

Sedentarism, overweight and gut microbiota: increased risk of type II diabetes mellitus in women with polycystic ovaries

Sedentarismo, sobrepeso e microbiota intestinal: risco aumentado de diabetes mellitus tipo II em mulheres com ovários policísticos

Sedentarismo, sobrepeso y microbiota intestinal: mayor riesgo de diabetes mellitus tipo II en mujeres con ovarios poliquisticos

RESUMO

Objetivo: Avaliar a influência do sedentarismo e sobrepeso na precocidade do Diabetes mellitus tipo 2 (DM II) em mulheres com Síndrome de Ovário Policístico (SOP). Método: estudo piloto observacional, de análise documental e entrevistas desenvolvido via plataforma GoogleForms® com 42 mulheres com SOP com idade entre 21 e 45 anos, com e sem diagnóstico de DM II. Resultados: 42 mulheres fizeram parte do estudo, sendo 23 diabéticas e 19 não diabéticas. Mulheres que gastam mais tempo em frente à televisão, ou usando o celular podem chegar a elevar o risco de obesidade em até 23% e de Diabetes mellitus 2 em mulheres com Síndrome do ovário policístico em até 14%. Conclusão: a prática da atividade física não demonstrou ser suficiente para reduzir o IMC, sendo o sobrepeso uma característica comum nas mulheres com SOP sem DM e com DM II. Desta forma controle de peso precisam ser melhor esclarecidas ao grupo.

DESCRITORES: Síndrome do Ovário Policístico; Diabetes; Sobrepeso.

ABSTRACT

Objective: To evaluate the influence of a sedentary lifestyle and overweight on the precocity of Type 2 Diabetes mellitus (DM II) in women with Polycystic Ovary Syndrome (PCOS). Method: observational pilot study, document analysis and interviews developed via the GoogleForms® platform with 42 women with PCOS aged between 21 and 45 years, with and without a diagnosis of DM II. Results: 42 women took part in the study, 23 diabetics and 19 non-diabetics. Women who spend more time in front of the television or using their cell phones can increase the risk of obesity by up to 23% and of Diabetes mellitus 2 in women with Polycystic Ovary Syndrome by up to 14%. Conclusion: the practice of physical activity has not been shown to be sufficient to reduce BMI, with overweight being a common characteristic in women with PCOS without DM and with DM II. Therefore, weight control needs to be better explained to the group.

DESCRIPTORS: Polycystic Ovary Syndrome; Diabetes; Overweight.

RESUMEN

Objetivo: Evaluar la influencia del sedentarismo y el sobrepeso en la precocidad de la Diabetes mellitus tipo 2 (DM II) en mujeres con Síndrome de Ovario Poliquistico (SOP). Método: estudio piloto observacional, análisis documental y entrevistas desarrolladas a través de la plataforma GoogleForms® con 42 mujeres con SOP de entre 21 y 45 años, con y sin diagnóstico de DM II. Resultados: Participaron en el estudio 42 mujeres, 23 diabéticas y 19 no diabéticas. Las mujeres que pasan más tiempo delante de la televisión o usando el móvil pueden aumentar el riesgo de obesidad hasta un 23% y de Diabetes mellitus 2 en mujeres con Síndrome de Ovarios Poliquisticos hasta un 14%. Conclusión: la práctica de actividad física no ha demostrado ser suficiente para reducir el IMC, siendo el sobrepeso una característica común en mujeres con SOP sin DM y con DM II. Por lo tanto, el control del peso necesita ser mejor explicado al grupo.

DESCRIPTORES: Síndrome de ovario poliquistico; Diabetes; Sobrepeso.

RECEBIDO EM: 16/01/2023 **APROVADO EM:** 14/03/2023

How cited: Massinhan BB, Giaretta DV, Giaretta FL, Lorenzi JB, Lima DD, Luciano Henrique Pinto LH. Sedentarism, overweight and gut microbiota: increased risk of type II diabetes mellitus in women with polycystic ovaries (Edição Brasileira) [Internet]. 2023 [acesso ano mês dia];13(88):13389-13400. Disponível em:

DOI: 10.36489/saudecoletiva.2023v13i88p13389-13400

ID **Beatriz Bittencourt Massinhan**
Bolsistas de Pesquisa Projeto ECOSAM, graduandas em Medicina.

