UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL
FACULDADE DE MEDICINA
PROGRAMA DE PÓS-GRADUAÇÃO EM CIÊNCIAS MÉDICAS: ENDOCRINOLOGIA

Scheila Karen Graff

Índice glicêmico e carga glicêmica da dieta de mulheres com a síndrome dos ovários policísticos: associações com variáveis metabólicas, antropométricas e de composição corporal

Porto Alegre, 2013

CIP - Catalogação na Publicação

Graff, Scheila Karen
Índice glicêmico e carga glicêmica da dieta de mulheres com a síndrome dos ovários policísticos: associações com variáveis metabólicas, antropométricas e de composição corporal / Scheila Karen Graff. -- 2013.
50 f.

Orientadora: Poli Mara Spritzer.

Dissertação (Mestrado) -- Universidade Federal do Rio Grande do Sul, Faculdade de Medicina, Programa de Pós-Graduação em Ciências Médicas: Endocrinologia, Porto Alegre, BR-RS, 2013.

1. Síndrome dos ovários policísticos. 2. Hiperandrogenismo. 3. Resistência insulínica. 4. Índice glicêmico. 5. Dieta. I. Spritzer, Poli Mara, orient. II. Título.

Elaborada pelo Sistema de Geração Automática de Ficha Catalográfica da UFRGS com os dados fornecidos pelo(a) autor(a).

Scheila Karen Graff

Índice glicêmico e carga glicêmica da dieta de mulheres com a síndrome dos ovários policísticos: associações com variáveis metabólicas, antropométricas e de composição corporal

Dissertação apresentada como requisito parcial para obtenção do título de mestre em Endocrinologia, à Universidade Federal do Rio Grande do Sul, Programa de Pós-Graduação em Ciências Médicas: Endocrinologia.

Orientadora: Prof[a] Dr[a] Poli Mara Spritzer

Porto Alegre, 2013

Agradecimentos

À minha orientadora, Profª Drª Poli Mara Spritzer, por seus ensinamentos e pela confiança que depositou em mim nos últimos 4 anos e meio.

Às colegas Bruna Cherrubini Alves e Fernanda Missio Mário, pelo apoio, amizade, compreensão e por tornarem os meus dias de trabalho mais alegres.

À Drª Denusa Wiltgen e Ramon Bossardi Ramos, colaboradores e amigos, pelo apoio e compreensão em diversos momentos.

Aos demais colegas da Unidade de Endocrinologia Ginecológica do Serviço de Endocrinologia do Hospital de Clínicas de Porto Alegre: Betânia Rodrigues dos Santos, Débora Martinho Morsch, Fabíola Satler, Fabrício Mattei, Fernanda do Amarante, Gislaine Casanova, Larissa Paixão, Lívia Paskulin, Marcela Metzdorf, Maria Augusta Maturana, Nathalia Cruz da Costa, Raquel Amaral Vieira, Sheila Lecke, Tássia Maciel, Thaís Mattuela Saraiva, Thaís Rasia da Silva, Vânia Andrade, Verônica Colpani, Vitor Fabris. Obrigada por proporcionarem um excelente ambiente de trabalho e pela amizade.

À Miriam Sant'Helena e Natália Goulart, sempre incansáveis em ajudar.

Aos meus pais, Gilberto e Íris Graff, o meu agradecimento pelo amor incondicional, me permitindo chegar até aqui.

Ao meu irmão, Luiz Henrique Graff, pela amizade e momentos de descontração.

Ao meu noivo, Frederico Birkholz, por estar sempre presente, mesmo que distante, e por me apoiar incondicionalmente nos momentos mais difíceis.

A todas as pessoas que, direta ou indiretamente, contribuíram para a execução desta dissertação de mestrado.

Esta dissertação de mestrado segue o modelo proposto pelo Programa de Pós-Graduação em Ciências Médicas: Endocrinologia, Faculdade de Medicina, Universidade Federal do Rio Grande do Sul, sendo apresentada na forma de uma revisão geral e um manuscrito sobre o tema da dissertação:

- Revisão: Síndrome dos ovários policísticos e índice glicêmico e carga glicêmica da dieta

- Artigo original: Dietary glycemic index is associated with less favorable anthropometric and metabolic profile in PCOS women with different phenotypes

SUMÁRIO

SÍNDROME DOS OVÁRIOS POLICÍSTICOS E ÍNDICE GLICÊMICO E CARGA GLICÊMICA DA DIETA

SÍNDROME DOS OVÁRIOS POLICÍSTICOS

A síndrome dos ovários policísticos (PCOS) é uma doença de apresentação clínica heterogênea cujas principais características clínicas são anovulação crônica e manifestações de hiperandrogenismo (THE ROTTERDAM ESHRE/ASRM-SPONSORED PCOS CONSENSUS WORKSHOP GROUP, 2004; APRIDONIDZE et al., 2005; AZZIZ et al., 2009). De acordo com o consenso de Rotterdam (THE ROTTERDAM ESHRE/ASRM-SPONSORED PCOS CONSENSUS WORKSHOP GROUP, 2004), a síndrome é definida pela presença de pelo menos dois dos seguintes critérios: oligo ou anovulação; hiperandrogenismo clínico e/ou bioquímico; presença de ovários policísticos ao ultrasom (12 ou mais folículos com 2 a 9 mm ou aumento do volume ovariano (>10cm³) em pelo menos um ovário). Ainda, devem ser excluídas outras patologias que apresentem hiperandrogenismo como: tumores secretores de androgênios, hiperplasia adrenal congênita, síndrome de cushing, hiperprolactinemia e alterações tireoidianas.

A determinação desses critérios levou ao reconhecimento de novos fenótipos da síndrome, além dos previamente descritos pelo National Institutes of Health (NIH), de 1990 (DUNAIF et al., 1992). Estes novos fenótipos incluem, por exemplo, mulheres hiperandrogênicas com ciclos menstruais ovulatórios ou mulheres com ciclos anovulatórios sem a presença de hiperandrogenismo. Usualmente, estes novos fenótipos apresentam formas mais brandas da síndrome em relação à forma “clássica” (mulheres anovulatórias e hiperandrogênicas), podendo diferir nos níveis de gonadotrofinas, secreção de hormônios esteróides, severidade da resistência à insulina, assim como no aumento do risco cardiovascular (RIZZO et al., 2009; BARBER et al., 2007; CARMINA et al., 2006; WILTGEN e SPRITZER, 2010; DI DOMENICO et al., 2012).

Estudos realizados em vários países estimam que de 5-10% das mulheres em idade reprodutiva apresentam esta síndrome (ASUNCION, 2000; AZZIZ et al., 2004a), o que a torna de grande importância clínica, em razão de sua prevalência ser semelhante à de doenças de grande impacto na saúde pública. Além dos distúrbios reprodutivos, as pacientes com PCOS apresentam frequentemente, alterações metabólicas que incluem resistência insulínica

(RI), obesidade e dislipidemia (DUNAIF et al., 1989; NORMAL et al., 2004; SPRITZER e WILTGEN, 2007; SATHYAPALAN e ATKIN, 2012).

O hiperandrogenismo, frequentemente presente nas mulheres com PCOS, está associado às alterações clínicas e metabólicas, em especial à RI, encontradas nestas pacientes, principalmente na forma "clássica" da doença (MORAN e TEEDE, 2009; DE ZEGHER e IBÁÑEZ, 2006; DOKRAS et al., 2006). A resistência à insulina (RI) tem sido documentada como uma característica altamente prevalente da doença há quase 30 anos e é vista em ambas as pacientes obesas e eutróficas. Tem sido teorizado que a resistência à insulina e a consequente hiperinsulinemia compensatória desempenham um papel inicial e central na patogênese das disfunções ovarianas e reprodutiva da PCOS (EHRMANN, 2005; STOVALL et al., 2011; LEGRO et al., 1999; NESTLER, 1997; DIAMANTI-KANDARAKIS et al., 2012).

A associação entre PCOS e diabetes mellitus tipo 2 (DM2) tem sido demonstrada em diversos estudos, inclusive pela International Diabetes Federation (IDF) (NORMAN et al., 2001). Em recente metanálise, a PCOS foi associada a um risco 2,5 e 4,5 vezes para intolerância à glicose e DM2, respectivamente, em relação a mulheres saudáveis (MORAN e TEEDE, 2009), agravado por presença concomitante de obesidade, diabetes gestacional e história familiar de DM2.

A obesidade e o sobrepeso são altamente prevalentes na população com PCOS, atingindo cerca de 60% destas mulheres, na sua grande maioria com padrão de distribuição central (NORMAN et al., 2004; MORAN, 2008; AZZIZ, 2004b). A presença de obesidade pode exacerbar as alterações metabólicas e reprodutivas associadas à síndrome (DUNAIF, 1999). O hiperandrogenismo está associado ao acúmulo de gordura nas porções superiores do corpo, independente do IMC, chamada distribuição de gordura andróide (TOSCANI et al., 2007). Este tipo de obesidade está associado à hiperinsulinemia, tolerância diminuída à glicose e DM2 (CALDERON-MARGALIT et al., 2010). Além disso, já é bem estabelecido que a obesidade está associada a uma maior incidência de anovulação, aborto espontâneo e complicações gestacionais (pré-eclâmpsia e diabetes gestacional). Estudos têm demonstrado que mulheres obesas com PCOS após diminuição de 5% do peso corporal apresentam uma maior taxa de ovulação e gestação espontânea (MOTTA, 2012).

A PCOS tem sido associada a uma alta prevalência de dislipidemia, que pode estar presente em até 70% dessas mulheres. Estudos têm demonstrado que mulheres com PCOS apresentam maiores níveis de TG e LDL-colesterol e menores níveis de HDL-colesterol

comparadas a mulheres controles, independentemente do índice de massa corporal (IMC) (WILD et al., 2011; SATHYAPALAN e ATKIN, 2012).

Evidências indicam que mulheres com PCOS apresentam elevação da pressão arterial sistêmica em relação a mulheres sem a síndrome, com maior risco de evolução precoce para hipertensão (FARRELL e ANTONI, 2010; LUQUE-RAMÍREZ et al., 2007; CHEN et al., 2007; LECKE et al., 2011).

ÍNDICE GLICÊMICO E CARGA GLICÊMICA

Os carboidratos variam em sua capacidade de aumentar os níveis circulantes de glicose e insulina pós-prandiais. O índice glicêmico (IG), proposto por Jenkins et al. (1981), é um parâmetro utilizado para classificar os alimentos contendo carboidratos de acordo com a resposta glicêmica que os mesmos promovem, em relação à resposta observada após consumo de um alimento de referência (pão branco ou glicose). O IG é, portanto, uma medida da qualidade do carboidrato ingerido.

