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Relationship of obesity-related disturbances with LH/FSH ratio among post-menopausal women in the United States

Hind Beydoun, PhD[a], **May Beydoun, PhD**[b], **Natasha Wiggins, MPH**[c], and **Laurel Stadtmauer, MD-PhD**[d]

[a]Graduate Program in Public Health, Eastern Virginia Medical School, Norfolk, VA

[b]National Institute on Aging, NIH/Intramural Research Program, Baltimore, MD

[c]ORISE/NMPHC, Portsmouth, VA

[d]Jones Institute for Reproductive Medicine, Eastern Virginia Medical School, Norfolk, VA

Abstract

Objectives—Although luteinizing hormone to follicular stimulating hormone (LH/FSH) ratio is a controversial criterion for identifying a sub-group of infertile women with polycystic ovary syndrome (PCOS) and abnormalities at the level of the hypothalamic-pituitary-ovarian axis, an elevated LH/FSH ratio is frequently observed in PCOS cases. Obesity and insulin resistance are highly prevalent among PCOS women. To date, no studies have examined the associations of LH/FSH ratio with these co-morbid conditions outside the context of pre- and peri-menopausal PCOS women. The objective of this study is to evaluate whether the LH/FSH ratio is associated with obesity, insulin resistance, metabolic disturbances and chronic inflammation among post-menopausal U.S. women, 35 to 60 years of age.

Study Design—Cross-sectional study of 693 women who participated in the 1999–2002 National Health and Nutrition Examination Survey.

Main Outcome Measures—body mass index, waist circumference, triglycerides, high-density lipoprotein (HDL) cholesterol, systolic and diastolic blood pressures, fasting glucose, metabolic syndrome, Homeostasis Model Assessment for Insulin Resistance and C-reactive protein (CRP).

Results—Age- and hysterectomy-adjusted regression models suggest that CRP level is positively associated with LH/FSH ratio and LH/FSH >1, high glucose level and LH/FSH>2 are inversely related and HDL<50 mg/dL is positively associated with both LH/FSH>1 and LH/FSH>2.

Conclusions—In a nationally representative sample of post-menopausal women, markers of chronic inflammation and dyslipidemia which are characteristics of PCOS-associated morbidities were also significantly associated with LH/FSH ratio, meriting further investigation.

Keywords

chronic inflammation; follicular stimulating hormone; insulin resistance; luteinizing hormone; obesity

Address of Correspondence: Hind A. Beydoun, PhD – Graduate Program in Public Health, Eastern Virginia Medical School, Post Office Box 1980, Norfolk, Virginia 23501-1980, Office phone: 757-446-7142; Fax: 757-446-6121; baydouha@evms.edu.

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1. Introduction

The ratio of circulating levels of luteinizing hormone to follicular stimulating hormone (LH/FSH ratio) is a controversial criterion for identifying a sub-group of infertile women with polycystic ovary syndrome (PCOS) and abnormalities at the level of the hypothalamic-pituitary-ovarian axis (1). PCOS is a clinically and biochemically heterogeneous condition characterized by dermatologic, reproductive and metabolic manifestations. PCOS features include menstrual cycle disturbances, anovulatory infertility, polycystic ovaries and clinical or biochemical hyperandrogenism (2–4). Among women of childbearing age, PCOS is the most frequent endocrine disorder with an estimated prevalence of 5% to 10%(2, 4). Women diagnosed with PCOS are at increased risk for adverse health outcomes later in life including type 2 diabetes, metabolic syndrome, cardiovascular disease, endometrial cancer, non-alcoholic fatty liver disease, sleep apnea and mood disorders (4, 5).

To date, three distinct sets of PCOS diagnostic criteria have been proposed, namely the 1990 National Institute of Health (NIH), the 2003 Rotterdam and the 2006 Androgen Excess Society (AES) criteria. The 1990 NIH criteria defining PCOS are “hyperandrogenism and/or hyperandrogenemia, chronic anovulation, and exclusion of all other conditions which may cause similar disorders”(6). According to the 2003 European Society of Human Reproduction (ESHRE)/American Society of Reproductive Medicine (ASRM) (Rotterdam) criteria, a PCOS diagnosis is established in the presence of two out of three of the following conditions: [1] oligo- or anovulation, [2] clinical and/or biochemical hyperandrogenism and [3] polycystic morphology of the ovaries. Finally, the 2006 Androgen Excess Society set the following criteria: [1] androgen excess (clinical and/or biochemical hyperandrogenism), [2] ovarian dysfunction (oligo-anovulation and/or polycystic morphology), and [3] exclusion of other conditions that may cause similar disorders (6). Factors to be considered in the differential diagnosis of PCOS include congenital adrenal hyperplasia, androgen-secreting tumors, exogenous androgens, Cushing’s syndrome, ancanthosis nigricans syndrome, thyroid disorders and hyperprolactinemia (7).