ID **Déborah Vanessa Giaretta**
Graduandas em Medicina.

ID **Fernanda Leonardi Giaretta**
Graduandas em Medicina.

ID **Jordany Bosse Lorenzi**
Graduandas em Medicina.

ID **Daniela Delwing de Lima**
Professor do Curso de Medicina.

ID **Luciano Henrique Pinto**
Professor do Curso de Medicina, 4 Coordenador do Projeto Integrado ECOSAM
Universidade da Região de Joinville – UNIVILLE.

INTRODUCTION

Polycystic Ovary Syndrome (PCOS) is a clinical condition whose etiology is multifactorial, having genetic origins and possible environmental conditions; including today exposure to Endocrine Disrupters (ED).¹ The main clinical manifestations include the presence of acne, hirsutism, alopecia, in addition to menstrual changes and infertility. There is also a greater predisposition to developing diseases such as Diabetes Mellitus (DM II)², in which modifiable risk factors (MRFs) such as excess weight and sedentary lifestyle add to an even greater chance of risk of DM II, especially in an “early” form (before an expected average age of 40 years).^{3,4}

It is known that this syndrome is common in menopausal women, and that its prevalence is estimated at 105 million women worldwide.¹ Guidelines based on multi-year evidence developed by the European Society of Human Reproduction and Embryology (ESHRE) and the American Society of Reproductive Medicine (ASRM), and endorsed by more than 40 international societies involved in PCOS have defined this clinical condition as being a set manifestations such as: [1]

oligo-ovulation and/or anovulation, [2] hyperandrogenism and [3] the presence of polycystic ovaries.²

In most cases, the clinical management of PCOS aims to control hyperandrogenism - resulting from the conversion of excess progesterone into testosterone - and normalize ovulatory cycles. However, a characteristic of PCOS is the presence of insulin resistance (IR) in some women; being a strong facilitator for the early development of DM II.^{3,5} Here it is emphasized that “early” DM II would be that acquired before the age of 40; an expected average age for the development of DM II among women predisposed to this disease and who do not deal with prevention through the management of modifiable risk factors (MRF).⁶ These factors include obesity and the adoption of sedentary practices, which can be reversed through changes in habits, especially physical activity.

Therefore, this work aims to investigate the following questions: *Does practicing any physical activity help control weight in women with PCOS, in order to avoid the “precociousness” of DM II?* This study intends to have an initial view on the issue to guide more in-depth studies in the future, in addition to theoretically discussing the issues in-

olved in the problem raised.

METHOD

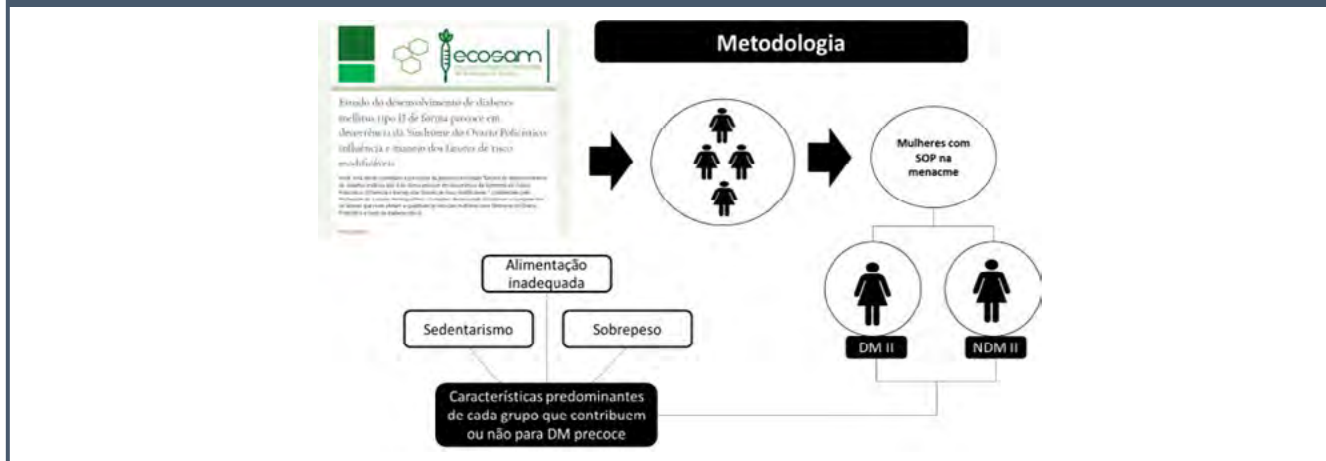
This study was carried out in an exploratory manner, as a pilot for subsequent studies. It was carried out through an online survey carried out among women diagnosed with PCOS, participants in the group “Convive – Polycystic Ovary Syndrome” on the social network Facebook®, which has more than 2 thousand women with this condition and is attended by health professionals who provide information about PCOS. The survey took place via the GoogleForms® platform, between May and June 2020. It was developed with the consent and agreement of the moderators of that group, who presented the research to the community members.

