Obesity and Insulin Resistance Are the Main Determinants of Postprandial Lipoprotein Dysmetabolism in Polycystic Ovary Syndrome

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Postprandial dyslipidaemia may be a plausible mechanism by which polycystic ovary syndrome (PCOS) increases cardiovascular risk. We sought to investigate whether the postprandial glucose and insulin and lipid and lipoprotein responses, including that of apolipoproteinB-48 (apoB-48) containing chylomicrons, to a mixed meal are different in obese PCOS women when compared to obese control subjects and whether differences, if any, are related to obesity, insulin resistance (IR), hyperandrogenaemia, or PCOS status. 26 women with PCOS (age 30.4±1.2 years (mean ± SEM), body mass index (BMI) 36.8±1.5 kg/m²) and 26 non-PCOS subjects (age 34.1±0.9 years, BMI 31.5±1.0 kg/m²) were studied before and up to 8 hours following a standard mixed meal. AUC-triglyceride (AUC-TG) was higher and AUC-high-density lipoprotein (AUC-HDL) lower in PCOS women. These differences were not apparent when BMI was accounted for. Insulin sensitivity (SI), AUC-apoB-48, and AUC-apolipoprotein B (AUC-apoB) were found to be independent predictors of AUC-TG, accounting for 55% of the variance. Only AUC-insulin remained significantly elevated following adjustment for BMI. Obesity related IR explains postprandial hypertriglyceridaemia and hyperinsulinaemic responses. Management of obesity in premenopausal women with PCOS is likely to reduce their cardiovascular risk burden.

1. Introduction

There is considerable evidence from epidemiological research, meta-analysis [1, 2], and prospective clinical trials [3, 4] to support an independent role for fasting and postprandial plasma triglycerides (TG) as a risk factor for cardiovascular disease (CVD). Increased plasma remnants of triglyceride-rich lipoproteins (TRLs), caused by delayed elimination of the same, has been shown to be prospectively associated with angiographic evidence of atherosclerosis and cardiac events [5]. Postprandial hypertriglyceridaemia is associated with two other well established cardiovascular risks—IR and obesity—both of which are prevalent in PCOS. An increase in postprandial lipoproteins is often found in IR states [6] and hyperinsulinaemia itself appears to delay and exacerbate postprandial accumulation of intestinally derived chylomicrons [7]. Obesity, especially visceral adiposity, also contributes to a magnified postprandial TG response [8, 9].

Postprandial hypertriglyceridaemia may be a plausible mechanism by which PCOS increases cardiovascular risk. Whilst numerous studies have investigated plasma lipid profile under fasting conditions in women with PCOS, few have investigated changes in the postprandial setting. In a previous study by Velázquez M et al. a strong positive correlation between postprandial TG and increasing waist-to-hip ratio (WHR) was demonstrated [10]. That study
evaluated overweight (BMI 27.41 ± 0.50 kg/m²) PCOS women and compared them to lean PCOS women and lean control subjects. There were no obese controls and there was no analysis of the influence of androgens on postprandial hypertriglyceridaemia [10]. A separate study by Bahceci et al. evaluated postprandial responses to an oral fat tolerance test, comparing lean PCOS women with lean controls (BMI 23.5 ± 2.6 kg/m² versus 23.1 ± 4.0 kg/m²; \( p > 0.05 \)) [11]. There were no obese or overweight controls in this study. They showed that PCOS women had higher baseline insulin levels, IR as assessed by homeostatic model assessment-IR (HOMA\(_{IR} \)), AUC-TG, AUC-total-cholesterol, AUC-veryslow-density lipoprotein cholesterol (AUC-VLDL-chol), and AUC-apoB. Surprisingly, though, AUC-insulin did not differ between the two groups. As with the study by Velázquez M et al., no analyses were reported between androgens and postprandial lipids [11].

It is also unclear whether postprandial hypertriglyceridaemia is mainly due to the contribution of intestinally derived apoB-48 containing chylomicrons or hepatically derived apoB-100 containing VLDL particles. Both VLDL and chylomicrons share a common lipolytic pathway and are hydrolysed by lipoprotein lipase (LPL), an enzyme predominantly found on the endothelial surfaces of the capillaries of adipose tissue, heart, and skeletal muscle. Hydrolysis results in the formation of a spectrum of smaller, denser particles. There are a number of described receptor mediated pathways through which these particles may eventually be cleared from the circulation [12]. Traditionally it has been difficult to assess what proportions of TRLs are chylomicrons and VLDLs. However, using ELISA, it is now possible to directly measure the quantity of apoB-48 and hence chylomicron particles, in whole plasma [13, 14].

We sought to investigate whether the postprandial glucose and insulin and lipid and lipoprotein responses, including that of apolipoprotein B-48 (apoB-48) containing chylomicrons, to a mixed meal are different in obese PCOS women when compared to obese control subjects and whether differences, if any, are related to obesity, insulin resistance (IR), hyperandrogenaemia, or PCOS status.

2. Methods

2.1. Subjects. Fifty-two obese premenopausal women with \( (n = 26) \) and without \( (n = 26) \) PCOS were recruited. Women with PCOS were recruited from the endocrinology outpatient clinics (Tallaght Hospital, Dublin, Ireland). Normal women were recruited by local advertisement. PCOS was defined according to the National Institute of Health (NIH) criteria as chronic oligomenorrhea (fewer than nine menstrual cycles per year) and clinical and/or biochemical evidence of hyperandrogenism, in the absence of other disorders causing the same phenotype [15]. Clinical criteria included hirsutism with a Ferriman–Gallwey score greater than 9, acne, or male pattern alopecia; biochemical criteria included total testosterone, androstenedione, or dehydroepiandrosterone sulphate (DHEAS) greater than the laboratory reference range. All normal subjects were eumenorrheic with testosterone levels within the normal range and were studied in the follicular phase of the menstrual cycle. Subjects were excluded if they were younger than 18 years old or older than 45 years old; were non-Caucasian, pregnant, or lactating; had a recent or chronic illness or medication likely to influence results; or were taking any medications likely to influence the results including hormonal contraception, antihypertensives, lipid-lowering medications, and antiplatelet or anti-inflammatory agents. Fourteen women in the PCOS group and 3 women without PCOS had a degree relative with type 2 diabetes mellitus. All study subjects gave their written signed consent to the study, which was approved by the Research Ethics Committee of Tallaght Hospital and St. James’s Hospital (Dublin, Ireland).

2.2. Clinical Protocol. This was a cross-sectional study. All subjects had their height measured with a Harpenden stadiometer and weight measured in light clothing. BMI was calculated as weight (kg)/height squared (m²). Waist circumference (WC) and hip circumference (HC) were measured with a nondistensible flexible tape, and WHR was calculated accordingly. All subjects also underwent estimation of body composition including percentage body fat (%BF) and percentage lean mass (%LM) using bioimpedance analysis using the Bodystat 1500 system (Bodystat Ltd., UK).