Whereas a substantial proportion of PCOS women are overweight/obese (40–70%) and/or insulin resistant (50–70%)(8–11), overweight/obesity and insulin resistance are not considered among the criteria that define PCOS. Furthermore, overweight and obesity are considered as co-morbid conditions of PCOS(8–10, 12) and insulin resistance which can lead to androgen excess is thought to play a key role in the pathophysiology of PCOS(4).

The LH/FSH ratio has been found to be elevated in a sub-group of PCOS women(13), and a limited number of studies have assessed the relationship of LH/FSH ratio with metabolic features of PCOS, including overweight, obesity and insulin resistance, yielding inconsistent results(13–19). To our knowledge, no studies have examined the associations of LH/FSH ratio with overweight, obesity and insulin resistance outside the context of a PCOS diagnosis. PCOS is frequently diagnosed among pre- or peri-menopausal women seeking various infertility treatments. Thus, little is known about the LH/FSH ratio and its association with obesity and related conditions after menopause. Unlike women in their pre- or peri-menopausal stage, gonadotrophin (FSH and LH) levels of post-menopausal women are relatively stable, allowing accurate quantification of the LH/FSH ratio. Accordingly, we performed secondary analyses of existing 1999–2002 National Health and Nutrition Examination Surveys (NHANES) data to evaluate whether the LH/FSH ratio was associated with obesity, insulin resistance, metabolic disturbances and chronic inflammation among post-menopausal U.S. women, 35 to 60 years of age.

2. Methods

2.1. Study population

The NHANES is a cross-sectional, nationally representative survey designed to assess the health and nutritional status of the U.S. civilian non-institutionalized population(20). Stratified, multistage, probability survey samples were obtained based on the selection of counties, blocks, households and persons within households(20), with over-sampling of individuals of low income, adults aged 60 years or older, African-Americans, and Mexican-Americans(21). Demographic, socioeconomic and health data were collected by trained staff using household interviews. In addition, a mobile examination center (MEC) run by health professionals collected numerous measurements including anthropometric, blood pressure, and laboratory tests, either on all or a subgroup of study participants. Informed consent was obtained for all participants and the institutional review board of the National Center for Health Statistics, Centers for Disease Control and Prevention, approved all protocols for the NHANES(22).

Since 1999, NHANES has become a continuous surveillance system. For the current analyses, we combined the 1999–2000 and 2001–2002 NHANES datasets, in which FSH and LH concentrations were determined in a sub-group of MEC participants, namely women 35 to 60 years of age. A total of 9 965 subjects participated in the 1999–2000 NHANES and 11 039 subjects participated in the 2001–2002 NHANES. Of those, 1748 consisted of females 35 to 60 years of age who had valid FSH and LH measurements. Of those, 964 were classified according to self-reported number of months since last menstrual period. After exclusion of pre-menopausal (< 2 months; n=190) and peri-menopausal (2–11 months; n=81) women, analyses were restricted to a study population of 693 post-menopausal (≥12 months) women.

2.2. Measures

Weight, height, waist circumference, systolic and diastolic blood pressure measurements were collected on all MEC participants during physical examination. Laboratory measurements were performed on sub-samples of MEC participants. These included a hormone profile (FSH, LH, thyroid stimulating hormone, thyroxin and pregnancy test), blood lipids (total cholesterol, high density lipoprotein (HDL) cholesterol, low density lipoprotein (LDL) cholesterol, triglycerides), diabetes profile (glucose, insulin, C-peptide, glycohemoglobin) and C-reactive protein (CRP). It is worth noting that glucose, insulin, HDL and triglycerides levels were obtained on a sub-sample of MEC participants after an overnight fast.

