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Endogenous sex steroid hormones and glucose in a South-Asian population without diabetes: the Metabolic Syndrome and Atherosclerosis in South-Asians Living in America pilot study

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Abstract

Aims—To examine the associations between endogenous sex steroid hormones (oestradiol, testosterone and sex hormone-binding globulin) with diabetes risk in a South-Asian population living in the USA.

Methods—We used data from the Metabolic Syndrome and Atherosclerosis in South-Asians Living in America pilot study. The analytical sample included 60 women and 45 men of Asian Indian origin living in the San Francisco Bay Area, who were free from diabetes and cardiovascular disease and did not use exogenous sex steroids. Sex steroid hormone levels were assessed by validated conventional radioimmunoassays, and visceral and hepatic adiposity were assessed by computed tomography. We used multivariable regression to examine the association between endogenous sex steroid hormone levels (log-transformed) and fasting glucose and 2-h glucose levels in a series of sex-stratified models adjusted for age, waist circumference, visceral and hepatic adiposity, and insulin resistance.

Results—In age-adjusted models, lower levels of sex hormone-binding globulin (β=−0.18, 95% CI −0.30, −0.06) and higher levels of free testosterone (β=0.14, 95% CI 0.02, 0.26) were associated with elevated fasting glucose levels in South-Asian women, whereas lower levels of sex hormone-binding globulin (β=−0.14, 95% CI −0.26, −0.02) and lower levels of total testosterone (β= −0.12, 95% CI −0.24, 0.00) were associated with elevated fasting glucose levels in South-Asian men. Adjustment for waist circumference, visceral adiposity and insulin resistance

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Competing interests

None declared.

attenuated most of these associations, while adjustment for hepatic adiposity strengthened some of the observed associations. Similar results were found for 2-h glucose levels.

Conclusions—Results were consistent with previous research, which suggests that endogenous sex steroid hormones are a risk factor for diabetes across multiple race/ethnic groups. Additional studies are needed to determine whether visceral fat is a mediator or confounder of associations between sex steroid hormone and glucose levels.

Introduction

The endogenous sex hormone profile of an individual, consisting of oestradiol, testosterone and sex hormone-binding globulin (SHBG), has emerged as a potential risk factor for diabetes. Despite the high prevalence of diabetes among South-Asian people in the USA [1], previous studies have not considered whether sex steroid hormone levels are associated with glucose levels in this population.

Using data from the Diabetes Prevention Program, we have reported that changes in sex steroid hormone levels, as well as their baseline levels, were associated with changes in fasting and post-challenge glucose levels among postmenopausal women [2,3]. In addition, multiple studies [4] have found that lower levels of SHBG and higher levels of testosterone and oestradiol were associated with an elevated diabetes risk in women, whereas lower levels of testosterone were associated with an elevated diabetes risk in men; therefore, the relationship between sex steroid hormones and diabetes appears to be sexually dimorphic.

Recent work in longitudinal cohorts suggests that adiposity and sex steroid hormones in mid-life women are strongly related, and this relationship may be bidirectional. In the Study of Women's Health Across the Nation (SWAN), increases in waist circumference around the menopausal transition predicted changes in SHBG, testosterone and oestradiol [5]. At the same time, decreasing oestradiol also predicted increases in waist circumference [5]. In SWAN, we reported that SHBG was strongly associated with hepatic adiposity, apart from waist circumference [6]; thus, assessments of the impact of endogenous sex steroid hormones and diabetes risk require adjustment for fat, optimally assessed with more precise measures than anthropometry. This is of particular importance in South-Asian people, who have higher levels of visceral fat relative to BMI compared with other racial/ethnic groups [7].

The aims of the present study were (1) to examine the associations between endogenous sex steroid hormones and fasting glucose and 2-h glucose levels in South-Asian women and men without diabetes in the USA and (2) to determine whether these associations were attenuated after adjusting for waist circumference, visceral and hepatic adiposity, and insulin resistance.

