Revista da
ASSOCIAÇÃO MÉDICA BRASILEIRA
www.ramb.org.br

Original article

Polycystic ovary syndrome and intervening factors in adolescents from 15 to 18 years old☆

Franciane Rocha de Faria[c,*], *Laís Silveira Gusmão*[b], *Eliane Rodrigues de Faria*[a], *Vivian Siqueira Santos Gonçalves*[b], *Roberta Stofeles Cecon*[a], *Sylvia do Carmo Castro Franceschini*[d], *Silvia Eloiza Priore*[d]

[a]*Graduate Program in Nutritional Sciences, Universidade Federal de Viçosa (UFV), Viçosa, MG, Brazil*
[b]*Enhancement Program (Higher Education), Department of Nutrition and Health, UFV, Viçosa, MG, Brazil*
[c]*Department of Nutrition, Universidade Federal do Espírito Santo, Alegre, ES, Brazil*
[d]*Department of Nutrition and Health, UFV, Viçosa, MG, Brazil*

ARTICLE INFO

Article history:
Received 17 July 2012
Accepted 1 February 2013

Keywords:
Polycystic ovary syndrome
Adolescent
Nutritional status
Menarche
Metabolic diseases

ABSTRACT

Objective: To assess the factors related to the presence of polycystic ovary syndrome (PCOS) in adolescents.
Methods: This was a cross-sectional study, with female adolescents from 15 to 18 years old, divided into: group 1 (with a medical diagnosis of PCOS) and group 2 (not diagnosed with PCOS). The height-for-age index and the body mass index were used for classifying the nutritional status, and a semi-structured questionnaire was applied. The Mann-Whitney test, Fisher's exact test, Spearman correlation coefficients, and logistic regression were used.
Results: This study evaluated 485 adolescents with an average age of 16.3 ± 0.9 years old. The prevalence of PCOS was 6.2%. No difference was found between the groups regarding anthropometric parameters and period of contraceptive use; however, there were differences regarding the age at menarche ($p < 0.004$). Older age at menarche was a protection factor against the syndrome.
Conclusion: An association was found between younger age at menarche and the development of the PCOS in adolescents.

Síndrome do ovário policístico e fatores relacionados em adolescentes de 15 a 18 anos

Palavras-chave:
Síndrome do ovário policístico
Adolescente
Estado nutricional

RESUMO

Objetivo: Avaliar os fatores relacionados à presença da síndrome do ovário policístico (SOP) em adolescentes.
Métodos: Estudo transversal, com adolescentes do sexo feminino de 15 a 18 anos, divididas em grupo 1 (com diagnóstico médico de SOP) e grupo 2 (sem diagnóstico da síndrome).

☆Study conducted at the Universidade Federal de Viçosa (UFV), Department of Nutrition and Health, Viçosa, MG, Brazil.

*Corresponding author.
E-mail: francianerdefaria@hotmail.com (F.R. Faria).

Menarca
Doenças metabólicas

Utilizou-se o índice estatura para idade e índice de massa corporal para classificação do estado nutricional, e aplicou-se questionário semiestruturado. Foram aplicados testes de *Mann-Whitney*, Exato de Fisher, correlação de *Spearman* e regressão logística.
Resultados: Foram avaliados 485 adolescentes, com idade média de 16,3 ± 0,9 anos. A prevalência de SOP foi de 6,2%. Não se encontrou diferença entre os grupos quanto aos parâmetros antropométricos e tempo de uso de anticoncepcionais, porém houve diferença quanto à idade da menarca ($p < 0,004$), e a mais tardia foi fator de proteção para síndrome.
Conclusão: Verificou-se associação entre a ocorrência da menarca precoce e o desenvolvimento da SOP em adolescentes.