The primary outcomes of interest were obesity, metabolic disturbances, insulin resistance and chronic inflammation. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2), and *obesity* was defined as BMI ≥ 30 kg/m^2. Metabolic syndrome was defined according to the updated National Cholesterol Education Program Adult Treatment Panel III criteria of an elevated blood pressure (≥130/85 mm Hg), increased waist circumference (≥35 inches), elevated fasting glucose levels (≥100 mg/dL), reduced HDL cholesterol level (≤50 mg/dL), and elevated triglyceride levels (≥150 mg/dL). Each of these metabolic syndrome criteria was considered as a *metabolic disturbance* and metabolic syndrome was diagnosed among women who satisfied at least three of those five criteria(7, 23). *Insulin resistance* was assessed using the Homeostasis Model Assessment for Insulin Resistance (HOMA-IR). HOMA-IR was calculated from fasting levels of insulin and glucose, using the formula [fasting serum insulin (μU/ml) × fasting plasma glucose (mmol/l)/22.5], and analyzed as a continuous variable (24). Chronic inflammation was measured using *C-reactive protein* (CRP) and analyzed as a continuous variable.

Serum levels of two gonadotrophins (FSH and LH) were originally used by NHANES investigators to classify women according to menopausal status. In the 1999–2002 NHANES datasets, serum FSH and LH concentrations (mIU/mL) were measured by a microparticle enzyme immunoassay technology (IMx FSH assay, IMx LH assay, Abbott Laboratories)(25, 26). This study relied on FSH and LH measurements to compute the LH/FSH ratio, the exposure of interest. LH/FSH>1 and LH/FSH>2 were alternatively considered to be abnormal and potentially indicative of PCOS.

A priori confounders of the hypothesized relationships included *age* (35–39, 40–44, 45–49, 50–54, 55–60 years), *race/ethnicity* (White, non-Hispanic; Black, non-Hispanic; Hispanic; Asian; Other), *education* (Less than high school, High school, More than High School), *marital status* (Ever-married, Never-married), *household income* (< $20,000, ≥$20,000) and *hysterectomy* (yes, no) of study participants.

2.3. Statistical analysis

All analyses were conducted using STATA version 8. Using survey commands, we applied recommended sub-sample weights for the period of 1999–2002. MEC exam weights were used for all analyses. For analyses involving metabolic syndrome, glucose, triglyceride and HDL levels, the 4-year fasting sample weights were applied. By contrast, the 4-year MEC weights were applied for analyses involving BMI, waist circumference, systolic blood pressure and diastolic blood pressure. Summary statistics included means and standard deviations for continuous variables or frequencies and percentages for categorical variables. Bivariate associations were analyzed using Pearson's Chi-square tests for independence and one-way analysis of variance tests, where appropriate. Unadjusted and adjusted beta coefficients and odds ratios (OR) were computed with their 95 percent confidence intervals (CI) using *svylogit* and *svyreg* commands, taking sampling weights into consideration. These weights were defined to represent the U.S. civilian, non-institutionalized population while accounting for over-sampling of certain age and ethnic groups and interview non-response. Two-sided statistical tests were performed at an alpha level of 0.05.

3. Results

The mean LH/FSH ratio was 0.73 with a standard deviation of 0.46. Of the 693 women who participated in the study, 15.2% had LH/FSH>1 and 2.6% had LH/FSH>2. Nearly 14.7% of study participants were less than 45 years of age, 47.9% were non-Hispanic white, 43.1% had more than high school education, 11.5% were never married and 25.6% had a household income of less than $20000. Furthermore, 52.1% of women had undergone a hysterectomy. Table 1 presents the LH/FSH ratio by demographic and socioeconomic characteristics of study participants. The mean LH/FSH ratio and the proportions of women having LH/FSH ratio above the designated cut-off points of 1 and 2 significantly declined with advancing age. Similarly, hysterectomized women had a higher LH/FSH ratio than their non-hysterectomized counterparts. There were no significant differences in LH/FSH ratio across racial or ethnic groups or according to level of education, marital status and household income. Because age and hysterectomy were the only a priori confounder which were consistently associated with the exposure variable of interest, no other covariate was included in adjusted linear and logistic regression models presented in Tables 2–6.

Nearly 42% of participants were obese and the mean BMI was 29.1 kg/m^2 with a standard deviation of 0.3 kg/m^2. Similarly, 69.5% had a waist circumference ≥35 inches, 34.8% had triglyceride level ≥ 150 mg/dL and 2.5% had HDL cholesterol level < 50 mg/dL. In addition, 42.4% had systolic blood pressure ≥ 130 mm Hg, 17.1% had diastolic blood pressure ≥ 85 mm Hg, 23.8% had fasting glucose level ≥ 100 mg/dL and 26.2% satisfied

criteria for the metabolic syndrome. Finally, the mean ± standard deviation of HOMA-IR and CRP levels were 3.0 ± 0.3 and 0.6 ± 0.03, respectively.