2.3. Frequently Sampled Intravenous Glucose Tolerance Test (fSIVGTT). Subjects attended the Clinical Investigation Unit after a 12-hour overnight fast and were requested to refrain from vigorous exercise and alcohol on the day prior to their fSIVGTT. On the morning of the fSIVGTT, two cannulae were inserted into the antecubital veins of both forearms. A fasting blood sample was taken from cannula 1. Then a bolus of 50% glucose solution (0.3 g/kg body weight (BW)) was infused into cannula 2 over a 1-minute period followed by 20 mL of 0.9% saline. Twenty minutes later, a dose of insulin (0.03 U/kg BW) was infused into the same cannula (cannula 2), which was then removed at 30 min after initiation of glucose administration. Meanwhile, blood was sampled through cannula 1 at frequent intervals over a 3-hour period (−5, 0, 2, 4, 8, 19, 22, 30, 40, 50, 70, 90, and 180 min after the start of the glucose injection) for determination of glucose and insulin at each time point. Blood samples were spun at 3000 rpm for 10 min after which the plasma was aliquoted and stored at −80°C until required for future analysis. Insulin sensitivity (\( S_i \)), glucose effectiveness (\( S_g \)), acute insulin response (AIR\(_{C_{2}} \)), and disposition index (DI) were estimated using the MINMOD computer program (version 3.0, copyright R. N. Bergman).

2.4. Mixed Meal and Sampling. Following a 12-hour overnight fast, subjects came to the Clinical Investigation Unit in Tallaght Hospital for blood sampling and a high caloric meal. The mixed meal was designed and analyzed by a qualified dietician. It consisted of 948 kcal. 48% of the total calories were derived from fat (20% saturated, 16% monounsaturated, and 8% polyunsaturated). 36% and 15% of the calories were derived from carbohydrate and protein, respectively. The meal was ingested within 20 minutes after baseline bloods. Bloods were taken at 2, 4, 6, and 8 hours after which the plasma was aliquoted and stored at −80°C until required for future analysis. Insulin sensitivity (\( S_i \)), glucose effectiveness (\( S_g \)), acute insulin response (AIR\(_{C_{2}} \)), and disposition index (DI) were estimated using the MINMOD computer program (version 3.0, copyright R. N. Bergman).
after ingestion of the meal. Subjects were advised to restrict their physical activity to the minimum until the end of the sampling period.

2.5. Laboratory Methods

2.5.1. Hormones, Glucose, HbAlc, Lipids, and Apolipoproteins

A-I, A-II, and B. Glucose was measured by an enzymatic (hexokinase) method on the Roche P Module (Roche, Stockholm, Sweden) and insulin was measured by electrochemiluminescence immunoassay on the Roche E Module (coefficients of variation (CVs) <5% for both). Glucose and insulin levels were used to calculate HOMAIR. Nonesterified fatty acids (NEFA) were measured by a kit using the Randox Colorimetric Method (Randox, Antrim, UK) and analyzed on a Hitachi modular analyzer (Tokyo, Japan) (CV <5%). Luteinising hormone (LH), follicle stimulating hormone (FSH), sex hormone binding globulin (SHBG), DHEAS, oestradiol, thyroid stimulating hormone (TSH), free thyroxine (T4), prolactin, and cortisol were measured by standard chemiluminescence immunoassays (CVs <5% for all). Total testosterone was measured by electrochemiluminescence immunoassay on the Roche E Module. Free androgen index (FAI) was calculated by the following formula: FAI = 100 x total testosterone/SHBG. Androstenedione was measured by radioimmunoassay (CV <5%). Total-cholesterol, TG, and HDL-C were measured using standard laboratory techniques (CV <5%). LDL-C was calculated using the Friedewald equation. Apolipoproteins A-I (apoA-I), A-II (apoA-II), and B (apoB) were measured by standard nephelometry on a BNII nephelometer (Dade Behring, Deerfield, IL) (CV <5%).

2.5.2. ApoB-48 ELISA. ApoB-48 was measured using a commercially available ELISA kit (AKHB48, Gentaur BVBA corporation) and using a modified version of the method described by Lorec et al. [13]. The anti-apoB-48 coated plate is initially washed to remove buffer. The appropriately diluted samples are added to the plate and left to react for one hour. Samples were diluted 1:250 to ensure that the concentration was not above the assay range. The plate was subsequently washed 4 times, and biotin-conjugated anti-apoB-48 antibody is added. This binds to human apoB-48 bound to the anti-apoB-48 antibody immobilised on the coated plate. This reaction is stopped after 1 hour and the plate washed 4 times. Finally a peroxidase-conjugated avidin is then added to the plate. The avidin and biotin readily bind to ensure that the horseradish peroxidase enzyme is immobilised on the plate. After washing, the chromogenic substrate tetramethyl benzidine (TMB) is added. This forms a blue colour on reaction with horseradish peroxidase enzyme. The reaction stopper (1M H2SO4) is added, resulting in a yellow colour formation which is proportional to substrate concentration. The plate was read at an absorbance of 450 nm. Interassay and intra-assay CVs were 14% and 9%, respectively.

2.6. Statistical Analysis. Data are presented as mean ± SEM. Skewed variables were logarithmically transformed to normalise data prior to analysis. Initial comparisons between groups were performed using independent t-test. Analysis of covariance (ANCOVA) was used to compare differences between the two groups adjusting for 3 separate covariates: BMI, HOMAIR, and S1. Correlations were made using Pearson’s correlation coefficient. Multiple linear regression analysis was used to identify independent contributors to postprandial TG, apoB-48, and HDL-chol. Independent variables that correlated significantly in univariate analysis were entered into the multiple regression models in forward stepwise fashion. Statistical significance was defined as p < 0.05.

3. Results

3.1. Baseline Demographic Data and Hormonal Profile. Table 1 shows the baseline data of both groups of subjects. Women with PCOS had greater BMI, WC, HC, and %BF. All androgens were higher whilst SHBG and FSH were lower in women with PCOS. Women with PCOS were more insulin resistant with a higher HOMAIR (4.40 ± 0.41 μmolL⁻² in PCOS versus 2.56 ± 0.30 μmolL⁻² in controls) and lower S1 (1.99 ± 0.18 × 10⁻⁴ min⁻¹mU/L in PCOS versus 4.05 ± 0.46 × 10⁻⁴ min⁻¹mU/L in controls).

3.2. Postprandial Lipids, NEFA, and Apolipoprotein. Table 2 shows the pre- and postprandial results of TG, HDL, and NEFA. Postprandial TG at 2 hours was significantly greater in
PCOS women (2.18±0.18 mmol/L versus 1.58±0.10 mmol/L, \( p = 0.019 \)) and nonsignificantly greater at the other time points compared to controls (Figure 1). AUC-TG, but not the iAUC-TG, was also significantly higher in women with PCOS. Conversely, HDL-cholesterol was significantly lower in PCOS women compared to controls at \( T = 0, 2, 4, \) and 6 hours (Figure 2). AUC-HDL was also significantly lower in PCOS compared with controls. NEFA levels did not differ significantly between the two groups. There were no significant differences in apoA-I, apoA-II, apoB, and apoB-48 at any of the time points and the AUC or iAUC of these apolipoproteins between the two groups.

3.3. Postprandial Glucose and Insulin. Table 3 shows the pre- and postprandial results for glucose and insulin. Glucose levels were nonsignificantly greater at 2 hours and significantly greater at 4 hours in women with PCOS compared to controls (Figure 3). AUC-glucose was also greater in PCOS. With the exception of insulin at 8 hours, insulin level at all other time points, AUC-insulin, and iAUC-insulin were all greater in women with PCOS (Figure 4).