Introduction

The main characteristics of adolescence, here understood as the period from ages 10 to 19 years, are rapid growth and puberty.[1]

Puberty is regarded as one of the first physiological processes of hormonal maturation and somatic growth that prepares the organism to procreate. The early signs of secondary sexual characteristics appear and develop during this period, and this phase extends until the morphological and physiological changes are similar to the adult stage.[2]

Polycystic ovary syndrome (PCOS) is a complex and heterogeneous endocrine disorder, whose prevalence in women ranges from 4% to 10% during the reproductive period, according to different diagnostic criteria.[3] It may result in health complications, such as menstrual dysfunction, infertility, hirsutism, acne, and metabolic syndrome, and it is considered a risk factor for diabetes mellitus type 2, arterial hypertension, and cardiovascular diseases.[4,5]

PCOS is fairly common in adolescents, and it is related to hormonal changes and/or morphological changes in the ovaries, as well as to the increased levels of insulin-like growth factor I (IGF-I) and insulin, which are common during puberty.[6]

There are several systemic changes that interact during PCOS, among which the changes in lipid metabolism (dyslipidemias) are noteworthy, in addition to those related to insulin sensitivity. Obesity defined as excess weight and/or body fat is associated with women affected by PCOS.[7-9]

Aiming at contributing to the research of PCOS, this study intended to assess the factors related to the presence of PCOS in adolescents from 15 to 18 years old who lived in Viçosa, Minas Gerais.

Methods

This was a cross-sectional and observational study with female adolescents in the age group of 15 to 18 years old who attended high school at private and public institutions in the urban area of the city of Viçosa, MG, Brazil.

The sample size was calculated through the software Epi Info version 6.04, based on a formula specific for cross-sectional studies. The population of 2,233 adolescents of the gender and age group required by the study, living in the urban area of Viçosa was considered,[10] with prevalence of 8%,[4] acceptable variability of 3%,[4,5] and confidence level of 99%, totaling 437 adolescents.

The adolescents were selected through intentional sampling, by convenience, and only those who had their menarche at least a year before were included in the study, resulting in a more homogeneous group.[11]

Weight and height were measured using the techniques proposed by the World Health Organization (WHO).[12] Weight was obtained with an electronic digital scale with maximum capacity of 150 kg and sensitivity of 50 g, and height was obtained using a portable stadiometer with a maximum length of 2.13 m and resolution of 0.1 cm; this measurement was performed twice, using the average value of both measurements. Should the difference between the measurements exceed 0.5 cm, new measurements were performed.

To evaluate the nutritional status, the height-for-age and body mass index (BMI)-for-age indices were used, classified according to the z-scores and pursuant to the WHO reference parameters for gender and age.[13] Adolescents with overweight and obesity (≥ z-score +1) were classified as excess weight.

A semi-structured questionnaire, including personal data, type of school (public or private), date of birth, age at menarche, medical diagnosis of PCOS, regular use of contraceptives and duration of use, diagnosis of chronic non-communicable diseases (CNCDs), pregnancy, and smoking.

The adolescents were grouped into group 1 (G1): with medical diagnosis of PCOS, and group 2 (G2): not diagnosed with PCOS.

Data was processed using the Excel software and analyzed through the Statistical Package for Social Sciences (SPSS), version 13.0 for Windows, and STATA, version 11.0. The Kolmogorov-Smirnov test for normality was used and, based on the result obtained, the Mann-Whitney test and Spearman's correlation coefficients were used. Fisher's exact test was used to verify the association between the variables analyzed. The level of rejection of the null hypothesis established was lower than 5% ($p < 0.05$).

Simple logistic regression was used to evaluate the association between PCOS (dependent variable) and the risk factors evaluated in this study (independent variables).

The project was approved in November 10, 2009 (Of. Ref. No. 084/2009) by the Human Research Ethics Committee of the Universidade Federal de Viçosa. Participants older than 18 years old or their guardians signed an informed consent.

Table 1 – Anthropometric parameters, age at menarche, and use of contraceptives – G1 and G2 adolescents. Viçosa, Minas Gerais, Brazil. 2010.

Variables	Group 1	Group 2	p
	Median (Min-Max)	Median (Min-Max)	
Weight (kg)	54.7 (40.5-78.3)	56.9 (38.0-71.8)	0.89
Height (cm)	162.4 (147.3-172.9)	161.0 (147.1-175.5)	0.82
BMI (kg/m^2)	20.2 (16.7-27.6)	20.4 (16.3-27.1)	0.95
Age at menarche (years)	12.0 (9.0-14.0)	12.0 (9.0-16.0)	**0.004**
Period of contraceptive use (months)	12.0 (1-36)	7.0 (1.0-36.0)	0.429

BMI, body mass index; G1, adolescents diagnosed with polycystic ovary syndrome; G2, adolescents not diagnosed with polycystic ovary syndrome.
Mann-Whitney test.