Table 2 presents linear regression models for the unadjusted and adjusted associations of LH/FSH ratio with continuous measures of obesity, metabolic disturbances and chronic inflammation. Unadjusted models suggested no significant associations of LH/FSH ratio with BMI, waist circumference, triglycerides, HDL cholesterol, diastolic blood pressure, glucose and HOMA-IR. Conversely, systolic blood pressure was significantly and negatively associated (β=−3.0; P = 0.033) and CRP level was marginally and positively associated (β=0.1, P=0.08) with LH/FSH ratio in the unadjusted models. After controlling for age and hysterectomy, CRP level remained marginally associated with LH/FSH ratio (β=0.1, P=0.07).

Tables 3 and 4 present linear regression models for the unadjusted and adjusted association of continuous measures of obesity, metabolic disturbances and chronic inflammation with LH/FSH>1 and LH/FSH>2, respectively. Both unadjusted and adjusted models revealed a significant and positive association of LH/FSH>1 with CRP level. Similarly, high LH/FSH ratios (LH/FSH>1 and LH/FSH>2) were associated with reduced glucose level, before adjustment for confounders. The inverse relationship of glucose level with LH/FSH>2 – but not with LH/FSH>1 – remained significant after adjustment for age and hysterectomy.

Table 5 presents logistic regression models for the unadjusted and adjusted association of LH/FSH ratio with dichotomous measures of obesity and metabolic disturbances. Clearly, all of the selected dichotomous outcomes were not significantly associated with LH/FSH ratio defined as a continuous variable, either before or after adjustment for confounders.

Table 6 presents logistic regression models for the unadjusted and adjusted association of LH/FSH>1 and LH/FSH>2 with dichotomous measures of obesity and metabolic disturbances. Again, most dichotomous outcomes were not significantly associated with LH/FSH>1 or LH/FSH>2 either in the unadjusted or in the adjusted models. Two exceptions were HDL cholesterol and metabolic syndrome. Specifically, an LH/FSH>1 was associated with greater odds of having HDL cholesterol<50 mg/dL (OR=1.49, 95% CI: 1.29–1.72) in the adjusted logistic model. Also, an LH/FSH>2 was associated with a greater odds of having HDL cholesterol<50 mg/dL (OR=1.52, 95% CI: 1.32–1.75) in the adjusted logistic model. Whereas metabolic syndrome was inversely associated with LH/FSH>1 in the unadjusted logistic model, this relationship became statistically non-significant after controlling for age and hysterectomy.

4. Discussion

In this cross-sectional study of post-menopausal U.S. women 35 to 60 years of age who participated in the 1999–2002 NHANES, we examined whether high LH/FSH ratio was predictive of obesity, insulin resistance, metabolic disturbances and chronic inflammation. High LH/FSH ratio, obesity and its co-morbid conditions have been previsouly found to be problematic in women diagnosed with PCOS. Age- and hysterectomy-adjusted models suggest that CRP level is positively associated with LH/FSH>1, an inverse relationship exists between glucose level and LH/FSH>2 and HDL<50 mg/dL is positively associated with both LH/FSH>1 and LH/FSH>2. By contrast, obesity, waist circumference, insulin resistance, systolic blood pressure, diastolic blood pressure, triglycerides and metabolic syndrome were not significantly associated with LH/FSH ratio, after controlling for confounders.

Disagreement persists among clinical practitioners from various medical specialties with respect to PCOS diagnosis, including usefulness of the LH/FSH ratio. Cussons and co-

workers(14) surveyed endocrinologists and gynecologists, and found discrepant practices among these two specialties. Whereas endocrinologists viewed androgen excess and menstrual irregularity as important diagnostic criteria, gynecologists considered polycystic ovaries, androgen excess, menstrual irregularity and an high LH/FSH ratio as essential diagnostic criteria(14).