Patients and methods

Study population

The data used for the present study were from the Metabolic Syndrome and Atherosclerosis in South-Asians Living in America (MASALA) pilot study. From August 2006 to October

2007, the study enrolled 150 community-dwelling individuals (75 men and 75 women) living in the San Francisco Bay area who self-identified as Asian Indian. Participants were aged 45–84 years and had no known cardiovascular disease. Detailed study methods have been described elsewhere [8]. Briefly, this pilot study was population-based, with random sampling of households in the San Francisco Bay Area with South-Asian surnames from the California Health Interview Survey. Subjects were eligible for the study if they were free from physician-diagnosed cardiovascular disease (myocardial infarction, stroke, transient ischaemic attack, congestive heart failure, angina, coronary artery bypass graft surgery, percutaneous cardiovascular interventions). Subjects were excluded if they could not speak or understand Hindi or English, and, for the purposes of this pilot study, people from other South-Asian countries were excluded. Ninety-eight percent of respondents were foreign-born. The Institutional Review Board at the University of California, San Francisco approved the study protocol and all study subjects provided written informed consent. For this analysis, we excluded people who used oestrogen therapy and those who had known diabetes, leaving a total of 60 women and 45 men.

Data collection

The study subjects were asked to provide blood samples after a 12-h fast. Steroid hormones and SHBG levels were measured at the Reproductive Endocrine Research Laboratory (University of Southern California). Oestradiol and testosterone levels were quantified in serum (0.5 ml) using a previously described radioimmunoassay method [9,10]. Prior to radioimmunoassay, steroids were extracted with hexane:ethyl acetate (3:2) and then oestradiol and testosterone were separated from each other and their metabolites by Celite column partition chromatography. The assay sensitivities for the oestradiol and testosterone radioimmunoassays are 2 pg/ml and 1.5 ng/dl, respectively. The interassay coefficients of variation for these assays are 11, 13 and 12% at 15, 36 and 101 pg/ml, respectively, and 8, 12 and 12% at 13, 30 and 96 ng/dl, respectively. SHBG was measured using a solid-phase, two-site chemiluminescent immunometric assay on the Immulite Analyzer (Siemens Healthcare Diagnostics, Deerfield, IL, USA). The SHBG assay sensitivity is 1 nmol/l and the interassay coefficient of variation is <10%. Free oestradiol and testosterone were calculated using a validated algorithm [11], based on derived equations [12], taking the concentrations of total testosterone, total oestradiol and SHBG into account and assuming a fixed albumin concentration of 3.5 g/dl.

Fasting glucose was measured using a glucose oxidase method. An oral glucose tolerance test was performed in which blood samples for plasma glucose were taken 120 min after participants consumed 75 g oral glucose solution.

Participant weight was determined using a digital scale, height was measured with a stadiometer and waist circumference was taken using a measuring tape halfway between the lower ribs and the anterior superior iliac spine, at the site of greatest circumference. Visceral and subcutaneous adiposity and hepatic liver-to-spleen attenuation ratio (values <1 represented higher amounts of hepatic fat) were measured using computed tomography (Philips Medical Systems, Best, the Netherlands). Visceral and subcutaneous abdominal fat were measured at the L4–L5 level after participants were positioned supine. Non-enhanced

computed tomography images of liver and spleen density were used to quantify hepatic fat content; a liver-to-spleen attenuation ratio of < 1 was used to define the presence of fatty liver. All computed tomography scans were digitally recorded for batched readings by a trained research assistant and intra-abdominal adipose tissue area was quantified by delineating the intra-abdominal cavity at the innermost aspect of the abdominal and oblique muscle walls surrounding the cavity [13]. Fasting serum insulin was measured by radioimmunoassay (Millipore, St. Charles, MO, USA) and homeostatic model assessment of insulin resistance was calculated as a proxy measure of insulin resistance as

$$[\mathrm{I0}\,(\mu\mathrm{IU/ml}) * \mathrm{G0}\,(\mathrm{mmol/1})/22.5],$$

where I0 is insulin and G0 is glucose at xxx [14]. Sociodemographic characteristics, medical history and medication use were assessed via questionnaire.