Posteriormente, em 1997, foi introduzido o conceito de carga glicêmica, por pesquisadores da Universidade de Harward, que é uma medida que incorpora não só a qualidade como também a quantidade dos carboidratos da dieta. É o produto do IG de um alimento e do teor de carboidratos disponíveis nele (SALMERON et al. 1997a; SALMERON et al. 1997b; LIU et al., 2000).

Tem sido sugerido que o consumo habitual de alimentos ricos em carboidratos, que promovem uma resposta glicêmica alta, pode aumentar o risco de obesidade (BRAND-MILLER et al., 2002; LUDWIG, 2002; LIVESEY, 2005). Uma meta-análise de ensaios clínicos mostrou que dietas de baixo IG e CG reduzem o IMC e a massa de gordura corporal mais do que dietas de alto IG ou CG. Foram vista reduções de 1,3 kg/m² no IMC (-2,0 a -0,5) e de 1,1 kg na massa gorda total (-1,9 a -0,4) (THOMAS, ELLIOTT e BAUR, 2007).

Um dos mecanismos propostos para a relação entre qualidade glicêmica da dieta e obesidade envolve a saciedade prolongada e conseqüente diminuição do consumo de energia a partir de dietas de baixo IG (PEREIRA, 2006). As propriedades das fibras solúveis presentes em cereais integrais e leguminosas, de formação de gel viscoso atenuam o aumento da glicose e níveis de insulina no sangue. Alimentos ricos em fibras solúveis viscosas têm um baixo índice glicêmico devido à sua capacidade de expandir e promover uma digestão

prolongada aumentando a saciedade (JENKINS et al., 2000; RIZKALLA, BELLISLE e SLAMA, 2002). Dessa maneira, um menor consumo de energia pode ser um fator causal da relação inversa entre obesidade e dietas de baixo IG (PEREIRA, 2006).

Recentemente Dong et al. (2012) mostraram que dietas de baixo IG e/ou baixa CG exercem, em mulheres adultas, um efeito protetor contra doenças cardiovasculares. O risco relativo para doenças cardiovasculares de dietas de alta CG foi de 1,69 (1,32 a 2,16) e de dietas de alto IG de 1,26 (1,12 a 1,43). Essa associação entre dietas de alto IG e CG e doenças cardiovasculares provavelmente é devida aos efeitos adversos dessas dietas nos níveis de lipídeos do sangue. Alguns estudos têm observado que as dietas com alto IG ou CG levam a um aumento dos triglicerídeos (SHIKANY et al., 2010; PEREIRA et al., 2004), do o LDL-colesterol (SHIKANY et al., 2010; THOMAS, ELLIOTT e BAUR, 2007; MCMILLAN-PRICE et al., 2006) e do colesterol total (THOMAS, ELLIOTT e BAUR, 2007) e reduzem o HDL-colesterol (SLYPER et al., 2005; FORD e LIU, 2001; AMANO et al., 2004), além de causar inflamação sistêmica (LEVITAN et al., 2008).

Até o momento, existem poucos estudos abordando as relações entre IG e distribuição da gordura corporal. Segundo Ludwig et al. (1999), a ingestão de alimentos de baixo IG pode diminuir a secreção de hormônios contra-regulatórios proteolíticos como o cortisol, hormônio do crescimento e glucagon, estimulando a síntese protéica. Bouché et al. (2002) referem que a regulação da massa de gordura corporal associada à ingestão de dietas de baixo IG pode estar relacionada à ativação de genes como o *ob*. Argumenta-se que a ingestão de tais dietas parece diminuir a expressão desses genes, diminuindo a secreção insulínica pós-prandial. Por esse motivo, observou-se que a ingestão de alimentos de baixo IG tende a aumentar o teor de massa magra e a diminuir, significativamente, o teor de massa gordurosa corporal.

Tem sido proposto que o consumo por tempo prolongado de alimentos de alto IG aumenta a demanda de insulina. Uma hiperinsulinemia crônica desempenha um papel crítico no desenvolvimento de resistência insulínica, prejudicando a função celular pancreática e, eventualmente, levando ao DM2 (NOAKES et al., 2006; SCHULZE et al., 2004).

No entanto, estudos de IG e CG da dieta em relação à resistência à insulina e o risco de DM2 têm tido resultados controversos. No estudo de Mckeown et al. (2004), ambos IG e CG da dieta foram correlacionados positivamente com resistência à insulina; Pereira et al. (2004) verificaram que dieta de baixa carga glicêmica melhorou mais o perfil de resistência à insulina em relação à dieta com restrição de lipídeos; Rizkalla et al. (2004) relataram que dieta de baixo IG induziu menores valores de glicose plasmática pós-prandial e melhores perfis insulinêmicos. Entretanto, nos estudos de Liese et al. (2005) e Lau et al. (2005) não

foram encontradas associações entre IG e CG e resistência à insulina. Uma recente meta-análise de Dong et al. (2011) concluiu que existem evidências para apoiar associações positivas entre dietas de alto IG e CG e risco de DM2. Este estudo demonstrou um risco relativo para DM2 de 1,16 (1,06 a 1,26) quando comparadas as categorias de maior IG contra a de menor IG, já para a CG o RR para DM2 foi de 1,20 (1,11 a 1,30).

A maioria das organizações internacionais de diabetes defendem o uso de dietas de baixo IG na prevenção e no tratamento da diabetes (FOSTER-POWELL, HOLT e BRAND-MILLER, 2002), mas a American Diabetes Association (ADA) não subscreve inteiramente o uso do IG, pois considera as evidências atuais insuficientes para sustentar uma relação entre IG ou CG da dieta e o desenvolvimento de diabetes (SHEARD et al., 2004; BANTLE et al., 2006).

ÍNDICE GLICÊMICO, CARGA GLICÊMICA e PCOS

Os benefícios da perda de peso em mulheres com PCOS já são bem documentados (HOEGER, 2007), porém uma dieta ideal ainda não foi estabelecida. Tem sido sugerido que reduzindo as concentrações de insulina pós-prandiais pode-se aumentar a oxidação de gordura por muitas horas após a refeição e, assim, reduzir a fome, o excesso de consumo alimentar e o ganho de peso (LUDWIG, 2002). Dessa forma, visto que a maioria das mulheres com PCOS apresentam uma hiperinsulinemia compensatória após a ingestão de carboidratos, pode haver vantagens no consumo de dietas de baixa CG neste grupo de pacientes (MARSH et al., 2010).

Apesar disso, ainda existem poucos estudos na literatura abordando o IG e a CG da dieta em relação à PCOS. Herriot, Whitcroft e Jeanes (2008) concluíram em seu estudo retrospectivo com 88 mulheres com PCOS que uma dieta de baixa CG combinada com medicamentos pode contribuir para uma melhoria no alívio dos sintomas dessas pacientes, como hipoglicemia, além de reduzir IMC e circunferência da cintura. Da mesma forma, Marsh et al. (2010) referem que o uso de uma dieta de baixo IG traz benefícios às mulheres com PCOS. Foram verificadas melhoras na regularidade do ciclo menstrual e na sensibilidade à insulina após 12 meses de dieta, entretanto, não foram encontradas diferenças na composição corporal e no perfil hormonal e metabólico entre as mulheres com dieta normal (20 pacientes) e de baixo IG (29 pacientes).

Barr et al. (2010a) se propuseram a avaliar a eficácia de uma dieta de baixo IG em mulheres com PCOS e sobrepeso, mantendo as calorias consumidas normalmente pelas pacientes, por um período de 12 semanas. Apesar de somente 21 pacientes terem concluído o estudo, foram demonstradas melhorias na sensibilidade à insulina das pacientes independentemente da perda de peso.

Da mesma forma, Mehrabani et al. (2012) verificaram que o tratamento por 12 semanas com uma dieta hipocalórica com a combinação de alto teor de proteína e baixa carga glicêmica causou um aumento significativo na sensibilidade à insulina em mulheres com PCOS (n=60) quando comparada com uma dieta hipocalórica convencional.

Um número ainda mais escasso de estudos se propuseram a avaliar diferenças entre mulheres com PCOS e controles no que diz respeito ao IG e CG da dieta habitual. Um estudo de Douglas et al. (2006) que se propôs a avaliar diferenças no consumo alimentar entre mulheres com e sem PCOS verificou que não houve diferença na quantidade total consumida de alimentos de elevado IG entre mulheres com e sem PCOS pareadas por idade, raça e IMC, entretanto, as mulheres com PCOS consumiram uma maior quantidade de alguns alimentos específicos com maior IG, como pão branco. Este estudo utilizou como método de investigação do consumo alimentar um questionário sobre a alimentação de múltipla escolha e um recordatório alimentar de 4 dias e teve como limitação um tamanho pequeno de amostra (30 mulheres com PCOS e 27 controles). Barr et al. (2010b) objetivaram descrever a dieta habitual de mulheres com PCOS (38 pacientes) comparando com a dieta de mulheres controles sem PCOS (28 pacientes) através de um diário alimentar de 7 dias e verificaram não haver diferenças no IG e CG da dieta entre os grupos. Recentemente, Altieri et al. (2013) realizaram estudo com objetivo de investigar os hábitos alimentares de mulheres com PCOS (100 pacientes) e controles (100 pacientes) através de diários alimentares de 7 dias. Os grupos não diferiram em termos de consumo calórico e de macronutrientes e, em relação ao IG, foi demonstrada apenas uma tendência das mulheres com PCOS de consumirem uma maior quantidade de carboidratos de alto IG. Barr et al. (2011), ao comparar mulheres com PCOS com obesidade a mulheres com PCOS eutróficas, verificou que as mulheres obesas consumiram dietas de maior IG.

Considerando que a síndrome dos ovários policísticos, além dos distúrbios reprodutivos, é caracterizada por distúrbios metabólicos, incluindo resistência à insulina, obesidade e dislipidemia, e que o consumo habitual de alimentos com alto IG e CG pode aumentar o risco para estes distúrbios metabólicos, mulheres com PCOS que tenham por hábito consumir este tipo de dieta podem ter prejuízos à saude. Portanto, sendo os estudos

nessa área escassos e incosistentes, há necessidade de mais estudos que avaliem o IG e CG da dieta habitual de mulheres com PCOS e sua relação com perfil antropométrico e metabólico.

REFERÊNCIAS BIBLIOGRÁFICAS

ALTIERI, P. et al. Dietary habits and their relationship with hormones and metabolism in overweight and obese women with polycystic ovary syndrome. **Clinical Endocrinology.** 78: 52–59, 2013.

