behavioral, and metabolic characteristics among Filipinas by probable NAFLD status. Filipinas with probable NAFLD ($n = 28$) were significantly younger (57.7 vs. 60.2 years, $p = 0.04$), had higher VAT (85.5 vs. 66.2 cm³, $p = 0.002$), waist girth, fasting glucose, postchallenge glucose, and total cholesterol compared to those without probable NAFLD ($n = 135$).

Levels of ALT (48.9 vs 16.9 U/L, $p < 0.0001$), GGT (82.5 vs. 27.6 iU/L, $p < 0.0001$) and AST (30.3 vs. 18 U/L, $p < 0.0001$) significantly differed by probable NAFLD status. Filipinas with probable NAFLD had a 2.3-fold greater diabetes prevalence compared to those without probable NAFLD (64.3 vs. 28.2%, $p = 0.0002$).

Table 3 reports the mean age-adjusted glucose variables, liver enzymes and diabetes, stratified by quintiles of VAT. Mean values of GGT ($p = 0.0008$), ALT ($p = 0.002$), fasting and postchallenge glucose (both $p = 0.004$) increased significantly with increasing VAT quintiles. The prevalence of diabetes significantly increased with increasing VAT levels ($p = 0.007$), but was already elevated (30.4%) among women with the least VAT (< 40 cm³).

Probable NAFLD was independently associated with diabetes, after adjusting for age, college education, exercise, family history of diabetes, VAT, total-to-HDL cholesterol, hypertension, adiponectin, GGT and AST (Table 4). Filipinas with probable NAFLD had a 6.32-fold increased odds of diabetes compared to those without probable NAFLD (95% CI 2.2 – 18.0, $p = 0.0006$). Other diabetes-associated risk factors included not having completed college (Adjusted OR (AOR): 0.34, 95% CI: 0.15 – 0.79), family history of diabetes (AOR: 7.19, 95% CI: 2.98 – 17.3), hypertension (AOR: 3.81, 95% CI: 1.50 – 9.67), and lower adiponectin levels (AOR: 0.08, 95% CI: 0.02 – 0.43).

The relationship between ALT, as a continuous variable, with diabetes was also examined after adjusting for the same risk factors (Data not shown). Elevated ALT remained significantly associated with diabetes independent of the above risk factors (AOR: 43.4, 95% CI 6.3 – 298.3, $p = 0.0001$). Other risk factors associated with diabetes persisted as

with the earlier multivariable model, and included not having completed college (AOR: 0.31, 95% CI: 0.13 – 0.75), family history of diabetes (AOR: 6.69, 95% CI: 2.78 – 16.1), hypertension (AOR: 4.18, 95% CI: 1.63 – 10.8), and lower adiponectin levels (AOR: 0.08, 95% CI: 0.02 – 0.43).

Figure 1 displays the association between probable NAFLD and diabetes with sequential adjustment. In model 1, Filipinas with probable NAFLD had a 4.53-fold increased odds of diabetes compared to those without probable NAFLD (95% CI 1.9 – 10.8), after adjusting for age. In model 2, this association was strengthened after including college education, exercise, family history of diabetes, hypertension, and total-to-HDL cholesterol (AOR: 5.67, 95% CI 2.01 – 16.0). The odds ratio for Model 3 remained similar to that of Model 2 after including adiponectin and VAT (AOR: 5.68, 95% CI 2.99 – 17.2). In the final model, the association was further strengthened by the addition of AST and GGT (AOR: 6.32, 95% CI 2.22 – 18). A positive linear relationship was seen between probable NAFLD and diabetes among the four models.

DISCUSSION

This is the first study to characterize hepatic enzymes and evaluate their association with type 2 diabetes in Filipino-American women. Assessment of probable NAFLD was possible since majority of this cohort (98.9%) did not drink alcohol. Filipino women with diabetes had three times higher prevalence of probable NAFLD relative to those without diabetes. Probable NAFLD was associated with six-fold higher odds of diabetes. The prevalence of probable NAFLD observed in our women (17.2%) mirrored that of Hispanic women (15%) and was twice as high as Caucasian and African-American women (both 7%, respectively) in a U.S. national study [33]; our result was also similar to the prevalence in a study of Asian-Americans (16.7%) where NAFLD was defined by liver biopsy [34]. In fact, these Filipino women with probable NAFLD had mean ALT levels (48.7 U/L) consistent with those of Filipinas in the Philippines with NAFLD defined using ultrasound (47.7 U/L) [21].