Statistical analysis

We used a series of sex-stratified multivariable regression models to examine the association between endogenous sex steroid hormones (log-transformed) and fasting glucose and 2-h glucose levels. Age, waist circumference, visceral and hepatic adiposity, and insulin resistance were modelled as continuous covariates. Model 1 was unadjusted for covariates, model 2 adjusted for age, model 3 adjusted for age and waist circumference, model 4 adjusted for age and visceral adiposity, model 5 adjusted for age and hepatic adiposity, model 6 adjusted for age and both visceral and hepatic adiposity, model 7 adjusted for age and insulin resistance and model 8 adjusted for age, insulin resistance, and visceral and hepatic adiposity. All regression models were examined for the presence of outliers and influential observations. The analysis was completed using SAS version 9.3, SAS Institute, Cary, NC, USA.

Results

Descriptive statistics stratified by sex are shown in Table 1. Due to skewness, we examined median differences for the sex steroid hormones and SHBG. For all other measures, we examined mean differences. Age did not differ significantly between women and men. Women had significantly lower fasting glucose than men, but there was no sex difference in 2-h glucose levels. Women had significantly lower total oestradiol, total testosterone, free oestradiol and free testosterone levels; whereas men had significantly lower SHBG levels. Women had significantly lower visceral fat, but there was no gender difference in waist circumference, continuous liver-to-spleen attenuation ratio or BMI. When examining a dichotomous measure of liver-to-spleen ratio, a higher percentage of men had a ratio < 1, indicating higher amounts of hepatic fat. Women had significantly lower homeostatic model assessment of insulin resistance values than men.

As shown in Table 2, total testosterone was inversely associated with fasting glucose levels among men but not women, and this association was attenuated after adjusting for waist circumference, visceral adiposity and insulin resistance. SBHG was inversely associated with fasting glucose among both women and men. The association among women was

attenuated after adjusting for waist circumference, visceral adiposity and insulin resistance; whereas adjusting for hepatic adiposity strengthened the association. Among men, the association between SHBG and fasting glucose was partially attenuated after adjusting for visceral adiposity and insulin resistance. Free testosterone was positively associated with fasting glucose among women but not men. This association was partially attenuated after adjusting for waist circumference, visceral adiposity and insulin resistance. There was no association between oestradiol or free oestradiol and fasting glucose levels for either women or men. As shown in Table 3, similar results were obtained for 2-h glucose.

Discussion

In this study in a middle-aged Asian Indian population without diabetes, living in the San Francisco Bay Area, a population at high-risk for dysglycaemia, we found that endogenous sex steroid hormone profile was cross-sectionally associated with both fasting and post-challenge 2-h glucose levels, and the nature of this association differed according to sex. Associations were most robust for SHBG, with lower levels of SHBG associated with higher levels of glucose in both men and women. Adjustment for visceral adiposity attenuated this relationship (more so for women than men), while adjustment for hepatic adiposity tended to strengthen this relationship. While lower total testosterone was associated with significantly higher fasting and 2-h glucose levels in men, total testosterone was not associated with glucose levels in women. Adjustment for visceral fat partially attenuated this relationship. Oestradiol, in either total or free form, was not associated with fasting or 2-h glucose levels in men or women before or after adjustment for adiposity. These patterns of associations parallel those in other racial/ethnic groups at lower risk of diabetes [4], despite the differences in fat deposition that distinguish South-Asian people.