AMANO, Y. et al. “Correlation between dietary glycemic index and cardiovascular disease risk factors among Japanese women,” **European Journal of Clinical Nutrition.** 58(11): 1472–1478, 2004.

APRIDONIDZE, T. et al. Prevalence and characteristics of the metabolic syndrome in women with polycystic ovary syndrome. **J Clin Endocrinol Metab.** 90(4): 1929-35, 2005.

ASUNCION, M. et al. A prospective study of the prevalence of the polycystic ovary syndrome in unselected Caucasian women from Spain. **J Clin Endocrinol Meta**b. 85: 2434–2438, 2000.

AZZIZ, R. et al. Task Force on the Phenotype of the Polycystic Ovary Syndrome of The Androgen Excess and PS**.** The Androgen Excess and PCOS Society criteria for the polycystic ovary syndrome: the complete task force report. **Fertil Steril.** 91: 456-488, 2009.

AZZIZ, R. et al. The prevalence and features of the polycystic ovary syndrome in an unselected population. **J Clin Endocrinol Metab.** 89: 2745-9, 2004a.

AZZIZ, R. et al. Androgen Excess in Women: Experience with Over 1000 Consecutive Patients. **The Journal of Clinical Endocrinology & Metabolism.** 89(2): 453– 462, 2004b.

BANTLE, J.P. et al. Nutrition recommendations and interventions for diabetes—2006: a position statement of the American Diabetes Association. **Diabetes Care.** 29(9): 2140–57, 2006.

BARBER, T.M. et al. Metabolic characteristics of women with polycystic ovary syndrome and oligo-amenorrhea but normal androgen levels: implication for the management of polycystic ovary syndrome. **Clin Endocrinol (Oxf).** 66: 513-517, 2007.

BARR, S. et al. Dietary glycaemic index, glycaemic load and insulin resistance in lean and overweight women with polycystic ovary syndrome and controls. **Proceedings of the Nutrition Society.** 69 (OCE1), E126, 2010b.

BARR, S. et al. Efficacy of a low-glycaemic index diet in women with polycystic ovary syndrome. **Proceedings of the Nutrition Society.** 69 (OCE6), E404, 2010a.

BARR, S. et al. Habitual dietary intake, eating pattern and physical activity of women with polycystic ovary syndrome. **Eur J Clin Nutr.** 65(10): 1126-32, 2011.

BOUCHÉ, C. et al. Five-week, low-glycemic index diet decreases total fat mass and improves plasma lipid profile in moderately overweight nondiabetic men. **Diabetes Care.** 25: 822-8, 2002.

BRAND-MILLER, J.C. et al. Glycemic index and obesity. **Am J Clin Nut**r. 76(suppl): 281S–5S, 2002.

CALDERON-MARGALIT, R. et al. Prospective Association of Serum Androgens and SHBG with subclinical cardiovascular disease in Young adult women: The "coronary artery risk development in young adults" Women's Study. **JCEM.** 95: 4424-4431, 2010.

CARMINA, E. The spectrum of androgen excess disorders. **Fertil Steril.** 85: 1582-85, 2006.

CHEN, M-J. et al. Relationship between androgen levels and blood pressure in young women with Polycystic Ovary Syndrome. **Hypertension.** 49: 1442-1447, 2007.

DE ZEGHER, F.; IBÁÑEZ, L. Prenatal growth restraint followed by catch-up of weigth: a hiperinsulinemic pathway to polycystic ovary syndrome. **Fertil Steril.** 86 Suppl 1:S4-5, 2006.

DIAMANTI-KANDARAKIS, E. et al. Insulin resistance and Polycystic Ovary Syndrome through life. **Current Pharmaceutical Design (Print)**, v. 18, p. 5569-5576, 2012.

DI DOMENICO, K. et al. Cardiac autonomic modulation in polycystic ovary syndrome: does the phenotype matter? **Fertility and Sterility.** v. 99, p. 286-292, 2012.

DOKRAS, A. et al. Obesity and insulin resistance but not hiperandrogenism mediates vascular dysfunction in women with polycystic ovary syndrome. **Fertil Steril.** 86(6): 1702-9, 2006.

DONG, J.-Y. et al. Dietary glycaemic index and glycaemic load in relation to the risk of type 2 diabetes: a meta-analysis of prospective cohort studies. **British Journal of Nutrition.** p. 1-6, 2011.

DONG, J.-Y. et al. Meta-Analysis of Dietary Glycemic Load and Glycemic Index in Relation to Risk of Coronary Heart Disease **Am J Cardiol.** 109: 1608 –1613, 2012.

DOUGLAS, C. et al. Difference in dietary intake between women with polycystic ovary syndrome and healthy controls. **Fertil Steril.** 86(2): 411– 7, 2006.

DUNAIF, A. Insulin action in the polycystic ovary syndrome. **Endocrinol Met Clin North Am.** 28: 341– 59, 1999.

DUNAIF, A. et al. Diagnostic criteria for polycystic ovary syndrome: towards a rational approach. Polycystic ovary syndrome. Boston: **Blackwell Scientific.** 377-84, 1992.

DUNAIF, A. et al. Profound peripheral insulin resistance, independent of obesity, in polycystic ovary syndrome. **Diabetes.** 38: 1165-1174, 1989.

EHRMANN, D.A. Polycystic ovary syndrome. **N Engl J Med**. 352:1223, 2005.

FARRELL, K; ANTONI, M. Insulin Resistance, Obesity, Inflammation, and Depression in Polycystic Ovary Syndrome: Biobehavioral Mechanisms and Interventions. **Fertil Steril.** 2010, 94(5): 1565–1574.

FORD, E.S.; LIU, S. "Glycemic index and serum high-density lipoprotein cholesterol concentration among US adults," **Archives of Internal Medicine.** 161(4): 572–576, 2001.

FOSTER-POWELL, K.; HOLT, S.H.; BRAND-MILLER, J.C. International Tables of Glycemic Index and Glycemic Load Values: 2008. **Am J Clin Nutr.** 76(1): 5-56, 2002.

HERRIOT, A.M.; WHITCROFT, S.; JEANES, Y. An retrospective audit of patients with polycystic ovary syndrome: the effects of a reduced glycaemic load diet. **J Hum Nutr Diet.** 21: 337–345, 2008.

HOEGER, K.M. Obesity and lifestyle management in polycystic ovary syndrome. **Clin Obstet Gynecol.** 50: 277–94, 2007.

JENKINS, D.J. et al. Glycemic index of foods: a physiological basis for carbohydrate exchange. **Am J Clin Nutr**. 34(3): 362-366, 1981.

JENKINS, D.J. et al. Viscous and nonviscous fibres, nonabsorbable and low glycaemic index carbohydrates, blood lipids and coronary heart disease. **Curr Opin Lipidol.** 11: 49–56, 2000.

LAU, C. et al. Dietary glycemic index, glycemic load, fiber, simple sugars, and insulin resistance: the Inter99 study. **Diabetes Care.** 28(6): 1397– 403, 2005.

LECKE, S.B.; MORSCH, D.M.; SPRITZER, P.M. Leptin and adiponectin in the female life course. **Brazilian journal of medical and biological research -on line.** v. 44, p. 381-387, 2011.

LEGRO, R.S. et al. Prevalence and predictors of risk for type 2 diabetes mellitus and impared glucose tolerance in polycystic ovary syndrome: a prospective, controlled study in 254 affected women. **JCEM.** 84(1): 165-69, 1999.

LEVITAN, E.B. et al., “Dietary glycemic index, dietary glycemic load, blood lipids, and Creactive protein,” **Metabolism.** 57(3): 437–443, 2008.

LIESE, A.D. et al. Dietary glycemic index and glycemic load, carbohydrate and fiber intake, and measures of insulin sensitivity, secretion, and adiposity in the Insulin Resistance Atherosclerosis Study. **Diabetes Care.** 28: 2832–8, 2005.

LIU, S. et al. A prospective study of dietary glycemic load, carbohydrate intake, and risk of coronary heart disease in US women. **Am J Clin Nutr.** 71: 1455–61, 2000.

LIVESEY, G. Low-glycaemic diets and health: implications for obesity. **Proc Nutr Soc.** 64: 105–13, 2005.

LUDWIG, D.S. et al. High glycemic index foods, overeating, and obesity. **Pediatrics.** 103(3): E26, 1999.

LUDWIG, D.S. The glycemic index. Physiological mechanisms relating to obesity, diabetes and cardiovascular disease. **JAMA.** 287: 2414–23, 2002.

LUQUE-RAMIRÉZ, M. et al. Obesity is the major determinant of the abnormalities in blood pressure found in young women with the polycystic ovary syndrome. **JCEM.** 92(6): 2141-8, 2007.

MARSH, K.A. et al. Effect of a low glycemic index compared with a conventional healthy diet on polycystic ovary syndrome. **Am J Clin Nutr.** 92: 83–92, 2010.

MCKEOWN, N.M. et al. Carbohydrate nutrition, insulin resistance, and the prevalence of the metabolic syndrome in the Framingham Offspring Cohort. **Diabetes Care.** 27(2): 538–46, 2004.

MCMILLAN-PRICE, J. et al. Comparison of 4 diets of varying glycemic load on weight loss and cardiovascular risk reduction in overweight and obese young adults: a randomized controlled trial. **Arch Intern Med.** 166(14): 1466-75, 2006.

MEHRABANI, H.H. et al. Beneficial effects of a high-protein, low-glycemic-load hypocaloric diet in overweight and obese women with polycystic ovary syndrome: a randomized controlled intervention study. **J Am Coll Nutr.** 31(2): 117-25, 2012.

MORAN, C. et al. Obesity differentially affects serum levels of androstenedione and testosterone in polycystic ovary syndrome. **Fertil Steril.** 90(6): 2310–7, 2008.

MORAN, L.; TEEDE, H. Metabolic features of the reproductive phenotypes of polycystic ovary syndrome. **Hum Reprod Update.** 15(4): 477-88, 2009.

MOTTA, A.B. The Role of Obesity in the Development of Polycystic Ovary Syndrome. **Curr Pharm Des.** 18(17): 2482-91, 2012.

NESTLER, J.E. Role of hiperinsulinemia in the pathogenesis of polycystic ovary syndrome, and its clinical implications. **Seminars in Reprodutive Endocrinology.** 15(2): 111-22, 1997.

NOAKES, M. et al. Comparison of isocaloric very low carbohydrate/high saturated fat and high carbohydrate/ low saturated fat diets on body composition and cardiovascular risk. **Nutr Metab.** 3: 7, 2006.

NORMAN, R.J. et al. Polycystic ovary syndrome. **Med J Aust.** 80: 132-137, 2004.