The relationship of LH/FSH ratio with obesity, insulin resistance, metabolic disturbances and chronic inflammation has not been explored outside the context of PCOS women. Current evidence suggests that high LH/FSH ratio and insulin resistance may be independent pathways leading to hyperandrogenism in PCOS women, although it remains inconclusive. The lack of association between LH/FSH ratio and insulin resistance is contrary to observations made by Marcondes and co-workers(27), namely that treatment of PCOS women with metformin can result in decrease of LH and increase of FSH levels. A study by Moran and co-workers(1) suggested that LH/FSH ratio was not significantly associated with BMI, waist-to-hip ratio and insulin resistance. In another study, Mor and co-workers(18) reported mean LH/FSH ratio to be significantly lower in PCOS with insulin resistance compared to PCOS women without insulin resistance, providing evidence for two distinct PCOS phenotypes, a low-LH and high-insulin group and a high-LH and low-insulin group(18). Similarly, Banaszewska and co-workers(13) examined the association of metabolic parameters with LH/FSH ratio among PCOS women, and found statistically significant differences among two groups of women (LH/FSH ratio>2 vs. LH/FSH ratio ≤ 2) with respect to BMI and insulin levels. In addition, most PCOS women with normal LH/FSH ratio were characteristically obese and/or hyperinsulinemic, and vice versa, confirming the idea of distinct pathways leading to hyperandrogenism in PCOS(13). The relationship of insulin resistance (HOMA-IR) with sex hormones, including LH and FSH, was longitudinally examined over the menstrual cycle in a recent study of 257 healthy pre-menopausal women by Yeung and co-workers(28). After adjustment for age, race, cycle, and other sex hormones, HOMA-IR was positively associated with estradiol and progesterone, and inversely associated with FSH, whereas LH was not associated with HOMA-IR(28).

The relationships of LH/FSH ratio with hyperglycemia and chronic inflammation have rarely been examined(15, 16, 29). Kurioka and co-workers(16) compared parameters of glucose intolerance among nine obese PCOS, 34 normal-weight PCOS (LH/FSH ratio >1.0), 11 normal-weight PCOS (LH/FSH ≤ 1.0) and 16 control women. Consistent with our study, they found a significant difference in total plasma glucose between LH-dominant, normal-weight PCOS and normal-LH PCOS women(16). In contrast, the finding of a direct relationship between LH/FSH ratio and CRP level is inconsistent with two studies of PCOS women. A study by Guzelmeric and co-workers (15) found CRP levels to be correlated with BMI, total cholesterol, triglycerides, LDL cholesterol, insulin levels and HOMA-IR, but not with testosterone or LH/FSH ratio(15). Similarly, a study by Lenarcik and co-workers(29) found a negative, rather than a positive, correlation between markers of chronic inflammation and LH/FSH ratio.

To our knowledge, this is the first study to examine LH/FSH ratio as a risk factor for post-menopausal obesity, insulin resistance and related metabolic disturbances outside the context of PCOS. However, study findings should be interpreted with caution and in light of several limitations. First of all, we performed secondary analyses of the 1999–2002 NHANES, which is a series of cross-sectional studies. Thus, the temporal relationship between the main exposure (LH/FSH ratio) and outcomes (obesity, insulin resistance, metabolic disturbances, and chronic inflammation) of interest could not be ascertained through a cross-sectional design. Second, the study population was restricted to post-menopausal women to minimize systematic changes in gonadotrophin levels according to

stage of the menstrual cycle, precluding generalization of study findings to pre- and peri-menopausal women. Third, selection bias may have occurred since a large proportion of NHANES women 35 to 60 years of age, were excluded from the study for lack of data on reproductive stage or because they did not participate in the MEC component and only a sub-sample of MEC participants took part in fasting measurements. Fourth, the statistically significant associations observed between LH/FSH ratio and various outcomes cannot be ruled out as chance findings, given the large number of hypotheses being tested. Finally, analyses of existing data precluded the distinction of women based on criteria that define PCOS including menstrual cycle disturbances, anovulatory infertility, polycystic ovaries and clinical or biochemical hyperandrogenism. Thus, it may be difficult to conclude that women with elevated LH/FSH ratios were indeed potential PCOS cases.

In conclusion, chronic inflammation and dyslipidemia are characteristic of PCOS-associated morbidities and were associated with LH/FSH ratio in the general population of post-menopausal U.S. women, meriting further investigation. The finding of an inverse relationship between LH/FSH ratio and hyperglycemia is in line with the idea that insulin resistance and LH/FSH ratio may constitute alternative pathways in the pathogenesis of PCOS. Similarly, the positive association between LH/FSH ratio and CRP is in line with the idea that PCOS women are more likely than their non-PCOS counterparts to exhibit chronic inflammation. The temporal relationships of LH/FSH ratio with obesity, insulin resistance and related metabolic disturbances can only be confirmed in the context of large prospective cohort studies of pre-, peri- and post-menopausal women, taking PCOS diagnosis into consideration.