The South-Asian population has been characterized as having higher glucose levels in relation to body fat compared with other racial/ethnic groups [15]. In a comparison of a larger US South-Asian cohort with that of the Multi-Ethnic Study of Atherosclerosis (MESA), a US cohort of mid-life adults, South-Asian people had a lower BMI and waist circumference than non-Hispanic white, African-American and Latino people, but a higher prevalence of Type 2 diabetes [15,16]. One explanation for this risk difference is that, despite their smaller body size, South-Asian people have a higher amount of visceral fat relative to overall body mass. In a 2013 review, Bhopal [17] noted that South-Asian people have lower birth weight and excess caloric intake in childhood and young adulthood compared with Northern Europeans, resulting in relatively greater ectopic fat deposition, which increases diabetes risk to a greater extent than does subcutaneous fat deposition [18]. This fat deposition is exacerbated by poor ongoing lifestyle behaviours. Immigrants may be at particular risk for these poor behaviours and additional stresses: in one cross-sectional examination of South-Asian people (consisting of people from India and Pakistan) in Kuwait, the prevalence of diabetes and other cardiovascular risk factors was higher compared with South-Asian people in their native countries [19]. Heald *et al*. [20] compared Gujarati men in India with men from the same villages living in the UK and found that migrants had higher waist circumferences compared with non-migrants, despite the younger age of the migrants.

Endogenous sex steroid hormones may be a possible mediator of the effect of this relative excess of ectopic fat on carbohydrate metabolism because of the actions of these hormones on skeletal muscle as well as on hepatic glucose metabolism [4]. Previous research examining sex steroid hormone levels among South-Asian people has shown that immigrant British Pakistani women had a significantly higher free androgen index than British-born Pakistani women and women of European origin [21], while South-Asian men in the UK had lower total testosterone levels than men of European origin [22]. Heald *et al*. [20] reported that higher levels of SHBG and higher levels of testosterone were correlated with waist circumference and higher insulin sensitivity in both migrant and non-migrant Indian populations in the UK. In the USA, the relationship between SHBG and waist circumference has been reported in children of South-Asian origin (move 24 here), but not among adults. We are not aware of any previous studies examining the relationship between sex hormone profiles and fasting or post-challenge glucose levels in South Asians in the USA [23] (remove cite here). Studies in other races/ethnic populations [4,24] have reported fairly consistent relationships between lower levels of SHBG and lower levels of glucose in both men and women, while higher levels of testosterone relative to oestradiol are related to lower glucose levels in men and an inverse, weaker relationship is observed in women. Our results are consistent with this previous work and extend it to the population of South-Asian migrants in the USA.

Aside from the MASALA study, we are not aware of any other studies in South-Asian populations that have data on sex hormones and ectopic fat deposition assessed by radiographic imaging. In other racial/ethnic populations, endogenous sex steroids in mid-life adults have been variably associated with glucose after consideration of visceral fat, although there are relatively few studies that have used imaging to measure fat mass. Peter *et al*. [24] noted that SHBG was correlated with fasting glucose levels, and this association was significant but somewhat attenuated after adjustment for hepatic fat; visceral fat was correlated with SHBG to a significantly lesser extent than hepatic fat. By contrast, Tschernof *et al*. [25] found that SHBG was not related to metabolic syndrome components, including glucose, after adjustment for visceral fat. Bonnet *et al*. [26] reported that the relationship between SHBG and fasting glycaemia was no longer significant after adjustment for hepatic fat, suggesting that SHBG, a protein produced by the liver, was a marker for hepatic fat. While our results are similar to other studies that found that adjustment for visceral fat on computed tomography generally attenuated relationships between sex steroid hormones and glucose, our results are conflicting in that adjustment for hepatic fat in the MASALA population tended to strengthen associations. These results suggest that SHBG has a different relationship with hepatic fat than that observed in other racial/ethnic groups but this should be interpreted with caution because of the small sample size and the risk of a type I error associated with multiple testing.

Post-challenge glucose is commonly believed to reflect skeletal muscle insulin sensitivity and later-phase insulin release, and is subject to greater intra-individual variation than fasting glucose [27]. We have previously reported weaker associations between changes in endogenous sex steroid hormone levels and changes in 2-h as opposed to fasting glucose levels [2]. Among participants in the pilot MASALA study, patterns of association were

similar between sex hormones and fasting and 2-h glucose levels, which may reflect the cross-sectional nature of the associations or stronger relationships between these hormones and post-challenge glucose levels than previously observed in other populations.