NORMAN, R.J. et al. Relative risk of conversion from normoglycaemic to impaired glucose tolerance or non-insulin dependent diabetes mellitus in polycystic ovary syndrome. **Hum Reprod.** 16: 1995-98, 2001.

PEREIRA, M.A et al. Effects of a low-glycemic load diet on resting energy expenditure and heart disease risk factors during weight loss. **JAMA.** 292(20): 2482-90, 2004.

PEREIRA, M.A. Weighing in on glycemic index and body weight. **Am J Clin Nutr.** 84: 677–9, 2006.

RIZKALLA, S.W. et al. Improved plasma glucose control, whole-body glucose utilization, and lipid profile on a low-glycemic index diet in type 2 diabetic men: a randomized controlled trial. **Diabetes Care.** 27: 1866–1872, 2004.

RIZKALLA, S.W.; BELLISLE, F.; SLAMA, G. Health benefits of low glycaemic index foods, such as pulses, in diabetic patients and healthy individuals**. Br J Nutr.** 88(Suppl 3): S255–262, 2002.

RIZZO, M. et al. Milder forms of atherogenic dyslipidemia in ovulatory versus anovulatory polycystic ovary syndrome phenotype. **Human Reproduction.** 24 (9): 2286-92, 2009.

SALMERON, J. et al. Dietary fiber, glycemic load, and risk of NIDDM in men. **Diabetes Care.** 20: 545–50, 1997a.

SALMERON, J. et al. Dietary fiber, glycemic load, and risk of non-insulin-dependent diabetes mellitus in women. **JAMA.** 277: 472–7, 1997b.

SATHYAPALAN, T.; ATKIN, S.L. Recent advances in cardiovascular aspects of polycystic ovary syndrome. **Eur J Endocrinol.** 166(4): 575-83, 2012.

SCHULZE, M.B. et al. Glycemic index, glycemic load, and dietary fiber intake and incidence of type 2 diabetes in younger and middle-aged women. **Am J Clin Nutr.** 80(2): 348–56, 2004.

SHEARD, N.F. et al. Dietary carbohydrate (amount and type) in the prevention and management of diabetes: a statement by the American Diabetes Association. **Diabetes Care.** 27(9): 2266 –71, 2004.

SHIKANY, J.M. et al. Association of glycemic load with cardiovascular disease risk factors: The Women's Health Initiative Observational Study. **Nutrition.** 26(6): 641-647, 2010.

SLYPER, A. et al. Influence of glycemic load on HDL cholesterol in youth. **Am J Clin Nutr.** 81: 376–9, 2005.

SPRITZER, P.; WILTGEN, D. Prevalência de Síndrome Metabólica em pacientes sul-brasileiras com Síndrome dos Ovários Policísticos. **Arquivos Brasileiros de Endocrinologia & Metabologia.** v. 51, p. 146-147, 2007.

STOVALL, D.W. et al. Assessment of insulin resistance and impared glucose tolerance in lean women with polycystic ovary syndrome. **J Womens Health (Larchmt).** 20(1): 27-43, 2011.

THE ROTTERDAM ESHRE/ASRM-SPONSORED PCOS CONSENSUS WORKSHOP GROUP. **Fertil and Steril.** 81(1): 19-24, 2004.

THOMAS, D.E.; ELLIOTT, E.J.; BAUR, L. Low glycaemic index or low glycaemic load diets for overweight and obesity. **Cochrane Database of Systematic Reviews.** CD005105, 2007.

TOSCANI, M. et al. Estimation of truncal adiposity using waist circumference or the sum of trunk skinfolds: a pilot study for insulin resistance screening in hirsute patients with or without polycystic ovary syndrome. **Metabolism.** 56(7): 992–7, 2007.

WILD, R.A. et al. Lipid levels in polycystic ovary syndrome: systematic review and meta-analysis. **Fertil Steril.** 95: 1073–79, 2011.

WILTGEN, D.; SPRITZER, P.M. Variation in metabolic and cardiovascular risk in women with different polycystic ovary syndrome phenotypes. **Fertility and Sterility.** v. 94, p. 2493-2496, 2010.

Dietary glycemic index is associated with less favorable anthropometric and metabolic profile in PCOS women with different phenotypes

Scheila Karen Graff, B.Sc.,[a] Fernanda Missio Mário, B.Sc.,[a] Bruna Cherubini Alves, B.Sc.,[a] and Poli Mara Spritzer, M.D., Ph.D.,[a,b,c*]

[a]Gynecologic Endocrinology Unit, Division of Endocrinology, Hospital de Clínicas de Porto Alegre (HCPA), Porto Alegre, Brazil; [b]Laboratory of Molecular Endocrinology, Department of Physiology, Universidade Federal do Rio Grande do Sul (UFRGS), Porto Alegre, Brazil; and-[c]National Institute of Hormones and Women's Health, Porto Alegre, Brazil.

***Corresponding author:**

Poli Mara Spritzer

Division of Endocrinology, Hospital de Clínicas de Porto Alegre

Rua Ramiro Barcelos, 2350

Porto Alegre, RS, Brazil

90035-003

Phone: +55 51 3359 8027 / Fax: +55 51 3359 8777

E-mail: spritzer@ufrgs.br

The authors declare no conflicts of interest.

Financial support:

This work was supported by grants from Conselho Nacional de Desenvolvimento Científico e Tecnológico [CNPq INCT 573747/2008-3] and Fundo de Apoio à Pesquisa do Hospital de Clínicas de Porto Alegre [FIPE-HCPA 11-0316], Brazil.

Capsule

Dietary glycemic index is increased in PCOS patients, especially in the classic PCOS phenotype. Increased dietary glycemic index is associated with a less favorable anthropometric and metabolic profile in PCOS.

ABSTRACT

Objective: To compare glycemic index and load (GI and GL) in the usual diet of PCOS and control women and to investigate whether dietary GI and GL are associated with body composition and anthropometric and metabolic variables across PCOS phenotypes.

Design: Cross-sectional study.

Setting: University hospital outpatient clinic.

Patients: 61 women with PCOS and 44 non-hirsute women with ovulatory cycles.

Interventions: Metabolic work-up, biochemical and hormonal assays, assessment of body composition and rest metabolic rate, physical activity (pedometer), and food consumption (food frequency questionnaire).

Main outcome measure(s): GI and GL.

Results: Mean age was 23.7±6.3 years. The prevalence of obesity was 44.3% in PCOS women and 31.8% in controls. Median GI for the group was 58. PCOS patients with GI>58 had higher BMI, worse metabolic profile, and lower intake of fibers. GI was correlated with BMI in controls and with lipid accumulation product (LAP) in the PCOS group, and was higher in classic PCOS vs. other groups.

Conclusions: Dietary GI is increased in PCOS patients, especially in the classic PCOS phenotype. Increased dietary GI is associated with a less favorable anthropometric and metabolic profile in PCOS.

Key words: Diet; insulin resistance; hyperandrogenism; glycemic index; polycystic ovary syndrome.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a complex heterogeneous condition that affects 5-10% of women of reproductive age and is primarily characterized by ovulatory dysfunction and hyperandrogenism (1, 2). Obesity is a prevalent characteristic of PCOS, found in 30 to 70% of these women, depending on the population studied (3, 4). The presence of obesity may exacerbate the metabolic and reproductive disorders associated with the syndrome (5), including insulin resistance and dyslipidemia (6-9). A meta-analysis (10) has shown that women with PCOS have higher levels of triglycerides (TG), LDL-cholesterol and total cholesterol (TC) and lower HDL-cholesterol levels compared to control women, regardless of body mass index (BMI).

It has been suggested that regular consumption of carbohydrate-rich foods, which promote a high glycemic response, increasing glucose and insulin levels (11-13), enhances the risk of obesity (14, 15). A meta-analysis of clinical trials has shown that diets based on foods with low glycemic response (or low glycemic index, GI) and low carbohydrate content (low glycemic load, GL) are more effective at reducing BMI and body fat mass than control diets (16). A recent study showed that low GI and/or GL diets exert a protective effect against cardiovascular disease in adult women (17). One possible explanation for the association between high dietary GI and GL and cardiovascular disease is the adverse effects of these diets on blood lipid levels. Some studies have found that high GI or GL diets lead to an increase in triglycerides (18) and LDL-cholesterol (18, 19) and to a reduction in HDL-cholesterol (20, 21), in addition to causing systemic inflammation (22).

Furthermore, it has been proposed that the prolonged consumption of high GI foods plays a critical role in the development of insulin resistance, eventually leading to type 2 diabetes (23). However, the few studies analyzing the association between reproductive or

metabolic disturbances in PCOS and dietary GI and GL in women with PCOS have produced inconsistent results.

Therefore, the aims of this study were to compare GI and GL in the usual diet of PCOS and control women and to investigate whether dietary GI and GL are associated with body composition as well as with anthropometric and metabolic variables in PCOS women with different phenotypes.

MATERIAL AND METHODS

Participants

This cross-sectional study was carried out with women aged 14 to 35 years, recruited not earlier than two years after menarche, between 2009 and 2012. We enrolled volunteers with hirsutism and irregular menses or with hirsutism and regular menses (in order to select both the ovulatory and classic PCOS phenotypes), and also volunteers without hirsutism and with regular menses (controls).

One hundred and five participants met the inclusion criteria. PCOS was diagnosed in 61 patients according to the Rotterdam criteria: 39 were classified as classic PCOS [biochemical and/or clinical hyperandrogenism and oligo/amenorrheic (< 9 cycles/year) or anovulatory cycles, with or without polycystic ovary (PCO) appearance at ultrasound] and 22 were characterized as ovulatory PCOS [hirsute women with normal androgen levels, regular, ovulatory cycles confirmed by luteal phase progesterone > 3.8 ng/mL, and PCO]. PCO was defined as ovarian volume greater than $10mm^3$ in at least one ovary. The control group included 44 non-hirsute women with regular and proven ovulatory cycles (luteal phase progesterone >3.8 ng/mL) Neither the PCOS participants nor controls had received any drugs known to interfere with hormonal levels for at least 3 months before the study. Women diagnosed with other hyperandrogenic disorders (nonclassic congenital adrenal hyperplasia,

Cushing's syndrome, androgen-secreting neoplasms), thyroid disorders or hyperprolactinemia were excluded, as previously reported (24-26). Other exclusion criteria were pregnancy, body mass index (BMI) >40 kg/m^2 and diabetes mellitus. The study protocol was approved by the local institutional review board. Written informed consent was obtained from all subjects.

Study protocol

Anthropometric measurements were performed in duplicate and included body weight, height and waist circumference (waist measured at the midpoint between the lower rib margin and the iliac crest in a plane that is perpendicular to the long axis of the body, with the subject standing balanced on both feet, approximately 20 cm apart, with both arms hanging freely) (27-30). BMI was calculated (current kg/m^2) according to WHO guidelines (31).