Recently, Prati et al. proposed a lowered ALT cut-point for women (ALT >19U/L) to improve sensitivity for NAFLD and chronic liver disease [35]. When Clark et al. applied the proposed reference to his study population, the prevalence of unexplained elevated aminotransferase levels increased from 5.4 to 21%. Likewise, the prevalence of probable NAFLD in our cohort of Filipinas increased from 17.2 to 36.8%. This value is similar to other reported NAFLD prevalence values detected by magnetic resonance (31%) among US adults [33] and by ultrasound (29%) in Japanese adults [36].

Probable NAFLD was significantly associated with diabetes independent of adiponectin, VAT, family history of diabetes, exercise, and other hepatic enzymes. Only two women reported ≥ 3 alcoholic beverages per week and were excluded from analysis which made it very unlikely that the association was due to or confounded by excessive alcohol consumption. Furthermore, these observations persisted when ALT was analyzed as a continuous variable in multivariate analysis. These findings suggest that elevated ALT, regardless of a defined cut-point, may play a role in diabetes pathogenesis.

Both GGT and ALT were significantly associated with increasing levels of VAT, and are consistent with previous findings [37, 38]. Although both liver enzymes are known to predict incident diabetes [8 – 11, 37, 39], only ALT was independently associated with increased odds of diabetes suggesting ALT may serve as the better biomarker for diabetes or NAFLD among Filipino women.

The significant associations between both glucose variables and VAT provide additional evidence of the role of VAT accumulation in diabetes pathogenesis. It is suggested that VAT influences hepatic fat infiltration in NAFLD through its role in cytokine production [25].

Decreased adiponectin levels have been associated with both diabetes [40] and NAFLD [26, 41]. Adiponectin, a protein hormone secreted from adipocytes, including VAT, has both insulin-sensitive and anti-inflammatory properties that play an important role in inflammation and NAFLD. Existing studies suggest hypoadiponectinemia in NAFLD enhances insulin resistance by decreasing hepatic insulin sensitivity [41] and increasing production of the inflammatory protein, tumor necrosis factor- α [42]. Hypoadiponectinemia may perpetuate hepatic fat accumulation through an influx of free fatty acids into the liver resulting in hepatic steatosis [42, 43]. Japanese women with NAFLD, defined by ultrasound, and mean ALT level of 45 U/L had significantly lower adiponectin concentration compared to those without NAFLD (7.2 vs. 9.0 ug/mL, $p < 0.005$) [26]. Lower adiponectin levels were observed in our cohort by diabetes and probable NAFLD status; however significant differences were seen only in women by diabetes status.

Since fatty liver in NAFLD is known to influence severity of hepatic insulin resistance and occurs commonly in individuals with diabetes [20], liver fat may serve as a therapeutic target [36]. Recent studies showed thiazolidinedione (TZD) therapy to enhance insulin sensitivity [36] and improve liver histology [44 – 46]. In diabetes patients, increased adiponectin levels after TZD use was associated with decreased hepatic fat content and increased hepatic insulin sensitivity and fatty acid metabolism [45]. Furthermore, TZD use significantly reduced the mean values of ALT, insulin resistance, fasting glucose and insulin in Taiwanese patients with diabetes and NAFLD, diagnosed by ultrasound, with no significant alcohol history and moderately elevated aminotransferase levels prior to TZD use [47].

This study had several limitations. Liver biopsy remains the gold standard for NAFLD [12 – 14]; however, this method is associated with bleeding complications and death [48]. Furthermore, utilization of liver biopsies in population-based studies is not feasible. Although imaging by ultrasound, computerized tomography and magnetic resonance have the ability to detect liver fat, these techniques cannot differentiate simple steatosis from non-alcoholic steatohepatitis [49]. We do not acknowledge the use of ALT levels alone for NAFLD diagnosis as it may underestimate the true burden of liver disease [17]. Studies have shown individuals may present with NAFLD-related conditions despite having “normal” ALT levels [33, 50]. The cross-sectional design of this study does not discern the temporal relationship of probable NAFLD with diabetes. Longitudinal studies with serial ALT measurements are needed to determine whether NAFLD explains the excess risk of incident diabetes in Filipino-American women.

Although liver diseases including Hepatitis B and Hepatitis C were not assessed, our cohort of women did not consume alcohol and have displayed NAFLD-associated comorbidities including metabolic syndrome, diabetes, and hypertension [4, 5, 27] which may allow elevated ALT levels to reflect NAFLD. Measuring liver enzymes is an inexpensive, convenient tool for routine clinical practice that may be used to assess premature liver disease and identify other associated comorbidities and macrovascular complications of diabetes.