3.4. Comparisons following Adjustment for BMI, HOMA\(_{IR}\), and \( S_I \). Tables 4 and 5 show results following adjustment for BMI, HOMA\(_{IR}\), and \( S_I \). After adjusting for BMI, androgens remained higher and SHBG lower in PCOS women compared to control subjects (Table 4). There were no differences in TG, HDL, and apoB-48 at any time points nor in AUC-TG, AUC-HDL, AUC-apoB-48. Insulin remained significantly higher at all time points except at 8 hours. AUC-insulin and iAUC-insulin were also significantly higher (Table 5). There were no differences in the other postprandial apolipoproteins.

Following adjustment for HOMA\(_{IR}\), androgens and SHBG were significantly different between the two groups (Table 4). ApoB-48 at 4 hours was significantly (\( p = 0.034 \)) higher in the PCOS women (19.8 ± 1.68 μg/mL) compared to controls (15.2 ± 1.64 μg/mL) and insulin at 4 and 6 hours as well as AUC-insulin and iAUC-insulin also remained significantly higher (Table 5).

Finally, following adjustment for \( S_I \), androgens remained significantly greater in PCOS women, but SHBG was no longer significantly different (Table 4). Only insulin at 4 hours was higher in the PCOS women, but AUC-insulin and iAUC-insulin were not different between the two groups (Table 5). ApoB-48 was nonsignificantly (\( p = 0.058 \)) greater at 4 hours in PCOS women (19.2 ± 1.90 μg/mL) compared to controls (16.8 ± 2.00 μg/mL) but not at other time points (Table 5). There were no significant differences in apoB, apoA-I, or apoA-II at any of the time points or in the AUC or iAUC between the two groups.

3.5. Correlations and Multiple Regression Analyses. Table 6 shows the correlations between AUC-TG, AUC-HDL, AUC-apoB-48, AUC-apoB, AUC-glucose, AUC-insulin, and all other variables. Taking the entire cohort of 52 subjects, AUC-TG correlated positively (\( p < 0.05 \) for all variables unless otherwise specified) with WC (\( r = 0.314 \)), weight (\( r = 0.357 \)), BMI (\( r = 0.316 \)), and body fat content (\( r = 0.378 \)) and negatively with body water content (\( r = -0.342 \)) and SHBG (\( r = -0.378, p < 0.01 \)). AUC-TG did not correlate with androgens except for FAI (\( r = 0.294 \)) and this is likely to be a
|                          | PCOS (n = 26) | Controls (n = 26) | p     |
|--------------------------|--------------|------------------|-------|
| TG 0 hrs (mmol/L)*       | 1.57 ± 0.15  | 1.20 ± 0.08      | 0.075 |
| TG 2 hrs (mmol/L)*       | 2.18 ± 0.18  | 1.58 ± 0.10      | 0.019 |
| TG 4 hrs (mmol/L)*       | 2.41 ± 0.22  | 1.83 ± 0.14      | 0.057 |
| TG 6 hrs (mmol/L)*       | 1.96 ± 0.23  | 1.49 ± 0.16      | 0.074 |
| TG 8 hrs (mmol/L)*       | 1.74 ± 0.22  | 1.30 ± 0.13      | 0.129 |
| AUC-TG (mmol/L-8 hrs)*   | 8.20 ± 0.77  | 6.15 ± 0.45      | 0.041 |
| iAUC-TG (mmol/L-8 hrs)   | 1.93 ± 0.28  | 1.35 ± 0.24      | 0.127 |
| HDL-chol 0 hrs (mmol/L)  | 1.34 ± 0.06  | 1.51 ± 0.06      | 0.046 |
| HDL-chol 2 hrs (mmol/L)  | 1.27 ± 0.06  | 1.44 ± 0.05      | 0.037 |
| HDL-chol 4 hrs (mmol/L)  | 1.22 ± 0.06  | 1.37 ± 0.05      | 0.043 |
| HDL-chol 6 hrs (mmol/L)  | 1.25 ± 0.06  | 1.42 ± 0.05      | 0.034 |
| HDL-chol 8 hrs (mmol/L)  | 1.30 ± 0.06  | 1.44 ± 0.05      | 0.092 |
| AUC-HDL-chol (mmol/L-8 hrs) | 5.06 ± 0.23 | 5.71 ± 0.21      | 0.041 |
| iAUC-HDL-chol (mmol/L-8 hrs) | −0.32 ± 0.03 | −0.33 ± 0.07     | 0.883 |
| NEFA 0 hrs (mmol/L)      | 0.65 ± 0.04  | 0.61 ± 0.05      | 0.644 |
| NEFA 2 hrs (mmol/L)      | 0.19 ± 0.02  | 0.18 ± 0.05      | 0.658 |
| NEFA 4 hrs (mmol/L)      | 0.33 ± 0.03  | 0.36 ± 0.05      | 0.524 |
| NEFA 6 hrs (mmol/L)      | 0.62 ± 0.05  | 0.67 ± 0.05      | 0.544 |
| NEFA 8 hrs (mmol/L)      | 0.81 ± 0.05  | 0.84 ± 0.05      | 0.698 |
| AUC NEFA (mmol/L-8 hrs)  | 1.87 ± 0.10  | 1.94 ± 0.05      | 0.681 |
| iAUC NEFA (mmol/L-8 hrs) | −0.72 ± 0.14 | −0.52 ± 0.05     | 0.400 |
| ApoB-48 0 hrs (µg/mL)*   | 11.9 ± 1.45  | 9.89 ± 1.29      | 0.252 |
| ApoB-48 2 hrs (µg/mL)*   | 17.0 ± 1.43  | 15.7 ± 1.08      | 0.468 |
| ApoB-48 4 hrs (µg/mL)*   | 19.2 ± 1.56  | 15.8 ± 1.55      | 0.058 |
| ApoB-48 6 hrs (µg/mL)*   | 18.3 ± 1.70  | 15.8 ± 1.93      | 0.184 |
| ApoB-48 8 hrs (µg/mL)*   | 12.9 ± 1.34  | 11.3 ± 1.48      | 0.239 |
| AUC-apoB-48 (µg/mL-8 hrs)* | 66.4 ± 5.32 | 57.6 ± 4.41      | 0.157 |
| iAUC-apoB-48 (µg/mL-8 hrs) | 19.35 ± 3.38 | 18.27 ± 2.45     | 0.796 |
| ApoB 0 hrs (g/dL)        | 0.73 ± 0.07  | 0.82 ± 0.06      | 0.328 |
| ApoB 2 hrs (g/dL)        | 0.76 ± 0.07  | 0.73 ± 0.06      | 0.816 |
| ApoB 4 hrs (g/dL)        | 0.83 ± 0.06  | 0.76 ± 0.06      | 0.364 |
| ApoB 6 hrs (g/dL)        | 0.79 ± 0.05  | 0.77 ± 0.05      | 0.779 |
| ApoB 8 hrs (g/dL)        | 0.83 ± 0.05  | 0.79 ± 0.05      | 0.603 |
| AUC-apoB (g/dL-8 hrs)    | 3.16 ± 0.17  | 3.07 ± 0.14      | 0.688 |
| iAUC-apoB (g/dL-8 hrs)   | 0.22 ± 0.22  | −0.22 ± 0.19     | 0.143 |
| ApoA-I 0 hrs (g/dL)      | 1.15 ± 0.07  | 1.10 ± 0.10      | 0.679 |
| ApoA-I 2 hrs (g/dL)      | 1.04 ± 0.09  | 1.14 ± 0.09      | 0.437 |
| ApoA-I 4 hrs (g/dL)      | 1.19 ± 0.08  | 1.28 ± 0.08      | 0.465 |
| ApoA-I 6 hrs (g/dL)      | 1.18 ± 0.08  | 1.22 ± 0.08      | 0.715 |
| ApoA-I 8 hrs (g/dL)      | 1.08 ± 0.08  | 1.16 ± 0.09      | 0.481 |
| AUC-apoA-I (g/dL-8 hrs)  | 4.52 ± 0.19  | 4.75 ± 0.18      | 0.391 |
| iAUC-apoA-I (g/dL-8 hrs) | −0.08 ± 0.30 | 0.35 ± 0.34      | 0.342 |
| ApoA-II 0 hrs (g/dL)     | 0.32 ± 0.02  | 0.30 ± 0.03      | 0.544 |
| ApoA-II 2 hrs (g/dL)     | 0.29 ± 0.03  | 0.30 ± 0.02      | 0.796 |
| ApoA-II 4 hrs (g/dL)     | 0.26 ± 0.03  | 0.25 ± 0.03      | 0.764 |
| ApoA-II 6 hrs (g/dL)     | 0.26 ± 0.02  | 0.30 ± 0.02      | 0.195 |
| ApoA-II 8 hrs (g/dL)     | 0.25 ± 0.02  | 0.26 ± 0.02      | 0.761 |
| AUC-apoA-II (g/dL-8 hrs) | 1.10 ± 0.04  | 1.13 ± 0.04      | 0.657 |
| iAUC-apoA-II (g/dL-8 hrs) | −0.19 ± 0.09 | −0.08 ± 0.09     | 0.410 |