Results

In the present study, 485 adolescents with average age of 16.3 ± 0.9 years old were included. The prevalence of PCOS found was 6.2% (n = 30).

No difference was found between the groups ($p > 0.05$) when comparing the anthropometric parameters and the period of contraceptive use. However, differences were found between the study groups regarding age at menarche ($p < 0.004$) (Table 1), and also an inverse correlation was found between weight and BMI values and age at menarche ($r = –0.150$; $p = 0.001$; $r = –0.195$; $p < 0.001$, respectively).

Figure 1 shows the adolescents' nutritional status; G1 presented a higher prevalence of short stature and overweight, but there was no difference between the groups ($p < 0.05$).

From the total sample, 10.3% (n = 50) of the adolescents used contraceptives on a regular basis; 78% of which (n = 39) belonged to G2. Regarding health condition and smoking habits, 2.7% (n = 13) had CNCDs, and 1.9% (n = 9) were smokers.

In the simple logistic regression analyses, the older age at menarche was a protection factor against PCOS. In this study, there was no association between BMI, height, duration of contraceptive use, and presence of CNCDs with PCOS (Table 2).

Table 2 – Simple logistic regression models for polycystic ovary syndrome in adolescents aged between 15 and 18 years (Viçosa, Minas Gerais, Brazil, 2010).

Independent variables	OR	95% CI	p
Age at menarche (years)	0.63	0.47-0.85	**0.003**
Body mass index (kg/m^2)	0.99	0.91-1.08	0.86
Height (cm)	0.99	0.94-1.06	0.94
Period of contraceptive use (months)	1.03	0.96-1.10	0.37
Presence of CNCD	1.26	0.16-10.1	0.82

CI, confidence interval; CNCD, chronic non-communicable diseases; OR, odds ratio.

Discussion

The hormonal changes and/or morphological changes in the ovaries appear to begin in childhood. The increase in levels of IGF-I and insulin during puberty may be related to the increased prevalence of PCOS in adolescence.[14]

The prevalences showed by population studies range from about 5% to 10% of women of reproductive age,[15] a range which encompasses the 6.2% found in this study. Bridges et al.,[16] when analyzing the growth of the ovaries and the prevalence of polycystic ovary in 358 girls in a pediatric endocrinology outpatient clinic of a hospital in the city of Middletown, in the United States, found a 6% prevalence of PCOS at 6 years of age and 26% at 15 years of age. Teixeira et al.,[17] when studying 140 pre- and post-pubertal healthy girls between 2 and 18 incomplete years of age in an endocrinology outpatient clinic in Rio de Janeiro, found a 4% positive result in pre-pubertal and 11% in post-pubertal girls.

Bouzas[18] warned that, unlike what happens in childhood, it is unusual in Brazil to bring teenagers to health services, even though sexuality, contraceptive methods, and body image are issues that concern them. Puberty is a phase in which hormonal changes occur with respect to insulin (relative insensitivity to insulin with compensatory hyperinsulinemia), gonadotropins, androgens, and estrogens, and the diagnosis of PCOS is a challenge, which may lead to the underestimation of prevalence of the disease in this population group.

Obesity and insulin-resistance are generally associated to PCOS. In a study with 49 women with PCOS, aged from 18 to 45 years, divided according to their BMI, Kuba et al.[19] found an association between obesity and higher prevalence of insulin resistance and diabetes mellitus. Martins et al.,[20] studying 60 women from 18 to 35 years presenting PCOS, revealed a higher cardiovascular risk in those who presented insulin resistance.

Obesity and insulin resistance are more and more present in the adolescent population,[21] and may persist into adulthood, triggering deleterious health effects. Thus, it is important to monitor this population, considering

the adoption of healthy habits, aiming at maintaining the appropriate weight and decreasing risk factors not only for PCOS, but also for cardiovascular diseases and metabolic changes.

Therefore, data on prevalence of PCOS provides knowledge about the distribution of the health problem in this population and draws attention to the investigation of its causes. It is a rational basis for helping with the choice of interventions to be implemented. They also draw the attention of healthcare professionals, responsible for quality care, mainly as to the measures to prevent such diseases in this population group to avoid non-reversible aggravations, as in the case of cardiovascular diseases.