The present report has several strengths and limitations. First, we examined cross-sectional data, so we were unable to determine whether baseline sex steroid hormone levels were associated with changes over time in fasting and 2-h glucose. Longitudinal data could provide stronger evidence for a causal association between sex steroid hormones and glucose, and would facilitate an examination of associations between these hormones and incident diabetes. Next, we did not adjust for multiple comparisons. Thus, some of the findings reported here may be attributable to chance and should be interpreted with caution; however, given the small sample size, we had limited power to detect associations. In the future, this work could be extended to the larger MASALA study (n=906) with the addition of sex steroid hormone data.

A key strength of the present study was its examination of a population-based sample of Asian Indians in the USA, an understudied and rapidly growing minority group with elevated risk of diabetes. Other strengths include adjustment for multiple measures of adiposity, including waist circumference and visceral and hepatic adiposity, and the inclusion of women and men, which allowed us to examine gender differences in associations between sex steroid hormones and glucose.

Learning more about the aetiology of glucose intolerance in the South-Asian population is important, as this may suggest racial/ethnic group-specific pathways for prevention and treatment. This study suggests that endogenous sex hormone profile is a risk factor for dysglycaemia in a population-based sample of US-dwelling South-Asian people in mid- to late life. Results were generally consistent with findings in other racial/ethnic groups; however, multi-ethnic studies are needed to determine whether sex steroid hormones are more strongly associated with glucose in South-Asian populations compared with other groups and whether sex steroid hormones contribute to the higher prevalence of diabetes among South-Asian people in the USA compared with African-American, Latino, Native American and non-Hispanic white people [1].

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What's new?

- This is the first study to examine the associations between sex steroid hormones and glucose levels in a population-based sample of South-Asian people without diabetes living in the USA.
- This work adds to a small body of literature examining sex steroid hormones in South-Asian people, a population at high risk for dysglycaemia.
- Although sex hormone-binding globulin has been hypothesized to be a marker of hepatic adiposity, associations of sex hormone-binding globulin with glucose were not attenuated by hepatic adiposity.

Table 1

Descriptive statistics for respondents without diabetes, stratified by sex

	Women				Men		
	n	**Mean (SD)**	**Median (IQR)**	***n***	**Mean (SD)**	**Median (IQR)**	***P***
Age, years	61	55.78 (7.11)	56.05 (13.08)	45	58.06 (9.23)	56.77 (14.89)	0.39*
Fasting glucose, mmol/l	61	5.28 (0.57)	5.21 (0.53)	45	5.66 (0.53)	5.58 (0.63)	<0.001*
2-h glucose, mmol/l	61	7.00 (1.57)	6.72 (2.25)	45	7.41 (1.98)	7.83 (3.30)	0.30*
Total oestradiol, pmol/l	59	195.66 (362.95)	47.72 (47.72)	45	154.07 (44.48)	146.84 (54.15)	< 0.001†
Total testosterone, nmol/l	59	0.88 (0.43)	0.76 (0.56)	45	18.82 (7.64)	17.64 (10.37)	< 0.001†
SHBG, nmol/l	60	44.84 (25.01)	41.85 (26.40)	45	32.04 (15.91)	28.60 (15.90)	< 0.001†
Free oestradiol, pmol/l	59	4.78 (9.21)	1.27 (1.06)	45	4.44 (1.28)	4.26 (1.62)	< 0.001†
Free testosterone, nmol/l	59	0.18 (0.08)	0.16 (0.09)	45	4.80 (1.50)	4.56 (0.21)	< 0.001†
Waist circumference, cm	61	93.77 (14.34)	90.2 (17.23)	45	96.62 (9.39)	95.3 (11.98)	0.06*
Visceral fat, per SD cm^2	61	106.23 (42.65)	99.53 (56.15)	45	145.86 (53.38)	139.77 (80.17)	< 0.001*
Liver-to-spleen attenuation ratio, HU	53	1.30 (0.20)	1.34 (0.22)	45	1.23 (0.18)	1.23 (0.17)	0.06*
Liver: spleen ratio < 1	53	8.20%		45	13.33%		0.00*
BMI, kg/m^2	61	26.39 (5.30)	24.34 (5.65)	45	25.92 (4.10)	25.21 (5.14)	0.86*
HOMA-IR	61	2.26 (1.45)	2.02 (1.13)	45	3.28 (2.32)	2.51 (2.53)	0.01*

SHBG, sex hormone-binding globulin; HU, Hounsfield unit; HOMA-IR, homeostatic model assessment of insulin resistance.