* t-tests analysis after log transformation.
Table 3: Postprandial glucose and insulin.

|                      | PCOS (n = 26) | Controls (n = 26) | p    |
|----------------------|--------------|------------------|------|
| Glucose 0 hrs (mmol/L) | 5.18 ± 0.11  | 4.99 ± 0.10     | 0.191|
| Glucose 2 hrs (mmol/L) | 5.67 ± 0.30  | 4.90 ± 0.25     | 0.053|
| Glucose 4 hrs (mmol/L) | 5.18 ± 0.18  | 4.73 ± 0.12     | 0.044|
| Glucose 6 hrs (mmol/L) | 4.66 ± 0.08  | 4.66 ± 0.06     | 0.959|
| Glucose 8 hrs (mmol/L) | 4.66 ± 0.06  | 4.62 ± 0.09     | 0.713|
| AUC-glucose (mmol/L⋅8 hrs) | 20.50 ± 0.48 | 19.10 ± 0.38   | 0.024|
| iAUC-glucose (mmol/L⋅8 hrs) | −0.33 ± 0.32 | −0.86 ± 0.40   | 0.306|
| Insulin 0 hrs (mU/L)* | 19.3 ± 1.80  | 11.7 ± 1.28     | <0.001|
| Insulin 2 hrs (mU/L)* | 105 ± 13.8   | 47.6 ± 5.41     | <0.001|
| Insulin 4 hrs (mU/L)* | 49.9 ± 7.02  | 21.4 ± 2.21     | <0.001|
| Insulin 6 hrs (mU/L)* | 21.7 ± 2.35  | 10.4 ± 0.85     | <0.001|
| Insulin 8 hrs (mU/L)* | 15.3 ± 1.59  | 12.6 ± 2.05     | 0.084|
| AUC-insulin (mU/L⋅8 hrs)* | 194 ± 21.6   | 91.5 ± 8.03     | <0.001|
| iAUC-insulin (mU/L⋅8 hrs)* | 117 ± 17.5   | 44.8 ± 5.70     | <0.001|

*t-tests analysis after log transformation.

result of the inverse correlation with SHBG, which causes FAI to be higher. Figures 5–8 show the correlations graphically between AUC-TG and SHBG (Figure 5), FAI (Figure 6), androstenedione (Figure 7), and DHEAS (Figure 8), respectively. As expected, AUC-TG also correlated strongly with HOMA_IR, S_I (r = −0.601, p < 0.01), and AUC-HDL (r = −0.540). Insulin at 0, 2, 4, and 6 hours, AUC-insulin, and iAUC-insulin also correlated significantly with AUC-TG (Figure 9). There were also positive correlations between AUC-TG and apoB-48 at 0, 2, 6, and 8 hours, AUC-apoB-48 (Figure 10), apoB at 2, 4, 6, and 8 hours, and AUC-apoB suggesting that both chylomicrons and VLDL contribute to postprandial hypertriglyceridaemia. Glucose at 0 and 2 hours, AUC-glucose, S_G, and DI also correlated with AUC-TG. Stepwise multiple regression analysis revealed that S_I, AUC-apoB-48, and AUC-apoB were independent predictors of AUC-TG, accounting for 55% of the overall variance. This suggests that postprandial chylomicron particles probably play an important role in contributing towards postprandial
Table 4: Baseline characteristics adjusted for BMI, HOMA<sub>IR</sub>, and log <i>S</i><sub>i</sub>.