Based on a survey with several questions regarding the presence of risk factors for DM II, such as overweight, diet and sedentary lifestyle in groups of women with diabetic and non-diabetic PCOS, for comparison purposes. This was an observational study, involving documentary analysis and interviews. The data and information collected corresponded to: [a] **Patient characteristics:** age, family history, general habits; [b] **General aspects:** Following

Artigo Original EN

Beatriz B. Massinhan, Déborah V. Giaretta, Fernanda L. Giaretta, Jordany B. Lorenzi, Daniela D. de Lima, Luciano H. Pinto
Sedentarism, overweight and gut microbiota: increased risk of type II diabetes mellitus in women with polycystic ovaries

Figure 1: Research process, which included a virtualized questionnaire made available to groups of women with PCOS via digital media. Of the total respondents, those diagnosed with DM and those without DM were separated, 2020



Source: data from authors, 2020

a diet, physical activity and BMI.

The population then corresponded to women who reported having been diagnosed with PCOS, and who expressed whether or not they had DM II. Women who did not meet these conditions, who did not agree to participate in the research or who completed the questionnaire incompletely were excluded from the research. The sample used was the convenience sample according to Miot⁷, seeking to reach a total of 40 women (Figure 1).

With regard to physical activity, the practice or not was only questioned according to the interviewee's understanding, as a way of evaluating her understanding of the topic. The data were expressed in graphic form for subsequent analysis and discussion of the results found.

As it involves human beings, the legislation in force in Brazil was respected, and this project was submitted to the Research Ethics Committee (CEP - Comitê de Ética em Pesquisa) of UNIVILLE, being assessed and evaluated as approved, obtaining an approval protocol with CAA registration 26897719.0.0000.5366.

RESULTS

A total of 42 women took part in

the investigation, 23 diabetics and 19 non-diabetics. Diabetics accounted for a total of 53.7% (Figure 2).

The average age of the diabetes group was 35 years, with the most frequent reported age of being diagnosed with diabetes being 30 years, an age considered early for the development of diabetes, highlighting the influence of PCOS on this condition, as on average it is expected to manifest around 40 years of age³ (Figure 3).

The fact that there is an average age of diagnosis of around 30 years for DM II among women with PCOS deserves