*P value generated from t-test for sex comparison.

†P value generated from nonparametric Wilcoxon–Mann–Whitney test for sex comparison.

Table 2

Associations of sex steroid hormones (log-transformed) with fasting glucose (mmol/l) in respondents without diabetes, stratified by sex

	Women					Men				
	n	**β**	**Lower**	**Upper**	***P***	***n***	**β**	**Lower**	**Upper**	***P***
Association with total oestradiol										
Model 1	59	−0.01	−0.13	0.11	0.86	45	−0.08	−0.20	0.04	0.19
Model 2	59	−0.02	−0.14	0.10	0.80	45	−0.08	−0.20	0.04	0.19
Model 3	59	−0.02	−0.14	0.10	0.74	45	−0.08	−0.21	0.04	0.17
Model 4	59	−0.04	−0.16	0.08	0.52	45	−0.07	−0.19	0.05	0.24
Model 5	51	−0.03	−0.15	0.09	0.65	45	−0.08	−0.20	0.04	0.18
Model 6	51	−0.04	−0.16	0.09	0.56	45	−0.07	−0.19	0.05	0.27
Model 7	59	−0.01	−0.13	0.11	0.90	45	−0.05	−0.17	0.07	0.42
Model 8	51	−0.02	−0.14	0.11	0.80	45	−0.03	−0.16	0.09	0.57
Association with total testosterone										
Model 1	59	0.04	−0.08	0.16	0.49	45	**−0.13**	**−0.26**	**−0.01**	**0.03**
Model 2	59	0.04	−0.08	0.16	0.49	45	**−0.12**	**−0.24**	**0.00**	**0.05**
Model 3	59	0.05	−0.07	0.17	0.44	45	−0.11	−0.23	0.01	0.07
Model 4	59	0.05	−0.07	0.17	0.38	45	−0.09	−0.21	0.03	0.14
Model 5	51	0.03	−0.09	0.15	0.67	45	**−0.12**	**−0.24**	**0.00**	**0.05**
Model 6	51	0.05	−0.08	0.17	0.45	45	−0.09	−0.21	0.03	0.16
Model 7	59	0.05	−0.07	0.17	0.41	45	−0.03	−0.15	0.09	0.64
Model 8	51	0.04	−0.08	0.16	0.50	45	−0.03	−0.16	0.09	0.57
Association with SHBG										
Model 1	60	**−0.18**	**−0.30**	**−0.06**	**0.01**	45	**−0.17**	**−0.29**	**−0.05**	**0.01**
Model 2	60	**−0.18**	**−0.30**	**−0.06**	**0.01**	45	**−0.14**	**−0.26**	**−0.02**	**0.03**
Model 3	60	−0.08	−0.20	0.04	0.18	45	**−0.13**	**−0.25**	**−0.01**	**0.04**
Model 4	60	−0.11	−0.23	0.01	0.07	45	−0.11	−0.23	0.01	0.08
Model 5	52	**−0.24**	**−0.36**	**−0.12**	**0.00**	45	**−0.14**	**−0.26**	**−0.01**	**0.03**
Model 6	52	**−0.17**	**−0.29**	**−0.05**	**0.01**	45	−0.10	−0.22	0.02	0.09
Model 7	60	−0.01	−0.13	0.11	0.87	45	−0.05	−0.17	0.07	0.38