Abbreviations

AES	Androgen Excess Society
ASRM	American Society of Reproductive Medicine
BMI	Body mass index
CRP	C-reactive protein
ESHRE	European Society of Human Reproduction
FSH	follicular stimulating hormone
HDL	high density lipoprotein
HOMA-IR	Homeostasis Model Assessment for Insulin Resistance
LDL	low density lipoprotein
LH	luteinizing hormone
MEC	mobile examination center
NHANES	National Health and Nutrition Examination Surveys
NIH	national institutes of health
PCOS	polycystic ovary syndrome

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Table 1

LH/FSH ratio by demographic and socioeconomic characteristics

	LH/FSH[a]		LH/FSH > 1[b]		LH/FSH > 2[b]		
	Mean (SD)	P[c]	%	P[d]	%	P[d]	Total N (%)[a]
Overall	0.73 (0.46)		15.2		2.6		693 (100)
Age (years):		< 0.0001		0.0001		0.029	628 (100)
35–39	1.04 (0.85)		45.9		9.4		33 (5.3)
40–44	0.94 (0.68)		21.0		4.4		59 (9.4)
45–49	0.85 (0.58)		21.1		5.5		117 (18.6)
50–54	0.68 (0.39)		11.8		1.1		212 (33.8)
55–60	0.66 (0.28)		8.9		0.8		207 (32.9)
Race/Ethnicity:		0.42		0.47		0.61	693 (100)
Hispanic	0.72 (0.35)		20.7		3.8		184 (26.6)
Non-Hispanic White	0.74 (0.52)		13.9		2.3		332 (47.9)
Non-Hispanic Black	0.76 (0.48)		19.4		4.1		147 (21.2)
Other	0.62 (0.32)		13.4		0.0		30 (4.3)
Education:		0.35		0.53		0.37	691 (100)
< High school	0.71 (0.49)		11.9		2.5		225 (32.6)
High school	0.71 (0.39)		15.6		4.2		168 (24.3)
> High school	0.76 (0.48)		16.2		1.7		298 (43.1)
Marital status:		0.37		0.46		0.70	654 (100)
Ever-married	0.72 (0.48)		14.7		2.6		579 (88.5)
Never-married	0.78 (0.45)		17.9		3.5		75 (11.5)
Household income:		0.40		0.59		0.89	606 (100)
< $20,000	0.71 (0.42)		13.8		2.9		155 (25.6)
≥$20,000	0.75 (0.49)		16.0		2.6		451 (74.4)
Hysterectomy:		< 0.0001		0.030		0.21	
Yes	0.84 (0.56)		25.6		4.3		361 (52.1)
No	0.62 (0.28)		3.3		0.0		332 (47.9)

[a] Unweighted analyses.

[b] Weighted analyses based on 4-year MEC weights for 1999–2002 NHANES data.

[c] Significance level for one-way ANOVA test.

[d] Significance level for Pearson's Chi-square test.

Table 2

Linear regression models for the unadjusted and adjusted associations of LH/FSH ratio with obesity, metabolic disturbances and chronic inflammation

	Mean (SEM)	Model I: Unadjusted		Model II: Adjusted	
		Log (LH/FSH ratio)			
		Beta (SEM)	P	Beta (SEM)	P
Body mass index[a]:	29.1 (0.3)	0.04 (0.4)	0.93	0.07 (0.4)	0.86
Waist Circumference[a]:	95.7 (0.8)	−0.2 (1.3)	0.88	0.1 (1.4)	0.92
Triglycerides[b]:	157.6 (13.6)	25.2 (31.7)	0.44	31.3 (31.3)	0.33
HDL cholesterol[b]:	56.8 (1.9)	−0.5 (2.0)	0.80	−1.8 (2.1)	0.40
Systolic blood pressure[a]:	126.0 (0.9)	−3.0 (1.4)	0.033	−0.6 (1.4)	0.69
Diastolic blood pressure[a]:	75.5 (0.5)	−0.3 (0.9)	0.78	−0.9 (0.9)	0.31
Glucose[b]:	96.3 (1.8)	−2.4 (1.4)	0.10	−1.4 (1.7)	0.41
HOMA-IR[b]:	3.0 (0.3)	−0.01 (0.3)	0.97	0.2 (0.3)	0.49
CRP[a]:	0.6 (0.03)	0.1 (0.07)	0.079	0.1 (0.07)	0.07

[a]Weighted linear regression analyses based on 4-year MEC weights for 1999–2002 NHANES data. Adjusted regression models include age (in years) and hysterectomy as covariates.

[b]Weighted linear regression analyses based on 4-year fasting sample weights for 1999–2002 NHANES data. Adjusted regression models include age (in years) and hysterectomy as covariates.