Hirsutism was defined as a modified Ferriman–Gallwey score ≥8 (32). Blood pressure was measured with a manual sphygmomanometer after a 10-minute rest, in the sitting position, with feet on the floor and the arm supported at heart level.

Hormonal and metabolic assessments were made between the 2^{nd} and 10^{th} days of the menstrual cycle, or on any day if the patient was amenorrheic. All samples were obtained between 8 and 10 a.m. Blood samples were drawn after an overnight 12-hour fast for determination of plasma cholesterol, HDL-cholesterol, and triglycerides. Glucose was measured before and 2 hours after the ingestion of a 75-g oral glucose load.

Blood samples were also drawn for measurements of insulin, sex hormone–binding globulin (SHBG) and total testosterone (TT). Insulin resistance (IR) was estimated by homeostasis model assessment (HOMA). HOMA index was calculated by multiplying insulin (μIU/mL) by glucose (mmol/L) and dividing the product by 22.5 (33). The lipid accumulation product index (LAP) was calculated using the formula [waist (cm) − 58] × triglyceride

concentration (mmol/l), as previously reported (28, 34, 35). Free androgen index (FAI) was estimated by dividing TT (in nanomoles per liter) by SHBG (in nanomoles per liter) × 100.

PCOS patients were stratified by GI, using as cut-off point the median GI value obtained for the group (GI=58).

Biochemical and hormonal assays

Total cholesterol, HDL-c, triglyceride, and glucose levels were determined by colorimetric-enzymatic methods (Bayer 1650 Advia System, Mannheim, Germany). Low-density lipoprotein cholesterol (LDL-c) was determined indirectly by using the formula LDL-c = total cholesterol − HDL-c - triglycerides/5 (36).

TT levels were measured by chemiluminescence (Siemens Advia Centaur XP, Deerfield, USA), with a sensitivity of 0.10 ng/mL and intra and inter assay coefficient of variation (CV) of 3.3 and 7.5% respectively. SHBG was measured by chemiluminescence (Immulite 2000 Siemens, Deerfield, USA), with a sensitivity of 0.02 nmol/L and intra and inter assay CV of 5.3 and 6.6% respectively. Plasma insulin levels were measured by electrochemiluminescence (Siemens Advia Centaur XP, Deerfield, USA), with a sensitivity of 0.50 U/mL and intra and inter assay CV of 2.8 and 2.1% respectively.

Assessment of body composition and rest metabolic rate

Body composition was assessed using bioimpedance (InBody 230, Biospace, Seoul, Korea). This device directly measures the impedance of each body segment to 20 KHz and 100 KHz. Assessments were performed in the morning, after a fast of at least 4 hours, with an empty bladder, using standard lab coat and stripped of all metal objects. Patients were instructed not to practice vigorous exercise the day before and on the day of the test.

Rest metabolic rate was assessed using the equipment FitMate™ (Cosmed, Rome, Italy). Patients were evaluated in the morning, after a fast of at least 5 hours, in a quiet, low light and temperature-controlled environment. Patients were also instructed not to exercise the day before and on the day of the test, and not to consume caffeine and alcohol the day before and on the day of the test.

Assessment of habitual physical activity

Habitual physical activity was estimated with a digital pedometer (BP 148 TECHLINE, São Paulo, Brazil). The device was configured individually according to the weight (kg) and step length of the individual.

Subjects were instructed to record the total number of steps taken each day in a recording sheet each night prior to sleep (37). Participants repeated this procedure over six consecutive days, generating an average weekly number of steps. They were encouraged not to alter their usual physical activity habits during the study.

Assessment of food consumption

The assessment of dietary intake was performed using a food frequency questionnaire (FFQ) previously validated in the adult population of the city of Porto Alegre, Rio Grande do Sul (38). This questionnaire assesses 121 items of food consumption during the month prior to application. Dietary GI and GL were estimated based on the FFQ as previously reported (39-42). Daily total energy, macro- and micronutrients were also calculated for PCOS and controls. We used as main reference the table of food composition *"Tabela Brasileira de Composição dos Alimentos"* (2006).

GI was calculated according to FAO/WHO (43). Firstly, the percentage of each food type in relation to the total carbohydrate content was determined; this value was multiplied by

the specific GI of each food type and divided by 100. The GI values for all foods listed in the FFQ were then added to predict the GI of the diet. The GL of each food type was calculated by multiplying the corresponding GI by the amount of carbohydrate contained in the daily serving of that food (g) and dividing this figure by 100. The daily or meal GL was obtained by adding the GL of all foods consumed during the day or the meal respectively. The GI values published in the International Table of Glycemic Index Values and Glycemic Load of Atkinson, Foster-Powell and Brand-Miller (2008) were used, with white bread as the standard reference.

Statistical analysis

The sample size was estimated based on a previous study with infertile patients (44), considering a power of 80% and alpha of 5%. To detect a difference of 2.0 points in GI between PCOS and controls, 88 women would be required (44 in each).

Results are expressed as mean±SD or median and interquartile range. Comparisons between the 2 group means were analyzed by Student's t test; comparisons between median values were analyzed with the Mann-Whitney U test; comparisons between 3 groups were analyzed by one-way analysis of variance (ANOVA). Bonferroni adjustment was used for multiple comparisons. Variables with non-Gaussian distribution were log-transformed for statistical analysis and back-transformed for data presentation. Pearson correlation coefficient or Spearman test was calculated between variables, according to Gaussian or non-Gaussian distribution, respectively. Comparisons between ratios were carried out using the χ^2 test. All analyses were performed using the Statistical Package for the Social Sciences 16 (SPSS, Chicago, IL, USA). Data from FFQ were entered in duplicate in the Epidata software, version 3.1 (The EpiData Association, Ondense, Denmark) and subsequently transported to the SPSS for analysis. Data were considered significant at $P < 0.05$.

RESULTS

One hundred and five women of childbearing age (23.7 ± 6.3 years) were studied. Most were Caucasian (87.6%). The remaining subjects were of mixed African and European ancestry. The prevalence of obesity was 44.3% in PCOS women and 31.8% in controls (P=0.288).

Overall PCOS group and controls

The clinical profile and metabolic variables of PCOS patients and controls are summarized in Table 1. The groups did not differ in age, BMI, waist circumference and glucose. Pedometer-measured physical activity and rest metabolic rate were also similar between the groups. PCOS women had higher body fat percentage, fasting insulin, HOMA-IR, and LAP in comparison to controls. As expected, PCOS patients also presented higher androgen and lower SHBG levels.

Table 1 also shows dietary GI and GL and calorie, macronutrient, and micronutrient intake in PCOS and controls. PCOS women had higher daily calorie intake and higher GI and GL. Fiber, macronutrient, and micronutrient intake did not differ between the groups, with the exception of sodium, whose consumption was higher in the PCOS group.

GI was correlated with BMI in controls and with LAP in the PCOS group (Figure 1).

PCOS patients stratified by median GI

When analyzing only PCOS women stratified by the median dietary GI observed in this sample, those with GI ≥ 58 had higher BMI, waist circumference, body fat percentage, LAP, glucose 120', and triglycerides (Table 2). HOMA-IR, fasting glucose and insulin, caloric intake and resting metabolic rate were similar between diet GI <58 or ≥ 58, but the

group with greater dietary GI had lower fiber intake [29.3 (22.9 – 40.9) vs 17.9 (13.4 – 26.0) g/day, P=0.0001].

Moreover, dietary carbohydrate, fat, and protein intake were similar between PCOS with GI ≥58 or <58 (52.1±8.0 % vs. 53.0±8.5%, P=0.671; 23.7±6.8% vs. 25.8±5.4%, P=0.168; 16.2±3.9% vs. 14.9±4.1%, P=0.227 respectively). The number of steps per day [5418 (3651-7789) vs. 5841 (3647-6892), P=0.935) and total cholesterol (167.8±32.8 vs. 179.0±36.7, P=0.218), LDL-c [98.4 (83.7-127.9) vs. 107.1 (88.2-122.1), P=0.205] and HDL-c (49.0±12.9 vs. 44.5±14.4, P=0.213) were also similar in PCOS with lower or higher median dietary GI respectively.

Classic PCOS patients, ovulatory PCOS patients, and controls

Table 3 shows the comparison between patients with classic PCOS, ovulatory PCOS and controls. Classic PCOS patients showed higher BMI and body fat percentage compared to both ovulatory PCOS and controls. Waist circumference differed significantly only between women with classic and ovulatory PCOS. Dietary GI was higher in the classic PCOS group compared to other groups. The difference in dietary GL between groups was not significant. Energy consumption was higher in the classic PCOS group compared to controls. Average daily steps or rate of resting metabolism did not differ between the 3 groups. Regarding insulin resistance indexes, HOMA-IR and insulin levels were higher in classic PCOS compared to controls and LAP was found to be higher in classic PCOS than in ovulatory PCOS and controls. Triglycerides were higher and HDL-cholesterol was lower in classic PCOS than in control group. Total testosterone was higher in PCOS, compared to the other groups. Ovulatory PCOS presented an intermediate metabolic and hormonal profile in relation to classic PCOS and controls.

Macronutrient and micronutrient intake was similar in classic and ovulatory PCOS phenotypes and controls.

DISCUSSION

The present study shows that the dietary habits of PCOS women are similar to those of non-PCOS women of the same age and BMI, except for the consumption of foods with higher GI and GL. While these results confirm the general notion that metabolic disturbances are not influenced by dietary preferences in PCOS (45-47), the present results indicate that consumption of carbohydrates with higher GI is associated with worse metabolic profile in PCOS, and that women with the more severe phenotype tend to eat more high-GI carbohydrate foods.

PCOS women also had higher daily calorie intake relative to controls. Because the percentage of macronutrients intake did not differ between groups, the increased GL found in the overall PCOS group probably resulted from a higher calorie consumption than that of the control group. The fact that GI takes into consideration the type of carbohydrate rather than the amount of carbohydrate ingested, indicates that PCOS patients in general may favor carbohydrates of lower quality. This result cannot be explained by a difference in dietary fiber content, since the groups did not differ in this respect. Other investigators (48, 49) have suggested that hunger and satiety might be impaired in PCOS. According to Farshchi et al. (50), many women with PCOS describe carbohydrate cravings and mention this as a cause of their difficulty in losing weight. This carbohydrate craving could explain a preference for a higher GI diet, as observed in our PCOS women.