|                                | Covariate: BMI | Covariate: HOMA<sub>IR</sub> | Covariate: <i>S</i><sub>i</sub> |
|--------------------------------|----------------|-------------------------------|-------------------------------|
|                                | PCOS           | Controls                      | PCOS                          | Controls                      | PCOS                          | Controls                      |
| Systolic BP (mmHg)             | 124.6 ± 2.2    | 123.3 ± 2.2                   | 124.4 ± 2.2                   | 123.5 ± 2.2                   | 125.0 ± 2.4                   | 123.0 ± 2.6                   |
| Diastolic BP (mmHg)            | 78.0 ± 1.9     | 78.9 ± 1.9                    | 78.6 ± 2.0                    | 78.2 ± 2.0                    | 78.6 ± 2.1                    | 78.9 ± 2.3                    |
| Waist (cm)                     | 107.3 ± 1.5    | 104.5 ± 1.5                   | 109.0 ± 2.2                   | 102.8 ± 2.2                   | 108.8 ± 2.4                   | 104.3 ± 2.6                   |
| Hip (cm)                       | 116.6 ± 1.1    | 114.8 ± 1.1                   | 118.7 ± 1.9<sup>a</sup>       | 116.2 ± 1.9                   | 118.4 ± 2.0                   | 113.3 ± 2.2                   |
| Waist : Hip                    | 0.920 ± 0.015  | 0.910 ± 0.015                 | 0.917 ± 0.015                 | 0.913 ± 0.015                 | 0.919 ± 0.016                 | 0.921 ± 0.017                 |
| Weight (kg)                    | 89.2 ± 1.4     | 89.5 ± 1.4                    | 91.2 ± 2.5                    | 87.4 ± 2.5                    | 91.0 ± 2.8                    | 88.9 ± 3.0                    |
| BMI (kg/m<sup>2</sup>)         | —              | —                             | 35.3 ± 1.0                    | 32.9 ± 0.9                    | 35.4 ± 1.1                    | 33.7 ± 1.2                    |
| % Body fat mass (%)            | 37.6 ± 1.2     | 36.2 ± 1.2                    | 38.2 ± 1.7                    | 35.7 ± 1.7                    | 38.5 ± 1.8                    | 36.2 ± 1.9                    |
| T (nmol/L)*                    | 3.37 ± 0.25<sup>b</sup> | 1.52 ± 0.24                   | 3.24 ± 0.25<sup>b</sup>       | 1.56 ± 0.25                   | 3.49 ± 0.27<sup>b</sup>       | 1.30 ± 0.279                  |
| SHBG (nmol/L)*                 | 32.2 ± 3.04<sup>b</sup> | 45.2 ± 2.98                   | 31.4 ± 2.98<sup>b</sup>       | 45.7 ± 2.98                   | 34.2 ± 3.19                   | 43.4 ± 3.45                   |
| FAI*                           | 12.2 ± 1.25<sup>b</sup> | 4.08 ± 1.22                   | 12.2 ± 1.24<sup>b</sup>       | 3.70 ± 1.24                   | 12.5 ± 1.38<sup>b</sup>       | 3.30 ± 1.50                   |
| Androstenedione (nmol/L)       | 15.67 ± 0.9<sup>b</sup> | 11.99 ± 0.89                  | 15.07 ± 0.92<sup>a</sup>      | 12.30 ± 0.90                  | 15.98 ± 0.99<sup>b</sup>      | 11.37 ± 1.05                  |
| DHEAS (μmol/L)                 | 8.00 ± 0.68<sup>b</sup> | 4.80 ± 0.66                   | 7.88 ± 0.66                   | 4.72 ± 0.66                   | 8.55 ± 0.66<sup>b</sup>       | 3.80 ± 0.72                   |
| HOMA<sub>IR</sub> (μmol<sup>2</sup>/L<sup>2</sup>)<sup>*</sup> | 3.99 ± 0.35<sup>a</sup> | 3.02 ± 0.34                   | —                             | 3.91 ± 0.38                   | 3.39 ± 0.41                   |
| <i>S</i><sub>i</sub> (×10<sup>-4</sup> min<sup>-1</sup>/mU/L)<sup>*</sup> | 2.23 ± 0.31<sup>b</sup> | 3.78 ± 0.34                   | 2.33 ± 0.30<sup>*</sup>       | 3.66 ± 0.32                   | —                             | —                             |
| <i>S</i><sub>Glucose</sub> (min<sup>-1</sup>) | 0.02 ± 0.00 | 0.02 ± 0.00 | 0.02 ± 0.00 | 0.02 ± 0.00 | 0.02 ± 0.00 | 0.02 ± 0.00 |
| AIR<sub>Glucose</sub> (mU/L<sup>-1</sup>·min<sup>-1</sup>) | 986 ± 144 | 612 ± 155 | 867 ± 133 | 747 ± 143 | 909 ± 149 | 700 ± 161 |
| DI                             | 1846 ± 321     | 2206 ± 345                    | 1893 ± 326                    | 2151 ± 351                    | 2174 ± 312                    | 1831 ± 338                    |

<sup>a</sup> ANCOVA analysis after log transformation. <sup>b</sup> p < 0.05 versus controls. <sup>*</sup> p < 0.01 versus controls.

Hypertriglyceridaemia, together with apoB and insulin sensitivity. AUC-TG was the only independent predictor of AUC-apoB-48, explaining 25.8% of the variance.

AUC-HDL correlated significantly negatively with WC (<i>r</i> = −0.439, <i>p</i> < 0.01), HC (<i>r</i> = −0.285), weight (<i>r</i> = −0.439, <i>p</i> < 0.01), BMI (<i>r</i> = −0.456, <i>p</i> < 0.01), body fat (<i>r</i> = −0.444), FAI (<i>r</i> = −0.350), HOMA<sub>IR</sub> (<i>r</i> = −0.499, <i>p</i> < 0.01), AUC-TG (<i>r</i> = −0.540, <i>p</i> < 0.01), AUC-glucose (<i>r</i> = −0.309), and AUC-insulin (<i>r</i> = −0.488, <i>p</i> < 0.01).

AUC-HDL correlated significantly positively with body water (<i>r</i> = 0.389), SHBG (<i>r</i> = 0.443, <i>p</i> < 0.01), and <i>S</i><sub>i</sub> (<i>r</i> = 0.454). AUC-HDL also correlated negatively with TG at all time points, iAUC-TG, iAUC-B48, apoA-1 at 2, 4, and 6 hours and AUC-apoA-1, glucose at 0 and 2 hours, AUC-glucose, insulin at 0, 2, 4, and 6 hours, AUC, and iAUC-insulin (results not shown). There was a nonsignificant negative correlation with androstenedione (<i>r</i> = −0.27, <i>p</i> = 0.055). AUC-TG and WC were the only independent predictors of AUC-HDL.
Table 5: Postprandial TG, HDL, apoB-48, glucose, and insulin levels adjusted for BMI, HOMA<sub>IR</sub>, and S<sub>I</sub>.