Table 3

Linear regression models for the unadjusted and adjusted association of LH/FSH ratio > 1 with obesity, metabolic disturbances and chronic inflammation

	Mean (SEM)	LH/FSH ratio > 1			
		Model I: Unadjusted		Model II: Adjusted	
		Beta (SEM)	P	Beta (SEM)	P
Body mass index[a]:	29.1 (0.3)	1.2 (0.8)	0.16	1.3 (0.8)	0.12
Waist Circumference[a]:	95.7 (0.8)	2.8 (2.1)	0.20	3.6 (2.2)	0.11
Triglycerides[b]:	157.6 (13.6)	20.6 (49.3)	0.68	31.3 (31.3)	0.33
HDL cholesterol[b]:	56.8 (1.9)	−0.08 (4.4)	0.98	−1.8 (2.1)	0.40
Systolic blood pressure[a]:	126.0 (0.9)	−2.9 (2.2)	0.21	0.7 (2.4)	0.76
Diastolic blood pressure[a]:	75.5 (0.5)	0.8 (1.5)	0.63	−0.2 (1.7)	0.91
Glucose[b]:	96.3 (1.8)	−7.1 (2.8)	0.022	−1.4 (1.7)	0.41
HOMA-IR[b]:	3.0 (0.3)	−0.3 (0.7)	0.62	0.2 (0.3)	0.49
CRP[a]:	0.6 (0.03)	0.2 (0.08)	0.02	0.2 (0.08)	0.02

[a]Weighted linear regression analyses based on 4-year MEC weights for 1999–2002 NHANES data. Adjusted regression models include age (in years) and hysterectomy as covariates.

[b]Weighted linear regression analyses based on 4-year fasting sample weights for 1999–2002 NHANES data. Adjusted regression models include age (in years) and hysterectomy as covariates.

Table 4

Linear regression models for the unadjusted and adjusted association of LH/FSH ratio > 2 with obesity, metabolic disturbances and chronic inflammation

	Mean (SEM)	LH/FSH ratio > 2			
		Model I: Unadjusted		Model II: Adjusted	
		Beta (SEM)	P	Beta (SEM)	P
Body mass index[a]:	29.1 (0.3)	−1.5 (0.9)	0.089	−1.4 (0.9)	0.14
Waist Circumference[a]:	95.7 (0.8)	−3.1 (3.4)	0.36	−2.5 (3.5)	0.50
Triglycerides[b]:	157.6 (13.6)	6.8 (18.3)	0.71	7.8 (24.9)	0.76
HDL cholesterol[b]:	56.8 (1.9)	0.8 (3.9)	0.84	−2.5 (4.6)	0.59
Systolic blood pressure[a]:	126.0 (0.9)	−2.4 (3.6)	0.50	2.9 (3.3)	0.39
Diastolic blood pressure[a]:	75.5 (0.5)	0.9 (3.0)	0.75	−0.2 (2.9)	0.95
Glucose[b]:	96.3 (1.8)	−8.8 (1.9)	0.001	−7.9 (2.6)	0.009
HOMA-IR[b]:	3.0 (0.3)	−0.9 (0.8)	0.28	−0.7 (0.8)	0.43
CRP[a]:	0.6 (0.03)	0.3 (0.2)	0.26	0.3 (0.2)	0.23

[a]Weighted linear regression analyses based on 4-year MEC weights for 1999–2002 NHANES data. Adjusted regression models include age (in years) and hysterectomy as covariates.

[b]Weighted linear regression analyses based on 4-year fasting sample weights for 1999–2002 NHANES data. Adjusted regression models include age (in years) and hysterectomy as covariates.

Table 5

Logistic regression models for the unadjusted and adjusted associations of LH/FSH ratio with obesity and metabolic disturbances

	Total N (%)‡	Logistic Models	
		Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Body mass index:[a]			
≥30 kg/m^2	286 (41.9)	0.94 (0.67–1.33)	0.96 (0.66–1.39)
< 30 kg/m^2	396 (58.1)	Ref.	Ref.
Waist Circumference:[a]			
≥35 inches	474 (69.5)	0.85 (0.55–1.28)	0.87 (0.56–1.33)
< 35 inches	208 (30.5)	Ref.	Ref.
Triglycerides: [b]			
≥150 mg/dL	241 (34.8)	1.45 (0.75–2.78)	1.61 (0.78–3.33)
< 150 mg/dL	452 (65.2)	Ref.	Ref.
HDL cholesterol: [b]			
< 50 mg/dL	17 (2.5)	0.23 (0.012–4.54)	0.41 (0.008–20.41)
≥50 mg/dL	676 (97.6)	Ref.	Ref.
Systolic blood pressure:[a]			
≥130 mm Hg	288 (42.4)	0.65 (0.39–1.09)	0.81 (0.48–1.39)
< 130 mm Hg	392 (57.7)	Ref.	Ref.
Diastolic blood pressure:[a]			
≥85 mm Hg	116 (17.1)	1.00 (0.63–1.58)	0.84 (0.50–2.01)
< 85 mm Hg	564 (82.9)	Ref.	Ref.
Glucose: [b]			
≥100 mg/dL	165 (23.8)	0.53 (0.13–2.08)	0.69 (0.19–2.43)
< 100 mg/dL	528 (76.2)	Ref.	Ref.
Metabolic syndrome: [b]			
3+	176 (26.2)	0.76 (0.36–1.64)	0.88 (0.34–2.33)
0–2	496 (73.8)	Ref.	Ref.