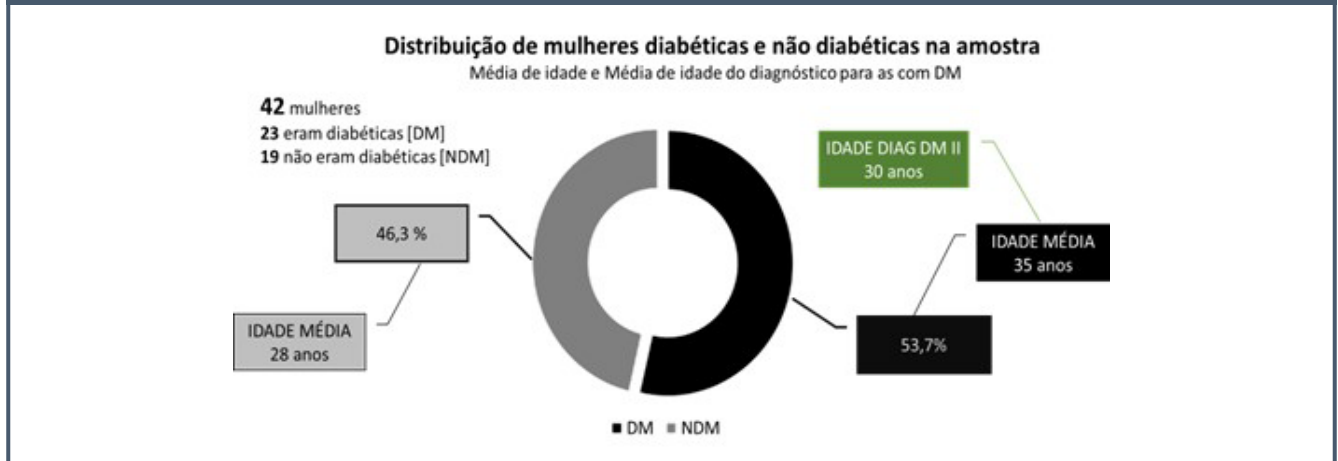
to be highlighted, given the condition in which the average age for developing such a clinical condition is approximately 40 years.³ It is true that the fact that they have PCOS affects the condition regarding Insulin Resistance (IR); which in itself becomes a warning.⁸ Furthermore, women with PCOS have a 3.26 times chance of having impaired glucose tolerance. Studies also indicate that up to 2.87 people have DM II compared to women who do not have PCOS.⁹ These facts draw even more attention to the importance of encouraging weight control and not being

Figure 2: Process of choosing participants. Goal was to reach at least 40 women (Miot convenience sample), 2022



Source: data from authors, 2020

Figure 3: Distribution of women with Diabetes and non-diabetes with their respective average ages in the studied sample, 2020



Source: data from authors, 2020

sedentary among women with PCOS. Therefore, physical activity becomes an important condition as it can be extremely useful in preventing obesity and the increased risk of DM II.

DISCUSSION

Physical activity versus sedentary lifestyle in women with PCOS

When asked about physical activity, women with PCOS and DM II (corresponding to the total of 23 women in the final sample), 16 women declared themselves sedentary, while 7 stated

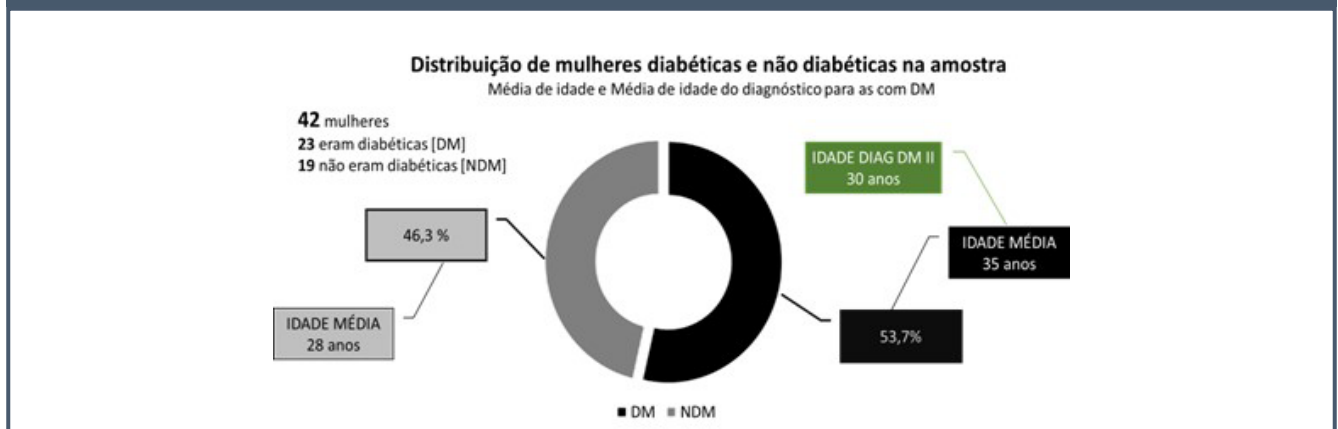
that they performed physical activities weekly (Figure 4). Regarding the Body Mass Index (BMI), 70% of women who declared themselves to be sedentary had an average BMI value of 34.9. The group that declared performing physical activity had a BMI of 33.8 (Figure 4). There was no absolute difference in BMIs between the groups.