For that purpose, it is highlighted that the treatment of PCOS is not limited to the approach to reproductive effects such as infertility, anovulation, and hirsutism, but it is also directed to the promotion of cardiovascular health. In this regard, non-pharmacological measures are being highlighted, especially nutritional counseling and regular practice of physical activities. Despite the fact that the long-term treatment strategies – which are more effective for PCOS – are not fully known, it appears that lifestyle changes, together with dietary changes, regular practice of physical activities, and weight loss, in addition to smoking cessation, stress management, and moderate alcohol consumption, are essential.[22,23]

In the 70's, the "critical weight hypothesis" was postulated in relation to the occurrence of the first menstruation, based on population studies, which suggest that a weight of approximately 48 kg was necessary for the occurrence of menarche. Thereafter, this hypothesis was modified based on the body composition, proposing that, for the occurrence of menarche, it would be required that at least 17% of the total body weight was composed of fat at age 13 years, and that at least 22% body fat would be necessary for the maintenance of menstrual cycles at age 16 years.[24]

In the present study, there was no association between the BMI and the presence of PCOS, unlike other studies,[3,18,25] which indicate that obese adolescents usually have higher chances to develop PCOS. Such result may be supported by the fact that the majority of adolescents in the present study had normal weight when classified by BMI/age, given that there was no difference between the groups.

With respect to age at menarche and excess adiposity, an inverse correlation between weight and BMI values and age at menarche was observed, showing that overweight may be related to the occurrence of early menarche. Fonseca, Sichieri, and Veiga,[26] when assessing 208 adolescents in Niterói, Brazil in the age group of 15 to 17 years old, found that the average age at menarche is 11 years and 5 months for overweight girls and 12 years and 4 months for girls with normal weight ($p = 0.002$). Accordingly, Vieira, et al.,[27] when analyzing adolescents of Viçosa with normal weight and high body fat percentage (% BF), found that the average age at menarche was lower in those with excess adiposity ($p < 0.002$), evidencing that early menarche is usually associated with excessive body fat.

The prevalence of nutritional disorders is highlighted in this study, and despite the lack of difference between the groups, there were a great number of adolescents with low weight, short stature, or excess weight, factors that may cause damages to the health of this population.

The increase in intra-abdominal adipose tissue, in the concentration of free testosterone, and in the insulin resistance in obese women occurs due to early menarche, which occurs earlier in obese women than in those with normal weight, as the menstruation, as previously reported, is probably initiated when the body reaches a certain body fat percentage.[28]

Huber-Buchholz, Carey, and Norman[29] emphasized in their study that the body fat redistribution appears to be even more important than its loss, as the decrease in abdominal obesity is followed by an improvement in insulin sensitivity, resulting in a positive impact on the restoration of ovarian function, and they also presented results that confirmed the association between PCOS and excess weight.

Hoffman and Ehrmann,[30] when analyzing the cardio-metabolic characteristics associated with PCOS, drew attention to the late metabolic changes in the syndrome, mainly in adolescence, by affirming that, although there is a lack of data in relation to the rates of cardiovascular events and mortality in these patients, a higher prevalence of cardiovascular risk factors has been well documented. In accordance with this study, Giordano[3] emphasized the favorable or determining conditions for cardiovascular diseases and diabetes in adolescents with PCOS, such as the presence of insulin resistance, excess weight, and increased blood pressure. Even though the present study did not find any association between PCOS and CNCDs, it cannot be affirmed that the syndrome is not related to these changes.

The clinical signs of PCOS differ and have several phenotypes, reflecting the varying degrees of metabolic dysfunction. History of low birth weight and early menarche confer increased risks that may lead to PCOS, which symptoms usually initiate during the period close to menarche. It may also begin after puberty, as a result of environmental modifiers, such as weight gain and sedentary lifestyle.[31,32]

The signs and symptoms of PCOS usually arise during peripubertal years with premature pubarche (PP) (appearance of pubic hair or jaws in girls before 8 years old with no other signs of puberty). Adolescents with medical history of PP have high risk to develop a complete phenotype of PCOS, including ovarian hyperandrogenism and chronic anovulation.[33]

In the study by Teixeira et al.,[17] conducted with 140 pre- and post-pubertal healthy girls between 2 and 18 incomplete years of age, most of those with polycystic ovaries had not menstruated yet, and two patients with history of menarche presented regular menstrual cycles and normal ovarian volumes, which shows the inconsistency of the results found in studies observed the influence of the age at menarche in the PCOS.