[a]Weighted logistic regression analyses based on 4-year MEC weights for 1999–2002 NHANES data. Adjusted regression models include age (in years) and hysterectomy as covariates.

[b]Weighted logistic regression analyses based on 4-year fasting sample weights for 1999–2002 NHANES data. Adjusted regression models include age (in years) and hysterectomy as covariates.

[c]Unweighted analyses.

Table 6

Logistic regression models for the unadjusted and adjusted associations of LH/FSH ratio > 1 and LH/FSH ratio > 2 with obesity and metabolic disturbances

	Total N (%)[c]	Unadjusted		Adjusted	
		LH/FSH > 1 OR (95% CI)	LH/FSH > 2 OR (95% CI)	LH/FSH > 1 OR (95% CI)	LH/FSH > 2 OR (95% CI)
Body mass index:[a]					
≥30 kg/m^2	286 (41.9)	1.15 (0.76–1.75)	2.25 (0.61–8.31)	1.20 (0.77–1.87)	2.16 (0.56–8.34)
< 30 kg/m^2	396 (58.1)	Ref.	Ref.	Ref.	Ref.
Waist Circumference:[a]					
≥35 inches	474 (69.5)	0.97 (0.55–1.72)	1.34 (0.39–4.53)	1.03 (0.58–1.86)	1.24 (0.36–4.26)
< 35 inches	208 (30.5)	Ref.	Ref.	Ref.	Ref.
Triglycerides: [b]					
≥150 mg/dL	241 (34.8)	0.80 (0.25–2.58)	0.45 (0.32–6.45)	0.88 (0.26–2.96)	0.39 (0.025–5.89)
< 150 mg/dL	452 (65.2)	Ref.	Ref.	Ref.	Ref.
HDL cholesterol: [b]					
< 50 mg/dL	17 (2.5)	--[d]	--[d]	1.49 (1.29–1.72)	1.52 (1.32–1.75)
≥50 mg/dL	676 (97.6)	Ref.	Ref.	Ref.	Ref.
Systolic blood pressure:[a]					
≥130 mm Hg	288 (42.4)	0.62 (0.29–1.36)	1.26 (0.37–4.26)	0.84 (0.34–2.09)	0.77 (0.20–2.98)
< 130 mm Hg	392 (57.7)	Ref.	Ref.	Ref.	Ref.
Diastolic blood pressure:[a]					
≥85 mm Hg	116 (17.1)	1.23 (0.69–2.20)	0.56 (0.15–2.08)	0.99 (0.50–1.94)	0.74 (0.19–2.91)
< 85 mm Hg	564 (82.9)	Ref.	Ref.	Ref.	Ref.
Glucose: [b]					
≥100 mg/dL	165 (23.8)	0.32 (0.07–1.53)	--[d]	0.45 (0.091–2.19)	0.99 (0.89–1.09)
< 100 mg/dL	528 (76.2)	Ref.	Ref.	Ref.	Ref.
Metabolic syndrome: [b]					
3+	176 (26.2)	0.36 (0.14–0.95)	1.79 (0.12–25.59)	0.45 (0.13–1.58)	1.54 (0.06–34.96)
0–2	496 (73.8)	Ref.	Ref.	Ref.	Ref.

[a] Weighted logistic regression analyses based on 4-year MEC weights for 1999–2002 NHANES data. Adjusted regression models include age (in years) and hysterectomy as covariates.

[b] Weighted logistic regression analyses based on 4-year fasting sample weights for 1999–2002 NHANES data. Adjusted regression models include age (in years) and hysterectomy as covariates.

[c] Unweighted analyses.

[d] Odds ratios and 95% confidence intervals could not be computed due to sample size limitations.