Interestingly, when stratified by phenotype, PCOS women with the classic, more severe phenotype had higher dietary GI than ovulatory PCOS women, even in the presence of similar energy intake. Classic PCOS patients also had higher BMI, waist circumference, and

total body fat. However, because of the study's cross-sectional design, the direction of the association between central adiposity and high dietary GI could not be determined.

Only a few studies have assessed dietary GI in women with PCOS. While Barr et al. (51) found no differences in dietary GI and GL between 38 PCOS and 28 controls, Douglas et al. (52), found that the dietary pattern of PCOS patients was characterized by consumption of a greater amount of specific foods with a high glycemic index, such as white bread. Recently, Altieri et al. (53) have shown that PCOS and controls did not differ regarding energy, macronutrient and advanced glycosylated end product intake, but PCOS individuals had higher consumption of high-GI foods.

The finding that the percentage of macronutrient intake did not differ between PCOS and controls is consistent with previous studies by our group (45) and others (52-55). Barr et al. (51) found that the percentage energy from carbohydrate intake was significantly lower and the percentage energy from fat significantly higher in lean PCOS patients compared to lean controls, but similar in overweight/obese PCOS patients and controls. Furthermore, Wright et al. (54) found that although women with PCOS had a higher BMI than controls, there was no difference in dietary macronutrient intake; however, lean women with PCOS reported significantly lower energy intake than lean women without PCOS. Tsai et al. (56) reported that Taiwanese women with PCOS consume lower energy and carbohydrate compared with those with non-PCOS-related infertility. These data should be interpreted with caution, because of different dietary habits as well as ethnic origins among different countries, which could account for the differences among the studies.

In the present study, total sodium intake was higher in the PCOS group compared to controls, probably due to increased food intake, as the PCOS group also had a higher calorie intake. Other studies did not find differences in sodium intake among PCOS and control groups (52, 55).

Our PCOS women consuming a diet with higher GI had higher BMI, waist circumference and body fat percentage, independent of total calorie intake and number of steps per day. Several authors suggest that regular consumption of carbohydrate-rich foods, which promote a high glycemic response, can increase the risk of obesity (14, 15, 57). A meta-analysis of clinical trials showed that diets low GI and GL reduce BMI and body fat mass than controls diets (16).

In fact, evidence indicates that a diet with higher GI seems to produce a worse lipid profile and increased cardiovascular risk that is independent of total calorie intake and level of physical activity. Recently, Dong et al. (17) showed that diets with low GI and/or low GL exert a protective effect against cardiovascular disease in adult women. This association between high dietary GI and GL and cardiovascular disease is probably due to the adverse effects of these diets on serum lipids (16, 18, 20, 21), causing systemic inflammation (22). Moreover, it is argued that a lower GI diet seems to reduce expression of genes related to insulin resistance (58).

The efficacy of low GI diets in improving insulin resistance and glucose control has been demonstrated (59, 60). In addition, a meta-analysis (61) concluded that there is evidence to support positive associations between diets high GI and GL and risk of type 2 diabetes. Mehrabani et al. (62) found that the combination of high-protein and low-glycemic-load foods in a modified diet for PCOS women caused a significant increase in insulin sensitivity when compared with a conventional diet.

Testosterone stimulates appetite (63), and high androgen levels in women could be associated with appetite dysregulation, together with a craving for carbohydrates. The higher testosterone levels of patients with classic PCOS may be one reason why these women have a preference for higher GI carbohydrates.

Hyperandrogenism seems to be essential for determining the cardiometabolic risk in the various PCOS phenotypes (26). A previous study by our group also indicated that androgen levels were three times higher in women with the classical anovulatory phenotype, who also had increased prevalence of impaired glucose tolerance and insulin resistance, compared to ovulatory women with PCO morphology (7). Furthermore, the clustering of more than one cardiovascular risk factor, appeared to be higher in the "classic" PCOS phenotype, coexisting with higher androgen levels (64, 65). In this sense, the present finding of a correlation of GI with insulin resistance only in PCOS, but not in controls, supports the notion that hyperandrogenism could play a role on this association.

Strengths of this study include the absence of previous analyses of dietary GI and GL in women with different phenotypes of PCOS and the use of a robust, validated FFQ that assesses 121 items of food consumption during the month prior to application. One limitation is the relatively small sample size, which did not allow a comparative analysis of obese vs. normal weight sub-groups of PCOS and controls.

In conclusion, the present results indicate that dietary GI is higher in patients with PCOS than controls. Also, patients with the classic PCOS phenotype present a higher dietary GI than ovulatory PCOS and control women, and a worse anthropometric and metabolic profile. Further studies are needed to clarify the mechanisms underlying the association between these abnormalities, high dietary GI, and hyperandrogenism in PCOS.

ACKNOWLEDGEMENTS

We would like to thank Denusa Wiltgen and Mariana Toscani for their support with data collection.

REFERENCES

1. Azziz R, Woods KS, Reyna R, Key TJ, Knochenhauer ES, Yildiz BO. The prevalence and features of the polycystic ovary syndrome in an unselected population. J Clin Endocrinol Metab 2004;89:2745-9.

2. Asuncion M, Calvo RM, San Millan JL, Sancho J, Avila S, Escobar-Morreale HF. A prospective study of the prevalence of the polycystic ovary syndrome in unselected Caucasian women from Spain. J Clin Endocrinol Metab 2000;85:2434-8.

3. Rotterdam EA-SPCWG. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. Fertil Steril 2004;81:19-25.

4. Apridonidze T, Essah PA, Iuorno MJ, Nestler JE. Prevalence and characteristics of the metabolic syndrome in women with polycystic ovary syndrome. J Clin Endocrinol Metab 2005;90:1929-35.

5. Dunaif A. Insulin action in the polycystic ovary syndrome. Endocrinol Metab Clin North Am 1999;28:341-59.

6. Azziz R, Sanchez LA, Knochenhauer ES, Moran C, Lazenby J, Stephens KC *et al.* Androgen excess in women: experience with over 1000 consecutive patients. J Clin Endocrinol Metab 2004;89:453-62.

7. Wiltgen D, Spritzer PM. Variation in metabolic and cardiovascular risk in women with different polycystic ovary syndrome phenotypes. Fertil Steril 2010;94:2493-6.

8. Moran L, Teede H. Metabolic features of the reproductive phenotypes of polycystic ovary syndrome. Hum Reprod Update 2009;15:477-88.

9. Wild RA, Carmina E, Diamanti-Kandarakis E, Dokras A, Escobar-Morreale HF, Futterweit W *et al.* Assessment of cardiovascular risk and prevention of cardiovascular disease in women with the polycystic ovary syndrome: a consensus statement by the

Androgen Excess and Polycystic Ovary Syndrome (AE-PCOS) Society. J Clin Endocrinol Metab 2010;95:2038-49.

10. Wild RA, Rizzo M, Clifton S, Carmina E. Lipid levels in polycystic ovary syndrome: systematic review and meta-analysis. Fertil Steril 2011;95:1073-9 e1-11.

11. Jenkins DJ, Wolever TM, Taylor RH, Barker H, Fielden H, Baldwin JM *et al.* Glycemic index of foods: a physiological basis for carbohydrate exchange. Am J Clin Nutr 1981;34:362-6.

12. Salmeron J, Manson JE, Stampfer MJ, Colditz GA, Wing AL, Willett WC. Dietary fiber, glycemic load, and risk of non-insulin-dependent diabetes mellitus in women. JAMA 1997;277:472-7.

13. Liu S, Willett WC, Stampfer MJ, Hu FB, Franz M, Sampson L *et al.* A prospective study of dietary glycemic load, carbohydrate intake, and risk of coronary heart disease in US women. Am J Clin Nutr 2000;71:1455-61.

14. Brand-Miller JC, Holt SH, Pawlak DB, McMillan J. Glycemic index and obesity. Am J Clin Nutr 2002;76:281S-5S.

15. Ludwig DS. The glycemic index: physiological mechanisms relating to obesity, diabetes, and cardiovascular disease. JAMA 2002;287:2414-23.

16. Thomas DE, Elliott EJ, Baur L. Low glycaemic index or low glycaemic load diets for overweight and obesity. Cochrane Database Syst Rev 2007:CD005105.

17. Dong JY, Zhang YH, Wang P, Qin LQ. Meta-analysis of dietary glycemic load and glycemic index in relation to risk of coronary heart disease. Am J Cardiol 2012;109:1608-13.

18. Shikany JM, Tinker LF, Neuhouser ML, Ma Y, Patterson RE, Phillips LS *et al.* Association of glycemic load with cardiovascular disease risk factors: the Women's Health Initiative Observational Study. Nutrition 2010;26:641-7.

19. McMillan-Price J, Petocz P, Atkinson F, O'Neill K, Samman S, Steinbeck K *et al.* Comparison of 4 diets of varying glycemic load on weight loss and cardiovascular risk reduction in overweight and obese young adults: a randomized controlled trial. Arch Intern Med 2006;166:1466-75.

20. Slyper A, Jurva J, Pleuss J, Hoffmann R, Gutterman D. Influence of glycemic load on HDL cholesterol in youth. Am J Clin Nutr 2005;81:376-9.

21. Ford ES, Liu S. Glycemic index and serum high-density lipoprotein cholesterol concentration among us adults. Arch Intern Med 2001;161:572-6.

22. Levitan EB, Cook NR, Stampfer MJ, Ridker PM, Rexrode KM, Buring JE *et al.* Dietary glycemic index, dietary glycemic load, blood lipids, and C-reactive protein. Metabolism 2008;57:437-43.

23. Schulze MB, Liu S, Rimm EB, Manson JE, Willett WC, Hu FB. Glycemic index, glycemic load, and dietary fiber intake and incidence of type 2 diabetes in younger and middle-aged women. Am J Clin Nutr 2004;80:348-56.

24. Spritzer P, Billaud L, Thalabard JC, Birman P, Mowszowicz I, Raux-Demay MC *et al.* Cyproterone acetate versus hydrocortisone treatment in late-onset adrenal hyperplasia. J Clin Endocrinol Metab 1990;70:642-6.

25. Nacul AP, Andrade CD, Schwarz P, de Bittencourt PI, Jr., Spritzer PM. Nitric oxide and fibrinogen in polycystic ovary syndrome: associations with insulin resistance and obesity. Eur J Obstet Gynecol Reprod Biol 2007;133:191-6.

26. Azziz R, Carmina E, Dewailly D, Diamanti-Kandarakis E, Escobar-Morreale HF, Futterweit W *et al.* The Androgen Excess and PCOS Society criteria for the polycystic ovary syndrome: the complete task force report. Fertil Steril 2009;91:456-88.