Even though the exploratory sample does not allow us to conclude that the practice of physical activity has an influence or not on BMI, reports on the important role of this habit in preventing DM II in women with PCOS

must be considered in the literature.⁷ Practicing aerobic activity contributes positively to preventing the occurrence of pre-diabetic events, such as reducing insulin resistance (IR).¹⁰ Authors also claim reduced glucose tolerance; which would also imply the prevention of DM II. The practice of physical activity would influence the metabolism of fatty acids, which in turn favors the translocation of GLUTs due to their adequate phosphorylation in the serine portion; allowing its translocation aiming at glucose uptake¹¹.

Observing the data found in figure 4

Figure 4: Women with PCOS and DM II. It is noted that the BMI does not vary between groups, 2020

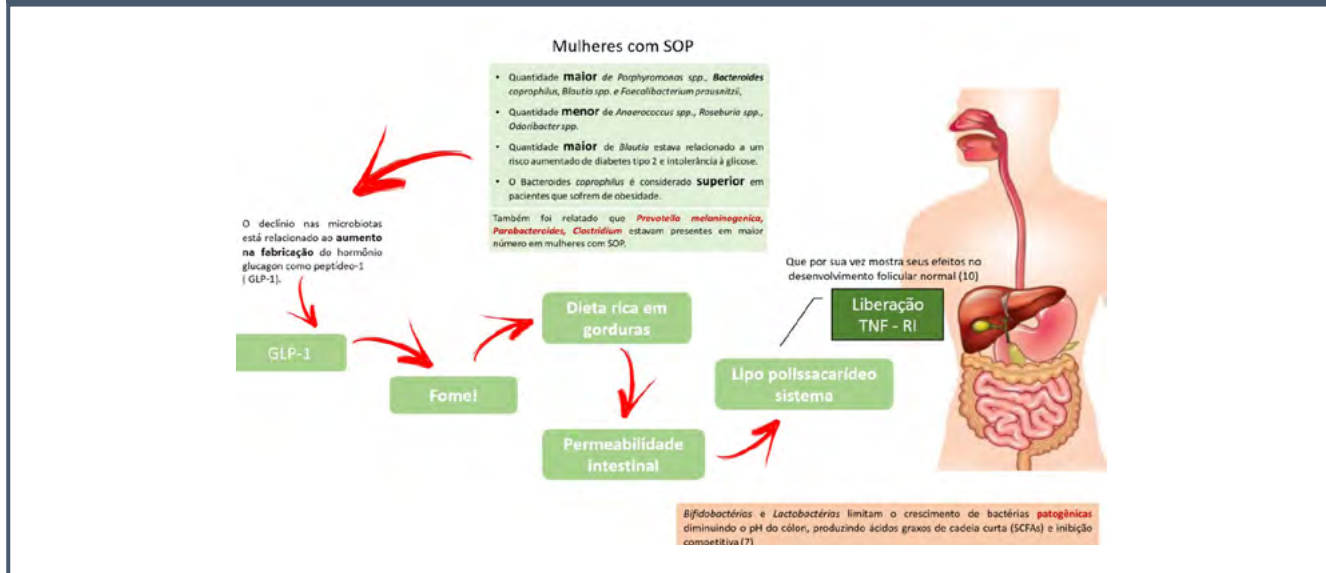


Source: data from authors, 2020

Artigo Original EN

Beatriz B. Massinhan, Déborah V. Giaretta, Fernanda L. Giaretta, Jordany B. Lorenzi, Daniela D. de Lima, Luciano H. Pinto
Sedentarism, overweight and gut microbiota: increased risk of type II diabetes mellitus in women with polycystic ovaries

Figura 5: Alteração na microbiota em mulheres com SOP que leva a fome e aumento de peso, além de RI (Arte: os autores), 2020



Source: data from authors, 2020

– however, considering the limitation of the study in view of the sample used but not refuting a discussion about the phenomena involved – the presence of high BMI is noted both in the group that claims to be engaged in physical activity and in the group that claims to be sedentary. This brings up the discussion about the influence of hormonal changes on weight control¹⁰, and the ideal type/frequency of physical activity for control; the latter being necessary and having to be carried out with adequate monitoring by qualified professionals.