Conclusion

It can be concluded that there is a relation between younger age at menarche and development of PCOS in adolescents.

It is necessary to identify and treat the factors that exert influence on the menarche, such as excess adiposity and hormonal changes, in order to mitigate the occurrence of PCOS and, as a result, prevent the deleterious effects of the disease (diabetes mellitus type 2, heart diseases, arterial hypertension, endometrial and ovarian cancers, infertility, among others). Therefore, the need to implement new prevention strategies at this life stage is reinforced, as they will reflect on adulthood.

Conflicts of interest

The authors declare no conflicts of interest.

Acknowledgements

The authors would like to thank the Fundação de Amparo à Pesquisa do Estado de Minas Gerais (FAPEMIG) for financing this study.

REFERENCES

1. World Health Organization. Nutrition in adolescence – issues and challenges for the health sector: issues in adolescent health and development. Geneve: World Health Organization; 2005.
2. Organización Panamericana de la Salud. La salud de los adolescentes y los jóvenes en las Américas: escrebiendo el futuro. OPS – Comunicación para la Salud, 6 Washington (DC); OPS: 1995 .
3. Giordano MG. Síndrome dos ovários policísticos na adolescência. Adolesc Saúde. 2009;6(4):6-10.
4. Norman RJ, Dewailly P, Legro RS, Hickey TE. Polycystic ovary syndrome. Lancet. 2007;370(9588):685-97.
5. Costa EC, Soares EMM, Lemos TMAM, Maranhão TMO, Azevedo GD. Índices de obesidad central y factores de riesgo cardiovascular em el síndrome de ovarios poliquísticos. Arq Bras Cardiol. 2010;94(5):615-20.
6. Nobels F, Dewailly D. Puberty and polycystic ovarian syndrome: the insulin/insulin-like growth factor I hypothesis. Fertil Steril. 1992;58(4):655-66.
7. Premoli ACG, Moura MD, Ferriani RA, Sá MFS, Reis RM. Perfil lipídico em pacientes portadoras da síndrome dos ovários policísticos. Rev Bras Ginecol Obstet. 2000;22(2):89-94.
8. Sathyapalan T, Atkin S. Mediators of inflammation in polycystic ovary syndrome in relation to adiposity. Mediators Inflammation. 2010;2010:Article ID 758656.
9. Tan S, Scherag A, Janssen OE, Hahn S, Lahner H, Dietz T, et al. Large effects on body mass index and insulin resistance of fat mass and obesity associated gene (FTO) variants in patients with polycystic ovary syndrome (PCOS). BMC Medical Genetics. 2010;11(12):1-9.
10. Instituto Brasileiro de Geografia e Estatística. IBGE. Censo 2010. Rio de Janeiro: IBGE; 2010.
11. Priore SE, Faria FR, Franceschinni SCC. Crescimento e desenvolvimento na adolescência. In: Priore SE, Oliveira RM, Faria ER, Franceschinni SCC, Pereira PF. Nutrição e saúde na adolescência. Rio de Janeiro: Rubio; 2010. p. 173-82.
12. World Health Organization. Physical status: the use and interpretation of anthropometry: report of a WHO Expert Committee. Geneve: World Health Organization; 1995. p. 263-311.
13. World Health Organization. Growth reference 5-19 years [accessed 9 May 2010]. Available from: http://who.org.int/growthref/who2007_bmi_for_age/en/index.html
14. Giorlandino C, Gleicher N, Taramanni C, Vizzone A, Gentili P, Mancuso S, et al. Ovarian development of the female child and adolescent: I. morphology. Int J Gynecol Obstet. 1989;29(1):57-63.
15. Spritzer PM, Morsch DM, Wiltgen D. Neoplasias associadas à síndrome dos ovários policísticos. Arq Bras Endocrinol Metab. 2005;49(5):805-10.