27. Toscani M, Migliavacca R, Sisson de Castro JA, Spritzer PM. Estimation of truncal adiposity using waist circumference or the sum of trunk skinfolds: a pilot study for insulin

resistance screening in hirsute patients with or without polycystic ovary syndrome. Metabolism 2007;56:992-7.

28. Wiltgen D, Benedetto IG, Mastella LS, Spritzer PM. Lipid accumulation product index: a reliable marker of cardiovascular risk in polycystic ovary syndrome. Hum Reprod 2009;24:1726-31.

29. Franz R, Maturana MA, Magalhaes JA, Moraes RS, Spritzer PM. Central adiposity and decreased heart rate variability in postmenopause: a cross-sectional study. Climacteric 2012.

30. Mario FM, do Amarante F, Toscani MK, Spritzer PM. Lean muscle mass in classic or ovulatory PCOS: association with central obesity and insulin resistance. Exp Clin Endocrinol Diabetes 2012;120:511-6.

31. WHO. Physical status: the use and interpretation of anthropometry. In: Report of a WHO Expert Committee. Vol. 854: World Health Organization Technical Report Series, 1995:1-452.

32. Ferriman D, Gallwey JD. Clinical assessment of body hair growth in women. J Clin Endocrinol Metab 1961;21:1440-7.

33. Wallace TM, Levy JC, Matthews DR. Use and abuse of HOMA modeling. Diabetes Care 2004;27:1487-95.

34. Kahn HS. The "lipid accumulation product" performs better than the body mass index for recognizing cardiovascular risk: a population-based comparison. BMC Cardiovasc Disord 2005;5:26.

35. Maturana MA, Moreira RM, Spritzer PM. Lipid accumulation product (LAP) is related to androgenicity and cardiovascular risk factors in postmenopausal women. Maturitas 2011;70:395-9.

36. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem 1972;18:499-502.

37. Graff SK, Alves BC, Toscani MK, Spritzer PM. Benefits of pedometer-measured habitual physical activity in healthy women. Appl Physiol Nutr Metab 2012;37:149-56.

38. Zanolla AF, Olinto MT, Henn RL, Wahrlich V, Anjos LA. Avaliação de reprodutibilidade e validade de um questionário de freqüência alimentar em adultos residentes em Porto Alegre, Rio Grande do Sul, Brasil. Cadernos de Saúde Pública 2009;25:840-8.

39. Sieri S, Krogh V, Berrino F, Evangelista A, Agnoli C, Brighenti F *et al.* Dietary glycemic load and index and risk of coronary heart disease in a large italian cohort: the EPICOR study. Arch Intern Med 2010;170:640-7.

40. Mendez MA, Covas MI, Marrugat J, Vila J, Schroder H. Glycemic load, glycemic index, and body mass index in Spanish adults. Am J Clin Nutr 2009;89:316-22.

41. Villegas R, Liu S, Gao YT, Yang G, Li H, Zheng W *et al.* Prospective study of dietary carbohydrates, glycemic index, glycemic load, and incidence of type 2 diabetes mellitus in middle-aged Chinese women. Arch Intern Med 2007;167:2310-6.

42. Liu S, Manson JE, Stampfer MJ, Holmes MD, Hu FB, Hankinson SE *et al.* Dietary glycemic load assessed by food-frequency questionnaire in relation to plasma high-density-lipoprotein cholesterol and fasting plasma triacylglycerols in postmenopausal women. Am J Clin Nutr 2001;73:560-6.

43. WHO. Preventing and Managing the Global Epidemic. In: WHO Technical Report Series 894. Geneva: World Health Organization, 1998:1-276.

44. Colombo O, Pinelli G, Comelli M, Marchetti P, Sieri S, Brighenti F *et al.* Dietary intakes in infertile women a pilot study. Nutr J 2009;8:53.

45. Toscani MK, Mario FM, Radavelli-Bagatini S, Spritzer PM. Insulin resistance is not strictly associated with energy intake or dietary macronutrient composition in women with polycystic ovary syndrome. Nutr Res 2011;31:97-103.

46. Fauser BC, Tarlatzis BC, Rebar RW, Legro RS, Balen AH, Lobo R *et al.* Consensus on women's health aspects of polycystic ovary syndrome (PCOS): the Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group. Fertil Steril 2012;97:28-38 e25.

47. Moran LJ, Ko H, Misso M, Marsh K, Noakes M, Talbot M *et al.* Dietary Composition in the Treatment of Polycystic Ovary Syndrome: A Systematic Review to Inform Evidence-Based Guidelines. J Acad Nutr Diet 2013.

48. Moran L, Norman RJ. Understanding and managing disturbances in insulin metabolism and body weight in women with polycystic ovary syndrome. Best Pract Res Clin Obstet Gynaecol 2004;18:719-36.

49. Herriot AM, Whitcroft S, Jeanes Y. An retrospective audit of patients with polycystic ovary syndrome: the effects of a reduced glycaemic load diet. J Hum Nutr Diet 2008;21:337-45.

50. Farshchi H, Rane A, Love A, Kennedy RL. Diet and nutrition in polycystic ovary syndrome (PCOS): pointers for nutritional management. J Obstet Gynaecol 2007;27:762-73.

51. Barr S, Hart K, Reeves S, Sharp K, Jeanes Y. Dietary glycaemic index, glycaemic load and insulin resistance in lean and overweight women with polycystic ovary syndrome and controls. Proceedings of the Nutrition Society 2010;69:E126.

52. Douglas CC, Norris LE, Oster RA, Darnell BE, Azziz R, Gower BA. Difference in dietary intake between women with polycystic ovary syndrome and healthy controls. Fertil Steril 2006;86:411-7.

53. Altieri P, Cavazza C, Pasqui F, Morselli AM, Gambineri A, Pasquali R. Dietary habits and their relationship with hormones and metabolism in overweight and obese women with polycystic ovary syndrome. Clin Endocrinol (Oxf) 2013;78:52-9.

54. Wright CE, Zborowski JV, Talbott EO, McHugh-Pemu K, Youk A. Dietary intake, physical activity, and obesity in women with polycystic ovary syndrome. Int J Obes Relat Metab Disord 2004;28:1026-32.

55. Alvarez-Blasco F, Luque-Ramirez M, Escobar-Morreale HF. Diet composition and physical activity in overweight and obese premenopausal women with or without polycystic ovary syndrome. Gynecol Endocrinol 2011;27:978-81.

56. Tsai YH, Wang TW, Wei HJ, Hsu CY, Ho HJ, Chen WH *et al.* Dietary intake, glucose metabolism and sex hormones in women with polycystic ovary syndrome (PCOS) compared with women with non-PCOS-related infertility. Br J Nutr 2012:1-9.

57. Mozaffarian D, Hao T, Rimm EB, Willett WC, Hu FB. Changes in diet and lifestyle and long-term weight gain in women and men. N Engl J Med 2011;364:2392-404.

58. Bouche C, Rizkalla SW, Luo J, Vidal H, Veronese A, Pacher N *et al*. Five-week, low-glycemic index diet decreases total fat mass and improves plasma lipid profile in moderately overweight nondiabetic men. Diabetes Care 2002;25:822-8.

59. Brand-Miller J, McMillan-Price J, Steinbeck K, Caterson I. Dietary glycemic index: health implications. J Am Coll Nutr 2009;28 Suppl:446S-9S.

60. Marsh KA, Steinbeck KS, Atkinson FS, Petocz P, Brand-Miller JC. Effect of a low glycemic index compared with a conventional healthy diet on polycystic ovary syndrome. Am J Clin Nutr 2010;92:83-92.

61. Dong JY, Zhang L, Zhang YH, Qin LQ. Dietary glycaemic index and glycaemic load in relation to the risk of type 2 diabetes: a meta-analysis of prospective cohort studies. Br J Nutr 2011;106:1649-54.

62. Mehrabani HH, Salehpour S, Amiri Z, Farahani SJ, Meyer BJ, Tahbaz F. Beneficial effects of a high-protein, low-glycemic-load hypocaloric diet in overweight and obese women with polycystic ovary syndrome: a randomized controlled intervention study. J Am Coll Nutr 2012;31:117-25.

63. Asarian L, Geary N. Modulation of appetite by gonadal steroid hormones. Philos Trans R Soc Lond B Biol Sci 2006;361:1251-63.

64. Jovanovic VP, Carmina E, Lobo RA. Not all women diagnosed with PCOS share the same cardiovascular risk profiles. Fertil Steril 2010;94:826-32.

65. Carmina E, Chu MC, Longo RA, Rini GB, Lobo RA. Phenotypic variation in hyperandrogenic women influences the findings of abnormal metabolic and cardiovascular risk parameters. J Clin Endocrinol Metab 2005;90:2545-9.

Figure legend

Figure 1. Correlation between glycemic index and BMI in women with PCOS (A) and controls (B). Correlation between glycemic index and LAP in women with PCOS (C) and controls (D).

Table 1. Clinical characteristics, metabolic variables, dietary glycemic index and load, energy, macro and micronutrient intake in PCOS patients and controls

Variable	PCOS (n=61)	Controls (n=44)	*P*
Age	22.7 ± 6.2	25.0 ± 6.3	0.070
BMI (kg/m²)	28.9 ± 5.6	27.1 ± 5.7	0.099
Waist circumference (cm)	85.4 ± 12.8	83.5 ± 12.7	0.464
Total body fat (%)	38.9 ± 7.4	34.7 ± 9.5	0.020
Steps/day	5519 (3658 – 7002)	5811 (4339 – 7267)	0.702
Resting metabolic rate	1469 ± 227	1453 ± 249	0.763
Glucose 0’ (mg/dL)	86.8 ± 9.1	87.0 ± 7.5	0.902
Insulin (µU/mL)	16.7 (9.8 – 21.2)	9.9 (6.8 – 12.5)	0.002
HOMA-IR	3.5 (2.1 – 4.7)	2.1 (1.4 – 2.8)	0.006
LAP	25.3 (16.0 – 54.6)	20.1 (10.3 – 31.7)	0.039
Total testosterone (ng/mL)	0.72 ± 0.25	0.54 ± 0.17	0.001
Free androgen index	15.1 (10.7 – 27.4)	7.2 (4.4 – 11.9)	0.001
SHBG (nmol/L)	27.1 (16.6 – 36.4)	40.2 (29.5 – 62.9)	0.001
Glycemic index	57.7 ± 5.3	55.7 ± 4.7	0.047
Glycemic load	176.3 (111.4 – 269.8)	143.8 (111.1 – 186.3)	0.049
Energy intake (Kcal/day)	2250 (1710 – 3786)	1984 (1620 – 2335)	0.034
Carbohydrate (%)	52.5 ± 8.2	53.4 ± 7.4	0.591
Fat (%)	24.8 ± 6.1	25.5 ± 5.5	0.649
Protein (%)	15.5 ± 4.1	15.9 ± 3.7	0.511
Fiber (g/day)	24.3 (17.4 – 35.5)	21.3 (17.4 – 29.5)	0.336
Cholesterol (mg/day)	222 (176 – 348)	221 (176 – 286)	0.585
Saturated fatty acids (%)	32.5 ± 5.9	31.5 ± 6.6	0.455
Monounsaturated fatty acids (%)	30.2 ± 4.7	31.0 ± 5.0	0.437
Polyunsaturated fatty acids (%)	12.9 ± 3.4	13.7 ± 3.3	0.251