In conclusion, probable NAFLD prevalence was elevated in this cohort of non-obese, non-alcohol consuming women. NAFLD, by ALT levels, was independently associated with diabetes independent of VAT, adiponectin, family history of diabetes and other known risk factors. Filipino women with probable NAFLD had similar mean ALT levels as ultrasound ascertained NAFLD patients in Asia. Our results show that elevated ALT may be a reasonable non-invasive surrogate marker for NAFLD, and diabetes risk in Filipinos, other Asians and other non-obese populations with elevated diabetes prevalence.

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Figure 1. Adjusted association between NAFLD, by ALT levels, and type 2 diabetes in a nested sequence of models

Model 1 is adjusted for age only. **Model 2** is model 1 plus family history of diabetes, education, exercise, hypertension and total:HDL cholesterol. **Model 3** is model 2 plus log-transformed adiponectin and visceral fat. **Model 4** is model 3 plus AST and GGT.

Table 1

Age-adjusted mean values of demographic, anthropometric, and metabolic variables in Filipino-American women by diabetes status aged 48 – 73 years, San Diego, CA, 1995–2002 (n = 163)

Variable	Type 2 diabetes		P-value
	Yes (n = 56)	No (n = 107)	
Age (years)	59.3	60	0.45
Exercise (% , 3x/wk)	75	72	0.69
College graduate (% , Yes)	33.9	49.5	0.06
Ever smoke (% , Yes)	10.7	15.9	0.37
Visceral fat (cm ³)	79.6	64.3	0.002 [*]
Subcutaneous fat (cm ³)	157.4	156.8	0.94
Visceral-to-Subcutaneous fat	0.52	0.44	0.06
Waist circumference (cm)	85.3	80.1	0.0009 [*]
Waist-to-hip ratio	0.87	0.84	0.003 [*]
BMI (kg/m ²)	26.3	25.1	0.04 [*]
Total body fat (% , by DEXA) [‡]	33.6	33.3	0.72
Fasting glucose (mg/dl) [†]	137.7	94.2	<0.0001 [*]
Postchallenge glucose (mg/dl) [§]	288.4	138.5	<0.0001 [*]
Fasting insulin (ng/dl) ^{††}	0.55	0.41	0.04 [*]
Postchallenge insulin (ng/dl) [†]	2.82	3.13	0.09
Insulin resistance (HOMA-IR)	4.67	2.37	<0.0001 [*]
Total:HDL cholesterol	4.67	4.08	0.005 [*]
LDL cholesterol (mg/dl)	144.6	137.7	0.003 [*]
HDL cholesterol (mg/dl)	52.7	54.5	0.38
Total cholesterol (mg/dl)	232.7	211.7	0.001 [*]
Triglycerides (mg/dl)	169.3	144.4	0.08
Systolic BP (mmHg)	138.6	130.8	0.02 [*]
Diastolic BP (mmHg)	80.6	78.6	0.21
ALT (U/L) [†]	28.7	19.1	0.0001 [*]
GGT (iu/L) [†]	47	31.9	0.02 [*]
AST (U/L) [†]	22.2	19.1	0.01 [*]
Adiponectin (ug/ml) [†]	5.75	8.0	0.0003 [*]
NAFLD (% , > 31 U/L)	32.1%	9.35%	0.0002 [*]

BMI, body-mass-index; **DEXA**, dual energy x-ray absorptiometry; **LDL**, low-density lipoprotein; **HDL**, high-density lipoprotein; **HOMA-IR**, homeostasis model assessment of insulin resistance; **BP**, blood pressure; **ALT**, alanine aminotransferase; **GGT**, gamma-glutamyltransferase; **AST**, aspartate aminotransferase; **NAFLD**, non-alcoholic fatty liver disease

^{*} P-values < 0.05 were statistically significant.

[†] Log transformed for analysis; back-transformed for presentation.

[‡] Total percent body fat is not presented among eleven women

§ Postchallenge glucose is not presented in six women with previously diagnosed diabetes

// Fasting insulin was not available for two women

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Table 2

Age-adjusted mean values of demographic, anthropometric, and metabolic variables in Filipino-American women by NAFLD status aged 48 – 73 years, San Diego, CA, 1995–2002