	Women					Men				
	n	**β**	**Lower**	**Upper**	***P***	***n***	**β**	**Lower**	**Upper**	***P***
Model 8	52	−0.05	−0.17	0.08	0.46	45	−0.06	−0.18	0.06	0.34
Association with free oestradiol										
Model 1	59	0.01	−0.11	0.13	0.68	45	−0.02	−0.14	0.10	0.35
Model 2	59	0.01	−0.11	0.13	0.71	45	−0.04	−0.16	0.08	0.32
Model 3	59	−0.01	−0.13	0.11	0.70	45	−0.05	−0.17	0.07	0.30
Model 4	59	−0.02	−0.15	0.10	0.71	45	−0.05	−0.17	0.07	0.31
Model 5	51	0.00	−0.12	0.12	0.74	45	−0.04	−0.16	0.08	0.35
Model 6	51	−0.02	−0.14	0.10	0.73	45	−0.04	−0.16	0.08	0.34
Model 7	59	−0.01	−0.13	0.11	0.88	45	−0.04	−0.17	0.08	0.54
Model 8	51	−0.01	−0.13	0.11	0.86	45	−0.02	−0.14	0.10	0.73
Association with free testosterone										
Model 1	59	**0.14**	**0.02**	**0.26**	**0.03**	45	−0.09	−0.21	0.03	0.14
Model 2	59	**0.14**	**0.02**	**0.26**	**0.02**	45	−0.10	−0.22	0.02	0.11
Model 3	59	0.09	−0.03	0.21	0.13	45	−0.09	−0.21	0.03	0.15
Model 4	59	0.11	−0.01	0.23	0.07	45	−0.07	−0.19	0.05	0.27
Model 5	51	**0.13**	**0.01**	**0.25**	**0.03**	45	−0.10	−0.22	0.02	0.11
Model 6	51	0.12	0.00	0.24	0.06	45	−0.06	−0.18	0.06	0.30
Model 7	59	0.05	−0.07	0.17	0.90	45	−0.01	−0.14	0.11	0.82
Model 8	51	0.06	−0.06	0.18	0.33	45	−0.02	−0.14	0.11	0.78

SHBG, sex hormone-binding globulin.

Model 1: unadjusted association; model 2: adjusted for age; model 3: adjusted for age and waist circumference; model 4: adjusted for age and visceral fat; model 5: adjusted for age and hepatic adiposity; model 6: adjusted for age, visceral fat and hepatic adiposity; model 7: adjusted for age and insulin resistance; model 8: adjusted for age, insulin resistance and visceral and hepatic adiposity.

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Table 3

Associations of sex steroid hormones (log-transformed) with 2-h glucose (mmol/l) in respondents without diabetes, stratified by sex

	Women					Men				
	n	**β**	**Lower**	**Upper**	***P***	***n***	**β**	**Lower**	**Upper**	***P***
Association with total oestradiol										
Model 1	59	−0.03	−0.15	0.09	0.67	45	−0.05	−0.17	0.08	0.46
Model 2	59	−0.04	−0.16	0.08	0.56	45	−0.05	−0.17	0.07	0.43
Model 3	59	−0.04	−0.16	0.08	0.54	45	−0.06	−0.18	0.06	0.33
Model 4	59	−0.05	−0.17	0.07	0.37	45	−0.03	−0.16	0.09	0.57
Model 5	51	−0.04	−0.16	0.08	0.54	45	−0.07	−0.19	0.05	0.26
Model 6	51	−0.04	−0.16	0.08	0.48	45	−0.05	−0.17	0.07	0.41
Model 7	59	−0.02	−0.14	0.10	0.71	45	−0.02	−0.14	0.10	0.72
Model 8	51	−0.03	−0.15	0.09	0.63	45	−0.03	−0.15	0.09	0.59
Association with total testosterone										
Model 1	59	−0.09	−0.21	0.03	0.13	45	**−0.14**	**−0.26**	**−0.02**	**0.03**
Model 2	59	−0.10	−0.22	0.02	0.12	45	**−0.16**	**−0.28**	**−0.03**	**0.01**
Model 3	59	−0.10	−0.22	0.02	0.11	45	−0.12	−0.24	0.01	0.06
Model 4	59	−0.09	−0.21	0.03	0.14	45	−0.10	−0.22	0.03	0.12
Model 5	51	−0.07	−0.19	0.05	0.28	45	**−0.15**	**−0.28**	**−0.03**	**0.01**
Model 6	51	−0.06	−0.18	0.06	0.34	45	−0.10	−0.23	0.02	0.09
Model 7	59	−0.09	−0.21	0.03	0.14	45	−0.09	−0.21	0.03	0.13
Model 8	51	−0.05	−0.17	0.07	0.39	45	−0.08	−0.20	0.04	0.20
Association with SHBG										
Model 1	60	**−0.18**	**−0.30**	**−0.06**	**0.00**	45	**−0.13**	**−0.25**	**−0.01**	**0.04**
Model 2	60	**−0.18**	**−0.30**	**−0.06**	**0.00**	45	**−0.19**	**−0.31**	**−0.07**	**0.00**
Model 3	60	**−0.15**	**−0.27**	**−0.03**	**0.02**	45	**−0.15**	**−0.27**	**−0.03**	**0.01**
Model 4	60	**−0.14**	**−0.26**	**−0.02**	**0.03**	45	**−0.14**	**−0.26**	**−0.02**	**0.03**
Model 5	52	**−0.18**	**−0.30**	**−0.05**	**0.01**	45	**−0.20**	**−0.32**	**−0.07**	**0.00**
Model 6	52	**−0.12**	**−0.24**	**0.00**	**0.05**	45	**−0.15**	**−0.27**	**−0.03**	**0.02**
Model 7	60	−0.10	−0.22	0.02	0.11	45	**−0.14**	**−0.26**	**−0.01**	**0.03**