Calcium (mg/day)	731 (524 – 1063)	648 (520 – 864)	0.363
Magnesium (mg/day)	256 (182 – 354)	227 (181 – 292)	0.308
Iron (mg/day)	9.6 (6.9 – 14.0)	8.7 (7.0 – 11.0)	0.104
Zinc (mg/day)	10.7 (7.4 – 14.3)	8.8 (7.1 – 11.9)	0.088
Folate (mcg/day)	501 (322 – 654)	429 (355 – 552)	0.471
Sodium (mg/day)	2329 (1680 – 3556)	1903 (1570 – 2406)	0.040

BMI = body mass index; HOMA = homeostasis model assessment; LAP = lipid accumulation product; SHBG = sex hormone-binding globulin. Values are expressed as mean ± SD (Student's t-test) or median and 25–75 inter-quartile range (Mann-Whitney test);

Table 2. Anthropometric, dietary and metabolic variables in PCOS women stratified by median diet GI

Variables	Median < 58 (n=29)	Median ≥ 58 (n=32)	*P*
BMI (kg/m²)	26.9 ± 4.7	30.9 ± 5.6	0.004
Waist circumference (cm)	80.8 ± 10.8	89.5 ± 13.2	0.007
Total body fat (%)	36.6 ± 7.9	40.7 ± 6.6	0.048
Energy intake (kcal/day)	2163 (1474 – 3786)	2300 (1768 – 4260)	0.447
Resting metabolic rate (kcal/day)	1446 ± 223	1489 ± 232	0.468
LAP	20.1 (10.3 – 31.7)	25.3 (16.0 – 54.6)	0.008
HOMA-IR	2.4 (1.4 – 4.2)	2.8 (1.8 – 4.6)	0.218
Glucose 0'(mg/dL)	84.9 ± 7.1	88.4 ± 10.3	0.144
Glucose 120' (mg/dL)	95.9 ± 22.5	110.5 ± 30.7	0.048
Insulin (μU/mL)	16.7 (9.8 – 21.8)	9.9 (6.8 – 12.5)	0.654
Triglycerides (mg/dL)	86.5 (66.3 – 134.0)	77.5 (52.0 – 102.0)	0.046
Total testosterone (ng/mL)	0.64 ± 0.21	0.65 ± 0.26	0.827
Free androgen index	10.1 (6.4 – 16.1)	13.5 (9.3 – 26.2)	0.073
SHBG (nmol/L)	36.1 (27.3 – 55.8)	29.1 (19.4 – 46.5)	0.101

BMI = body mass index; LAP = lipid accumulation product; HOMA = homeostasis model assessment; SHBG = sex hormone-binding globulin. Values are expressed as mean ± SD (Student's t-test) or median and 25–75 inter-quartile range (Mann-Whitney test).

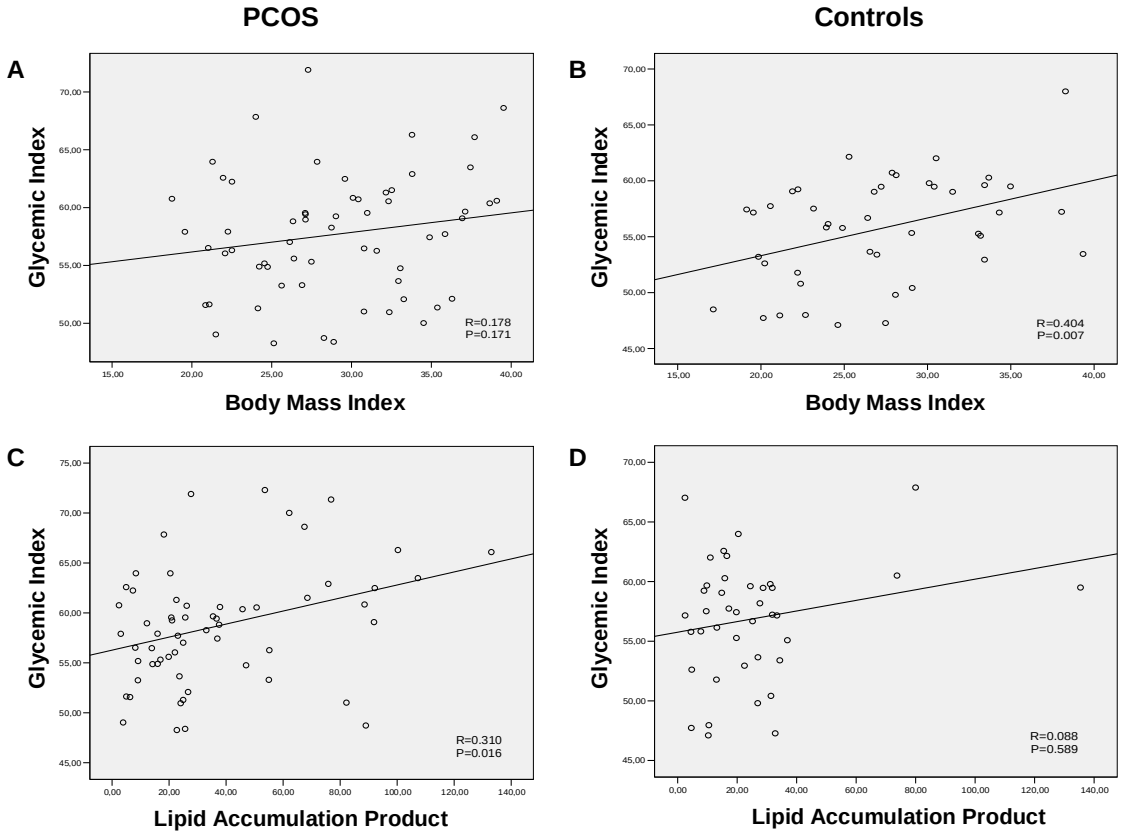
Table 3. Clinical profile, anthropometric and metabolic variables in women with classic or ovulatory PCOS and controls

Variables	Classic PCOS (n=39)	Ovulatory PCOS (n=22)	Controls (n=44)	*P*
BMI (kg/m²)	30.6 ± 5.6 [a]	26.0 ± 4.3 [b]	27.0 ± 5.6 [b]	0.002
Waist circumference (cm)	89.2 ± 12.9 [a]	78.6 ± 9.6 [b]	83.2 ± 12.6 [a,b]	0.004
Total body fat (%)	41.2 ± 6.3 [a]	34.5 ± 7.4 [b]	34.5 ± 9.3 [b]	0.001
Glycemic index	59.1 ± 5.6 [a]	56.9 ± 5.0 [b]	55.8 ± 4.7 [b]	0.044
Glycemic load	176.3 (101.9 – 281.5)	173.5 (118.7 – 228.3)	143,8 (110.4 – 187.8)	0.127
Energy intake (kcal/day)	2449 (1681 – 3872) [a]	2141 (1650 – 3485) [a,b]	1984 (1620 – 2335) [b]	0.023
Systolic blood pressure (mmHg)	120.3 ± 12.4 [a]	116.1 ± 14.0 [a,b]	111,9 ± 11,3 [b]	0.011
Diastolic blood pressure (mmHg)	80.0 ± 8.7 [a]	73.2 ± 9.7 [b]	72.3 ± 10.0 [b]	0.001
Steps/day	5642 (3595 – 7113)	5486 (3755 – 6915)	5955 (4385 – 7377)	0.820
Resting metabolic rate (kcal/day)	1481 ± 38.0	1453 ± 35.8	1447 ± 50.7	0.822
LAP	36.8 (22.0 – 70.3) [a]	20.6 (8.1 – 25.8) [b]	19.7 (10.3 – 31.3) [b]	0.002
HOMA-IR	3.8 (2.4 – 5.3) [a]	2.7 (1.3 - 4.1) [a,b]	2.1 (1.4 – 2.8) [b]	0.007
Glucose 0'(mg/dL)	87.5 ± 9.9	85.5 ± 7.5	87.1 ± 7.8	0.681
Glucose 120' (mg/dL)	107.9 ± 31.8	97.0 ± 18.6	98.4 ± 19.4	0.160
Insulin (µU/mL)	18.1 (11.8 – 23.1) [a]	12.8 (6.5 – 18.9) [a,b]	10.3 (6.8 – 13.3) [b]	0.006
Triglycerides (mg/dL)	107.0 (70.3 – 161.3) [a]	76.5 (61.0 – 101.3) [a,b]	77.5 (52.0 – 102.0) [b]	0.014
Total cholesterol (mg/dL)	178.7 ± 37.4	165.4 ± 29.7	175.7 ± 28.0	0.296
LDL-c (mg/dL)	110.5 ± 28.4	96.6 ± 27.6	106.8 ± 22.5	0.138
HDL-c(mg/dL)	44.1 ± 14.0 [a]	51.0 ± 12.4 [a,b]	51.0 ± 11.2 [b]	0.032

Total testosterone (ng/mL)	0.77 ± 0.27 [a]	0.62 ± 0.18 [b]	0.54 ± 0.17 [b]	0.001
Free androgen index	16.5 (11.9 – 27.8) [a]	12.6 (8.8 – 27.0) [a]	7.2 (4.4 – 11.9) [b]	0.001
SHBG (nmol/L)	27.2 (16.7 – 33.2) [a]	26.1 (15.4 – 44.1) [a]	40.2 (29.5 – 62.9) [b]	0.001

LAP = lipid accumulation product; HOMA = homeostasis model assessment; LDL-c = LDL-cholesterol; HDL-c = HDL-cholesterol; SHBG = sex hormone-binding globulin; BMI= body mass index. Values are expressed as mean ± SD or median and 25–75 inter-quartile range (One-way ANOVA; Multiple comparisons by Bonferroni test). Different letters represent statistically significant difference ($P < 0.05$).

Figure 1


PCOS
Controls
A
B
C
D
Glycemic Index
Body Mass Index
Lipid Accumulation Product
R=0.178
P=0.171
R=0.404
P=0.007
R=0.310
P=0.016
R=0.088
P=0.589