Variable	Probable NAFLD		P-value
	Yes (n = 28)	No (n = 135)	
Age (years)	57.7	60.2	0.04*
Exercise (% 3x/wk)	82.1	71.1	0.23
College graduate (% Yes)	42.9	44.4	0.06
Ever smoke (% Yes)	17.9	13.3	0.53
Visceral fat (cm ³)	85.5	66.2	0.002*
Subcutaneous fat (cm ³)	164.6	155.4	0.43
Visceral-to-Subcutaneous fat	0.53	0.45	0.16
Waist circumference (cm)	85.8	81.1	0.02*
Waist-to-hip ratio	0.27	0.25	0.08
BMI (kg/m ²)	26.5	25.4	0.13
Total body fat (% by DEXA) [‡]	34.2	33.2	0.40
Fasting glucose (mg/dl) [†]	138.4	103.1	<0.0001*
Postchallenge glucose (mg/dl) [§]	257	173.3	<0.0001*
Fasting insulin (ng/dl) ^{††}	0.49	0.45	0.31
Postchallenge insulin (ng/dl) [†]	2.50	3.13	0.15
Insulin resistance (HOMA-IR)	4.23	2.94	0.06
Total:HDL cholesterol	4.70	4.20	0.07
LDL cholesterol (mg/dl)	143.9	131.3	0.09
HDL cholesterol (mg/dl)	52.7	54.1	0.59
Total cholesterol (mg/dl)	233.5	215.9	0.04*
Triglycerides (mg/dl)	177.9	147.7	0.10
Systolic BP (mmHg)	131.4	133.9	0.55
Diastolic BP (mmHg)	78.7	79.4	0.71
ALT (U/L) [†]	48.9	16.9	<0.0001*
GGT (iu/L) [†]	82.5	27.6	<0.0001*
AST (U/L) [†]	30.3	18	<0.0001*
Adiponectin (ug/ml) [†]	7.09	7.28	0.27
Type 2 diabetes	64.3	28.2	0.0002*

NAFLD, non-alcoholic fatty liver disease; **BMI**, body-mass-index; **DEXA**, dual energy x-ray absorptiometry; **LDL**, low-density lipoprotein; **HDL**, high-density lipoprotein; **HOMA-IR**, homeostasis model assessment of insulin resistance; **BP**, blood pressure; **ALT**, alanine aminotransferase; **GGT**, gamma-glutamyltransferase; **AST**, aspartate aminotransferase

* P-values < 0.05 were statistically significant.

[†] Log transformed for analysis; back-transformed for presentation.

[‡] Total percent body fat is not presented among eleven women

§ Postchallenge glucose is not presented in six women with previously diagnosed diabetes

// Fasting insulin was not available for two women

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Table 3

Age-adjusted means of liver enzymes and glucose variables by quintiles of visceral fat

VAT Quintile	1: <40 cm ³ (n = 23)	2: 40–59cm ³ (n = 42)	3: 60–79cm ³ (n = 45)	4: 80–99cm ³ (n = 28)	5: 100 cm ³ (n = 25)	ptrend
Age	60.2	60.1	60.4	58	59.8	0.45
Fasting glucose [†]	102.5	97.7	113	107.2	129.3	0.004
Postchallenge glucose	167.8	155.4	198.1	193.3	233.6	0.004
ALT [‡]	19.0	17.9	22.5	25.1	29.4	0.002
AST [‡]	19.5	19.1	20.2	20.4	22	0.46
GGT [‡]	36.7	26.4	34.7	35.4	61.2	0.0008
Type 2 diabetes [‡]	30.4	16.7	33.3	42.9	60	0.007*

* Significance determined by Chi-square test

[†] Log transformed for analysis; back-transformed for presentation.[‡] Values are presented as percent

Table 4

Multivariate logistic regression of risk factors for type 2 diabetes in Filipino-American women aged 48 – 73 years, San Diego, CA, 1995–2002

Variable	Odds Ratio	95% Confidence Interval	p-value
Age (years)	1.01	0.94 – 1.09	0.75
College graduate			0.01*
No [†]	1		
Yes	0.34	0.15 – 0.79	
Exercise			0.36
< 3 times per week [†]	1		
3 times per week	1.59	0.59 – 4.28	
Family history of diabetes			<0.0001*
No [†]	1		
Yes	7.19	2.98 – 17.3	
Visceral fat (cm ³)	1.00	0.98 – 1.02	0.96
Total:HDL cholesterol	1.17	0.84 – 1.64	0.35
Hypertension			0.005*
No [†]	1		
Yes	3.81	1.50 – 9.67	
Adiponectin (ug/mL)	0.08	0.02 – 0.43	0.003*
GGT (iU/L)	3.52	0.74 – 16.8	0.11
AST (U/L)	1.45	0.02 – 9.41	0.86
Probable NAFLD			0.0006*
ALT 31 U/L [†]	1		
ALT > 31 U/L	6.32	2.22 – 18.0	

HDL, high-density lipoprotein; **GGT**, gamma-glutamyltransferase; **AST**, aspartate aminotransferase; **NAFLD**, non-alcoholic fatty liver disease; **ALT**, alanine aminotransferase

* *P*-values < 0.05 were statistically significant.

[†] Reference level