| Covariate: BMI | Covariate: HOMA<sub>IR</sub> | Covariate: S<sub>I</sub> |
|----------------|------------------|------------------|
| TG 0 hrs (mmol/L)* | 1.54 ± 0.13 | 1.25 ± 0.12 | 1.40 ± 0.11 | 1.36 ± 0.11 | 1.47 ± 0.13 | 1.33 ± 0.14 |
| TG 2 hrs (mmol/L)* | 2.14 ± 0.16 | 1.66 ± 0.16 | 1.97 ± 0.14 | 1.79 ± 0.14 | 2.04 ± 0.17 | 1.73 ± 0.18 |
| TG 4 hrs (mmol/L)* | 2.37 ± 0.20 | 1.90 ± 0.19 | 2.14 ± 0.16 | 2.10 ± 0.16 | 2.24 ± 0.20 | 2.10 ± 0.22 |
| TG 6 hrs (mmol/L)* | 1.92 ± 0.21 | 1.57 ± 0.21 | 1.70 ± 0.18 | 1.75 ± 0.18 | 1.80 ± 0.22 | 1.77 ± 0.24 |
| TG 8 hrs (mmol/L)* | 1.71 ± 0.19 | 1.37 ± 0.19 | 1.48 ± 0.16 | 1.56 ± 0.16 | 1.60 ± 0.20 | 1.56 ± 0.22 |
| AUC-TG (mmol/L/8 hrs)* | 8.06 ± 0.68 | 6.45 ± 0.66 | 7.25 ± 0.54 | 7.10 ± 0.54 | 7.61 ± 0.70 | 7.04 ± 0.76 |
| iAUC-TG (mmol/L/8 hrs) | 1.87 ± 0.29 | 1.45 ± 0.29 | 1.63 ± 0.27 | 1.65 ± 0.27 | 1.64 ± 0.31 | 1.82 ± 0.33 |
| HDL-chol 0 hrs (mmol/L) | 1.40 ± 0.16 | 1.45 ± 0.16 | 1.41 ± 0.06 | 1.44 ± 0.06 | 1.40 ± 0.06 | 1.38 ± 0.07 |
| HDL-chol 2 hrs (mmol/L) | 1.33 ± 0.06 | 1.38 ± 0.06 | 1.34 ± 0.05 | 1.37 ± 0.05 | 1.34 ± 0.06 | 1.33 ± 0.07 |
| HDL-chol 4 hrs (mmol/L) | 1.27 ± 0.06 | 1.32 ± 0.05 | 1.28 ± 0.05 | 1.31 ± 0.05 | 1.28 ± 0.06 | 1.27 ± 0.06 |
| HDL-chol 6 hrs (mmol/L) | 1.30 ± 0.06 | 1.37 ± 0.06 | 1.32 ± 0.06 | 1.36 ± 0.06 | 1.31 ± 0.06 | 1.31 ± 0.07 |
| HDL-chol 8 hrs (mmol/L) | 1.35 ± 0.06 | 1.38 ± 0.06 | 1.36 ± 0.06 | 1.37 ± 0.06 | 1.36 ± 0.06 | 1.32 ± 0.07 |
| AUC-HDL-chol (mmol/L/8 hrs) | 5.28 ± 0.23 | 5.49 ± 0.22 | 5.33 ± 0.22 | 5.44 ± 0.22 | 5.31 ± 0.24 | 5.26 ± 0.26 |
| iAUC-HDL-chol (mmol/L/8 hrs) | −0.33 ± 0.06 | −0.31 ± 0.06 | −0.33 ± 0.06 | −0.32 ± 0.06 | −0.30 ± 0.06 | −0.27 ± 0.07 |
| Log ApoB-48 0 hrs (μg/mL)* | 12.4 ± 1.54 | 9.70 ± 1.47 | 11.9 ± 1.49 | 9.86 ± 1.46 | 11.9 ± 1.70 | 10.4 ± 1.80 |
| Log ApoB-48 2 hrs (μg/mL)* | 17.3 ± 1.43 | 15.6 ± 1.36 | 17.0 ± 1.37 | 15.7 ± 1.34 | 16.5 ± 1.53 | 16.9 ± 1.62 |
| Log ApoB-48 4 hrs (μg/mL)* | 19.6 ± 1.77 | 15.5 ± 1.69 | 19.8 ± 1.68<sup>a</sup> | 15.2 ± 1.64 | 19.2 ± 1.90 | 16.8 ± 2.00 |
| Log ApoB-48 6 hrs (μg/mL)* | 18.9 ± 2.06 | 15.6 ± 1.97 | 17.2 ± 1.94 | 16.9 ± 1.90 | 17.9 ± 2.22 | 17.5 ± 2.34 |
| Log ApoB-48 8 hrs (μg/mL)* | 13.2 ± 1.60 | 11.2 ± 1.53 | 11.7 ± 1.47 | 12.4 ± 1.44 | 12.3 ± 1.70 | 12.5 ± 1.79 |
| Log ApoB-48 (μg/mL/8 hrs)* | 67.8 ± 5.51 | 57.1 ± 5.26 | 65.6 ± 5.30 | 58.4 ± 5.18 | 65.0 ± 5.97 | 62.5 ± 6.30 |
| iAUC apoB-48 (μg/mL/8 hrs) | 19.02 ± 3.33 | 18.31 ± 3.18 | 17.57 ± 3.19 | 19.98 ± 3.12 | 17.92 ± 3.70 | 21.06 ± 3.91 |
| Log Insulin 0 hrs (pmol/L)* | 17.9 ± 1.56<sup>a</sup> | 13.4 ± 1.12 | 15.4 ± 0.30 | 15.6 ± 0.30 | 17.5 ± 1.66 | 15.1 ± 1.79 |
| Log Insulin 2 hrs (pmol/L)* | 95.7 ± 10.3<sup>a</sup> | 59.5 ± 10.1 | 88.7 ± 8.91 | 63.8 ± 8.91 | 91.6 ± 11.3 | 64.1 ± 12.2 |
| Log Insulin 4 hrs (pmol/L)* | 47.6 ± 5.59<sup>b</sup> | 24.6 ± 5.47 | 43.7 ± 4.92<sup>a</sup> | 27.6 ± 4.92 | 45.7 ± 5.94<sup>b</sup> | 27.7 ± 6.42 |
| Log Insulin 6 hrs (pmol/L)* | 20.9 ± 1.90<sup>b</sup> | 11.6 ± 1.86 | 19.2 ± 1.57<sup>b</sup> | 12.9 ± 1.57 | 19.9 ± 1.94 | 13.2 ± 2.11 |
| Log Insulin 8 hrs (pmol/L)* | 13.6 ± 1.89 | 14.4 ± 1.84 | 13.4 ± 1.81 | 14.3 ± 1.81 | 14.1 ± 2.17 | 14.7 ± 2.35 |
| AUC-insulin (pmol/L/8 hrs)* | 180 ± 16.2<sup>b</sup> | 110 ± 15.8 | 166 ± 13.0<sup>a</sup> | 119 ± 13.0 | 173 ± 17.5 | 120 ± 18.9 |
| iAUC-insulin (pmol/L/8 hrs)* | 108 ± 13.5<sup>a</sup> | 55.9 ± 13.2 | 104 ± 13.0<sup>a</sup> | 57.0 ± 13.0 | 103 ± 14.7 | 59.6 ± 15.9 |

* ANCOVA analysis after log transformation. <sup>a</sup><sup>p</sup> < 0.05 versus controls. <sup>b</sup><sup>p</sup> < 0.01 versus controls.

Figure 8: Correlation between AUC-TG and DHEAS.

Figure 9: Correlation between AUC-TG and AUC-insulin.
### 4. Discussion

Dyslipidaemia, including both increased TG and low HDL-cholesterol, is common in PCOS [16, 17] and is a well-recognized feature of the metabolic syndrome which confers increased risk of cardiovascular disease [18, 19]. Hypertriglyceridaemia signifies the presence of excess TRL. TRL consists of hepatically derived VLDL, characterised by the presence of apoB-100, and intestine-derived chylomicrons, which contain apoB-48. Both VLDL and chylomicrons share a common lipolytic pathway and are hydrolysed by lipoprotein lipase (LPL) and there are a number of described receptor-mediated pathways through which these particles may eventually be cleared from the circulation [12]. It is postulated that an excess production and/or a delay in clearance of postprandial lipoproteins of both TRL particles may be implicated in atherosclerosis [20, 21].

To the best of the author’s knowledge, this is the first study to compare the postprandial responses in obese PCOS women with that of obese control subjects. Although some

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**Table 6: Correlations between AUC-TG, AUC-HDL-chol, AUC-apoB-48, AUC-apoB, AUC-glucose, AUC-insulin, and other variables.**

|                      | AUC-TG*        | AUC-HDL-chol | AUC-apoB-48* | AUC-B          | AUC-glucose | AUC-insulin* |
|----------------------|---------------|-------------|--------------|----------------|-------------|--------------|
|                      | (mmol/L 8 hrs) | (mmol/L 8 hrs) | (μg/mL 8 hrs) | (g/dL 8 hrs) | (mmol/L 8 hrs) | (pmol/L 8 hrs) |
| AUC-TG* (mmol/L 8 hrs) | 1.000         | −0.540a     | 0.524a       | 0.484b         | 0.304a       | 0.542b        |
| AUC-HDL-chol (mmol/L 8 hrs) | −0.540b   | 1.000       | −0.229       | −0.225         | −0.309a      | −0.488b       |
| AUC-apoB-48* (μg/mL 8 hrs) | 0.524b      | −0.229      | 1.000        | 0.294a         | 0.171        | 0.165         |
| AUC-insulin (g/dL 8 hrs) | 0.484a       | −0.225      | 0.294a       | 1.000          | 0.038        | 0.206         |
| AUC-glucose (mmol/L 8 hrs) | 0.304a       | −0.309a     | 0.171        | 0.038          | 1.000        | 0.634b        |
| AUC-insulin (pmol/L 8 hrs) | 0.542b       | −0.488b     | 0.165        | 0.206          | 0.634b       | 1.000         |