16. Bridges NA, Cooke A, Healy MJ, Hindmarsh PC, Brook CG. Standards for ovarian volume in childhood and puberty. Fertil. Steril. 1993;60(3): 456-60.
17. Teixeira RJ, Silva VCG, Freitas JR, Henriques JLM, Guimarães MM. Ovários policísticos em meninas e adolescentes normais: uma avaliação ultra-sonográfica. Radiol Bras. 2001;34(4):217-20.
18. Bouzas I. Síndrome dos ovários policísticos na adolescência. Adolesc Saúde. 2007;4(2):43-8.
19. Kuba VM, Cavaliere PM, Christóforo AC, Faria Júnior R, Caetano R, Coeli CM, et al. Resistência insulínica e perfil metabólico em pacientes com síndrome dos ovários policísticos de peso normal e sobrepeso/obesidade. Arq Bras Endocrinol Metab. 2006;50(6):1026-33.
20. Martins WP, Soares GM, Vieira CS, Reis RM, Sá MFS, Ferriani RA. Resistência à insulina em mulheres com síndrome dos ovários policísticos modifica fatores de risco cardiovascular. Rev Bras Ginecol Obstet. 2009;31(3):111-6.
21. Faria ER, Franceschini SCC, Peluzio MCG, Priore SE. Síndrome metabólica em adolescentes: uma atualização. Nutrire: Rev Soc Bras Alim Nutr (J Braz Soc Food Nutr). 2009;34(2):179-94.
22. Norman RJ, Davies MJ, Lord J, Moran LJ. The role of lifestyle modification in polycystic ovary syndrome. Trends Endocrinol Metab. 2002;13(6):251-7.
23. Hoeger KM, Kochman L, Wixom N, Craig K, Miller RK, Guzick DS. A randomized, 48-week, placebo-controlled trial of intensive lifestyle modification and/or metformin therapy in overweight women with polycystic ovary syndrome: a pilot study. Fertil Steril. 2004;82(2):421-9
24. Vitalle MSS, Tomioka CY, Juliano Y, Amancio OMS. Índice de massa corporal, desenvolvimento puberal e sua relação com a menarca. Rev Assoc Med Bras. 2003;49(4):429-33.
25. Fernandes JBF, Soares GM, Martins WP, Sá MFS, Ferriani RA, Reis RM, et al. Obesidade e alteração da estrutura arterial em mulheres jovens com síndrome dos ovários micropolicísticos. Rev Bras Ginecol Obstet. 2009;31(7):342-8.
26. Fonseca VM, Sichieri R, Veiga GV. Fatores associados à obesidade em adolescentes. Rev Saúde Pública. 1998;32(6): 541-9.
27. Vieira PR, Faria E, Faria F, Sperandio N, Araújo C, Stofeles R, et al. Fatores associados à adiposidade em adolescentes do sexo feminino eutróficas com adequado e elevado percentual de gordura corporal: elaboração de um modelo de risco. Arch Latinoamericanos Nutrición. 2011;6(3):279-87.
28. Jung R. Obesity as a disease. Br Med Bull. 1997;53(2):307-321.
29. Huber-Buchholz MM, Carey DGP, Norman RJ. Restoration of reproductive potential by lifestyle modification in obese polycystic ovary syndrome: role of insulin sensitivity and luteinizing hormone. J Clin Endocrinol Metab. 1999;84(4):1470-4.
30. Hoffman LK, Ehrmann DA. Cardiometabolic features of polycystic ovary syndrome. Nat Clin Pract Endocrinol Metab. 2008;4(2):215-22.

31. Rosenfield RL, Barnes RB. Menstrual disorders in adolescence. Endocrinol Metab Clin North Am. 1993;22(3):491-505.
32. Ibánez L, Valls C, Marcos MV, Ong K, Dunger DB, Zegher F. Insulin sensitization for girls with precocious pubarche and with risk for polycystic ovary syndrome: effects of prepubertal initiation and postpubertal discontinuation of metformin treatment. J Clin Endocrinol Metab. 2004;89(9):4331-7.
33. Allahbadia GN, Merchant R. Polycystic ovary syndrome and impact on health. Middle East Fertil Soc J. 2011;16(1):19-37.