	Women					Men				
	n	**β**	**Lower**	**Upper**	***P***	***n***	**β**	**Lower**	**Upper**	***P***
Model 8	52	−0.06	−0.18	0.06	0.30	45	**−0.13**	**−0.25**	**−0.01**	**0.04**
Association with free oestradiol										
Model 1	59	0.00	−0.12	0.12	0.95	45	0.00	−0.13	0.12	0.94
Model 2	59	−0.01	−0.13	0.11	0.88	45	0.01	−0.11	0.13	0.88
Model 3	59	−0.02	−0.14	0.10	0.72	45	−0.02	−0.14	0.10	0.73
Model 4	59	−0.04	−0.16	0.08	0.52	45	0.00	−0.13	0.12	0.94
Model 5	51	−0.01	−0.13	0.11	0.82	45	−0.01	−0.13	0.11	0.87
Model 6	51	−0.03	−0.15	0.09	0.63	45	−0.02	−0.14	0.11	0.79
Model 7	59	−0.03	−0.15	0.09	0.65	45	0.00	−0.13	0.12	0.95
Model 8	51	−0.02	−0.14	0.10	0.77	45	0.01	−0.11	0.14	0.82
Association with free testosterone:										
Model 1	60	0.00	−0.12	0.12	0.94	45	**−0.12**	**−0.24**	**0.00**	**0.05**
Model 2	60	0.00	−0.12	0.12	0.97	45	**−0.12**	**−0.24**	**0.00**	**0.05**
Model 3	60	−0.03	−0.15	0.09	0.61	45	−0.09	−0.21	0.04	0.16
Model 4	60	−0.03	−0.15	0.09	0.65	45	−0.06	−0.18	0.06	0.30
Model 5	52	0.02	−0.10	0.14	0.77	45	−0.12	−0.24	0.00	0.06
Model 6	52	−0.20	−0.41	0.00	0.96	45	−0.07	−0.19	0.05	0.26
Model 7	59	−0.05	−0.17	0.07	0.41	45	−0.06	−0.18	0.06	0.31
Model 8	51	−0.03	−0.15	0.09	0.66	45	−0.05	−0.17	0.08	0.45

SHBG, sex hormone-binding globulin.

Model 1: unadjusted association; model 2: adjusted for age; model 3: adjusted for age and waist circumference; model 4: adjusted for age and visceral fat; model 5: adjusted for age and hepatic adiposity; model 6: adjusted for age, visceral fat and hepatic adiposity; model 7: adjusted for age and insulin resistance; model 8: adjusted for age, insulin resistance and visceral and hepatic adiposity.