**Age, PCOS status**

|                      | Age (years) | PCOS |
|----------------------|-------------|------|
|                      | 0.125       | 0.284a |
|                      | −0.010      | −0.284a |
|                      | −0.015      | 0.201 |
|                      | 0.134       | 0.057 |
|                      | 0.314       | 0.315b |
|                      | −0.014      | 0.125 |
|                      | −0.289b     | 0.158 |

**Androgens, SHBG**

|                      | T* (nmol/L) | SHBG* (nmol/L) | FAI* | Androstenedione (nmol/L) | DHEAS (μmol/L) |
|----------------------|-------------|----------------|------|--------------------------|---------------|
|                      | 0.133       | −0.163         | 0.115 | 0.015                   | 0.026         |
|                      | 0.133       | −0.350a        | 0.227 | −0.014                  | 0.108         |
|                      | 0.078       | −0.271         | 0.014 | −0.056                  | −0.289b       |
|                      | 0.078       | −0.456b        | 0.033 | 0.146                   | 0.125         |

**Anthropometrics**

|                      | Waist (cm) | Hip (cm) | Waist : Hip | Weight (kg) | BMI (kg/m²) | % Body fat mass (%) | % Body lean mass (%) | % Body water (%) |
|----------------------|------------|----------|-------------|-------------|-------------|---------------------|---------------------|-----------------|
|                      | 0.314a     | −0.483b  | 0.063       | 0.064       | 0.139       | 0.012               | 0.018               | −0.342a |
|                      | 0.216      | −0.285a  | 0.154       | 0.154       | 0.356c      | 0.092               | 0.092               | 0.661b |
|                      | 0.237      | −0.439b  | 0.163       | 0.047       | 0.193       | 0.030b              | 0.360a              | 0.609b |
|                      | 0.357a     | −0.378b  | 0.059       | 0.276       | 0.271       | 0.030a              | 0.364a              | 0.836b |
|                      | 0.316a     | −0.456b  | 0.033       | 0.184       | 0.414b      | 0.030a              | 0.453b              | 0.810b |
|                      | 0.378a     | −0.444b  | 0.009       | 0.164       | 0.368a      | 0.030a              | 0.381a              | 0.487b |

**IR, insulin sensitivity, and variables derived from the f3IVGTT**

|                      | HOMAIR* (μmol/L²) | S (×10⁻⁴ min⁻¹/mU/L)* | S (min⁻¹) | AIC (mU/L⁻¹·min)* | DI |
|----------------------|-------------------|------------------------|-----------|-------------------|----|
|                      | 0.568b            | −0.499b                | 0.130     | 0.229             | 0.366b |
|                      | 0.601b            | 0.454b                 | 0.223     | −0.262            | −0.433b |
|                      | −0.364a           | 0.159                  | −0.266    | −0.232            | −0.083 |
|                      | 0.029             | −0.090                 | −0.282    | 0.100             | −0.141b |
|                      | −0.364a           | 0.226                  | −0.328b   | −0.139            | −0.558b |

*a Correlations after log transformation.

b p < 0.05.  
**Correlations after log transformation.**
Postprandial studies in PCOS women have been done previously, this is the first one to evaluate the contribution of the two main metabolic/endocrine disturbances in PCOS women—IR and hyperandrogenaemia—to postprandial dyslipidaemia in obese women with PCOS. Both are implicated in accelerated atherosclerosis but the relative contribution of either is a subject of controversy [22–24]. Obesity, in particular central obesity, is strongly associated with insulin resistance, whilst androgens are also associated with an android distribution of fat. In a previous study by Velázquez M et al. a strong correlation between postprandial triglycerides and waist-to-hip ratio was demonstrated. That study evaluated overweight (BMI 27.41 ± 0.50 kg/m²) PCOS women and compared them to lean PCOS women and lean controls. Only free testosterone was measured, and there was no analysis between this and postprandial hypertriglyceridaemia [10]. A separate study by Bahcecici et al. evaluated postprandial responses to an oral fat tolerance test, in lean PCOS women with lean controls (BMI 23.5 ± 2.6 kg/m² versus 23.1 ± 4.0 kg/m²; p > 0.05). They showed that PCOS women had higher baseline insulin, HOMAIR, AUC-TG, AUC-total-cholesterol, AUC-VLDL-cholesterol, and AUC-apoB. Surprisingly, though, AUC-insulin did not differ between the two groups. Again, no analyses were reported between androgens and postprandial lipids [11].

In this study, comparing obese women with PCOS with obese control subjects, AUC-TG, AUC-HDL, AUC-glucose, and AUC-insulin were all significantly different. HDL-chol and insulin were different at most of the time points, but TG was only different at 2 hours. Independent predictors of AUC-TG included $S_I$, AUC-apoB-48, and AUC-apoB, accounting for 55% of the variance. This suggests that postprandial chylomicron particles have an important role to play in postprandial hypertriglyceridaemia, together with insulin sensitivity and apoB. On the other hand, AUC-TG was the only independent predictor of AUC-apoB-48, explaining 25.8% of the variance.

Following adjustment for BMI, lipid differences were no longer noted but insulin levels at all time points and AUC-insulin and iAUC-insulin were still much greater in PCOS women consistent with the fact that PCOS women are more insulin resistant than their BMI matched counterparts [25, 26]. In this study, IR was determined by the more convenient HOMAIR and insulin sensitivity was determined by the more sophisticated fsIVGTT derived $S_I$. When comparisons were made adjusting for HOMAIR, postprandial insulin was not significantly higher in the PCOS group. However, these differences were largely no longer present when adjustments were made for $S_I$, which may be a better marker for insulin sensitivity than HOMAIR, since the latter is calculated from fasting values of insulin and glucose.

There was only weak or no correlation between androgens and TG, HDL-chol, apoB-48, apoA-I, apoA-II, and apoB. There were very strong correlations between SHBG and TG, HDL-chol, AUC-apoB-48, AUC-apoB, and AUC-apoA-II. FAL but not testosterone per se also strongly correlated with HDL at all time points, TG at 0 and 2 hours, and both AUC-HDL-chol and AUC-TG. This suggests that IR, and perhaps obesity, both of which are strongly negatively correlated with SHBG, rather than androgens, may be the major determinant of postprandial lipids.

This study had certain limitations. PCOS women and the controls were not entirely matched for BMI. However, both groups were obese and results were analyzed with BMI as a covariate. The two groups did not match for IR as assessed by HOMAIR or $S_I$ as assessed by the fsIVGTT. However this is to be expected based on the well accepted notion that women with PCOS are more insulin resistant than BMI matched counterparts. In addition, after using HOMAIR and $S_I$ as covariates, results still revealed that hyperinsulinaemia and possibly a low SHBG level are the main factors influencing postprandial hypertriglyceridaemia. Postprandial chylomicrons also appear to play a significant role in postprandial hypertriglyceridaemia in premenopausal women with and without PCOS.

In conclusion, this study provides evidence that, in obese women with PCOS, IR plays a more important role than hyperandrogenaemia in postprandial dyslipidaemia and cardiovascular risk. Targeting obesity and thereby improving IR by lifestyle measures and perhaps the use of agents such as metformin should be a priority in the treatment of obese PCOS women.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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References

[1] M. A. Austin, “Epidemiology of hypertriglyceridemia and cardiovascular disease,” *The American Journal of Cardiology*, vol. 83, no. 9, pp. 13F–16F, 1999.

[2] J. E. Hokanson and M. A. Austin, “Plasma triglyceride level is a risk factor for cardiovascular disease independent of high-density lipoprotein cholesterol level: a meta-analysis of population-based prospective studies,” *Journal of Cardiovascular Risk*, vol. 3, no. 2, pp. 213–219, 1996.

[3] A. Fontbonne, E. Eschwege, F. Cambien et al., “Hypertriglyceridemia as a risk factor of coronary heart disease mortality in subjects with impaired glucose tolerance or diabetes. Results from the 11-year follow-up of the Paris Prospective Study,” *Diabetologia*, vol. 32, no. 5, pp. 300–304, 1989.

[4] L. E. Eberly, J. Stampler, and J. D. Neaton, “Relation of triglyceride levels, fasting and nonfasting, to fatal and nonfatal coronary heart disease,” *Archives of Internal Medicine*, vol. 163, no. 9, pp. 1077–1083, 2003.

[5] N. R. Phillips, D. Waters, and R. J. Havel, “Plasma lipoproteins and progression of coronary artery disease evaluated by angiography and clinical events,” *Circulation*, vol. 88, no. 6, pp. 2762–2770, 1993.

[6] J. Jeppesen, C. B. Hollenbeck, M.-Y. Zhou et al., “Relation between insulin resistance, hyperinsulinemia, postheparin plasma lipoprotein lipase activity, and postprandial lipemia,” *Arteriosclerosis, Thrombosis, and Vascular Biology*, vol. 15, no. 3, pp. 320–324, 1995.

[7] A. Harbis, C. Defoort, H. Narbonne et al., “Acute hyperinsulinism modulates plasma apolipoprotein B-48 triglyceride-rich lipoproteins in healthy subjects during the postprandial period,” *Diabetes*, vol. 50, no. 2, pp. 462–469, 2001.

[8] C. Couillard, N. Bergeron, A. Pascot et al., “Evidence for impaired lipolysis in abdominally obese men: postprandial study of apolipoprotein B-48- and B-100-containing lipoproteins,” *The American Journal of Clinical Nutrition*, vol. 76, no. 2, pp. 311–318, 2002.

[9] C. Couillard, N. Bergeron, D. Prud’homme et al., “Gender difference in postprandial lipemia: importance of visceral adipose tissue accumulation,” *Arteriosclerosis, Thrombosis, and Vascular Biology*, vol. 19, no. 10, pp. 2448–2455, 1999.

[10] E. Velázquez M, G. A. Bellabarba, S. Mendoza, and L. Sánchez, “Postprandial triglyceride response in patients with polycystic ovary syndrome: relationship with waist-to-hip ratio and insulin,” *Fertility and Sterility*, vol. 74, no. 6, pp. 1159–1163, 2000.

[11] M. Bahcici, M. Aydemir, and A. Tuzcu, “Effects of oral fat and glucose tolerance test on serum lipid profile, apolipoprotein, and CRP concentration, and insulin resistance in patients with polycystic ovary syndrome,” *Fertility and Sterility*, vol. 87, no. 6, pp. 1363–1368, 2007.

[12] R. W. Mahley and Z. S. Ji, “Remnant lipoprotein metabolism: key pathways involving cell-surface heparan sulfate proteoglycans and apolipoprotein E,” *The Journal of Lipid Research*, vol. 40, no. 1, pp. 1–16, 1999.

[13] A.-M. Lorec, C. Juhel, Y. Pafumi et al., “Determination of apolipoprotein B-48 in plasma by a competitive ELISA,” *Clinical Chemistry*, vol. 46, no. 10, pp. 1638–1642, 2000.

[14] N. Sakai, Y. Uchida, K. Ohashi et al., “Measurement of fasting serum apoB-48 levels in normolipidemic and hyperlipidemic subjects by ELISA,” *Journal of Lipid Research*, vol. 44, no. 6, pp. 1256–1262, 2003.

[15] J. K. Zawadzki and A. Dunai, “Diagnostic criteria for polycystic ovary syndrome: towards a rational approach,” in *Polycystic Ovary Syndrome*, A. Dunai, J. R. Givens, F. P. Haselton, and G. R. Merriam, Eds., pp. 377–384, Blackwell Scientific, Boston, Mass, USA, 1992.

[16] R. S. Legro, A. R. Kunselman, and A. Dunai, “Prevalence and predictors of dyslipidemia in women with polycystic ovary syndrome,” *The American Journal of Medicine*, vol. 113, no. 8, pp. 607–613, 2001.

[17] T. Apridonidze, P. A. Essah, M. J. Juorno, and J. E. Nestler, “Prevalence and characteristics of the metabolic syndrome in women with polycystic ovary syndrome,” *The Journal of Clinical Endocrinology & Metabolism*, vol. 90, no. 4, pp. 1929–1935, 2005.

[18] E. S. Ford, “The metabolic syndrome and mortality from cardiovascular disease and all-causes: findings from the National Health and Nutrition Examination Survey II Mortality study,” *Atherosclerosis*, vol. 173, no. 2, pp. 309–314, 2004.

[19] B. Isomaa, P. Almgren, T. Tuomi et al., “Cardiovascular morbidity and mortality associated with the metabolic syndrome,” *Diabetes Care*, vol. 24, no. 4, pp. 683–689, 2001.

[20] D. B. Zilversmit, “Atherosclerosis: a postprandial phenomenon,” *Circulation*, vol. 60, no. 3, pp. 473–485, 1979.

[21] P. H. E. Groot, W. A. H. J. Van Stiphout, X. H. Krauss et al., “Postprandial lipoprotein metabolism in normolipidemic men with and without coronary artery disease,” *Arteriosclerosis, Thrombosis, and Vascular Biology*, vol. 11, no. 3, pp. 653–662, 1991.

[22] A. Dunai, “Insulin resistance and the polycystic ovary syndrome: mechanism and implications for pathogenesis,” *Endocrine Reviews*, vol. 18, no. 6, pp. 774–800, 1997.

[23] L. C. Morin-Papunen, I. Vauhkonen, R. M. Koivunen, A. Ruokonen, and J. S. Tapanainen, “Insulin sensitivity, insulin secretion, and metabolic and hormonal parameters in healthy women and women with polycystic ovarian syndrome,” *Human Reproduction*, vol. 15, no. 6, pp. 1266–1274, 2000.

[24] A. D. Covelli, R. S. Legro, and A. Dunai, “Adolescent girls with polycystic ovary syndrome have an increased risk of the metabolic syndrome associated with increasing androgen levels independent of obesity and insulin resistance,” *The Journal of Clinical Endocrinology & Metabolism*, vol. 91, no. 2, pp. 492–497, 2006.

[25] A. Dunai, K. R. Segal, W. Futterweit, and A. Dobrjansky, “Profound peripheral insulin resistance, independent of obesity, in polycystic ovary syndrome,” *Diabetes*, vol. 38, no. 9, pp. 1165–1174, 1989.

[26] E. Carmina and R. A. Lobo, “Use of fasting blood to assess the prevalence of insulin resistance in women with polycystic ovary syndrome,” *Fertility and Sterility*, vol. 82, no. 3, pp. 661–665, 2004.