Despite the ability to temporarily compensate IR with hyperinsulinemia, the fact that women with PCOS are overweight may favor the onset of DM II.¹¹ Again, when observing PCOS with DM II, (Figure 4), it is clear that the presence of DM is more present in women with a BMI above 30; a condition that implies affectation in IR.¹² The accumulation of adipose tissue, in turn, affects insulin resistance. Guided by the research question of this work, in which the practice of some physical activity and its collaboration in weight control are questioned with a view to

avoiding the “precociousness” of DM II, the discussion also begins to involve the issue of the limits of physical activity to control weight and reverse IR, and the competition of other factors predisposing to excess weight that need to be worked on together.

Therefore, even though it is understood that physical activity is positive for weight reduction¹⁰, It is necessary to discuss the influence of other factors that contribute to weight gain, and which are also subject to change (thus being MRF). This discussion becomes important since the adoption of a more reductionist thinking can lead to insistence on certain guidelines – from professionals or found in social media¹³ – which would be limiting in its intended purpose: weight reduction and prevention of DM II. It is essential to know other ways that contribute to weight gain that can be managed together with physical activity, always with scientific support.

In the difficulty of weight control through physical activity: The intestinal microbiota of women with PCOS and its influence on weight,

and how to overcome this problem: perspective within science

In an analysis of the microbiota present in the intestine of a healthy woman, *Bacteroides*, *Prevotella*, *Porphyromonas*, *Clostridium* and *Eubacterium* are found, being *Lactobacilli* and *Bifidobacterium* the main beneficial bacteria, which under normal conditions maintain a dynamic balance.¹⁴ Meanwhile, in the intestine of women with PCOS, the microbiota shows reduced alpha dysbiosis and increased beta dysbiosis, with an increase in pro-inflammatory *Bacteroides* and a decrease in *Prevotella*, and also bacteria from the lactobacilli and bifidobacteria families, this IM alpha dysbiosis contributes to low-grade chronic inflammation, which may be a driver for the development of inflammatory diseases (Figure 5).

The effects of using probiotics have already been analyzed in 3 aspects: Weight loss, glycemic reduction and lipid profile control in women with PCOS. A double blind randomized clinical trial with 60 women, in which 30 of them received a capsule of *Lactobacillus acidophilus*, *Lactobacillus casei*,

Bifidobacterium bifidum, were compared with 30 women who received only placebo. In the probiotic group there was a significant reduction in weight compared to placebo. There was also a reduction in fasting plasma glucose, serum insulin concentrations and also serum triglyceride levels¹⁵.

Obesity and abdominal fat distribution play an important role in the maintenance of PCOS.¹⁶ Therefore, just the manifestation of “practicing physical activity” and “not being sedentary” are not absolute for the issue regarding preventing early DM II, but they also cannot be discarded given the contribution they can bring along with other measures, which include food and the use of probiotics, the latter being better evaluated.

CONCLUSION

The study showed – in a small convenience sample – that women with PCOS developed DM II at an age around 11 years earlier than expected, being a trend in this group. Regarding the theme of the article, the declaration of physical activity did not prove to be sufficient to reduce BMI, and overweight is a common characteristic in women with PCOS and DM II. Given this scenario, forms of weight control need to be better explained to the group, regarding the practice of physical activities, and that hormonal changes should not be disregarded. Attention to eating habits also needs to be considered, and the use of probiotics may be a promi-

sing condition, requiring further studies at the moment.

This study has limitations regarding sampling, indicating trends rather than evidence. Not only sedentary lifestyle but other factors together contribute to excess weight and risk of early DM II. New studies including eating habits and adoption of probiotics will be carried out in larger samples.

REFERENCES

1. Palioura E, Diamanti-Kandarakis E. Polycystic ovary syndrome (PCOS) and endocrine disrupting chemicals (EDCs). *Rev Endocr Metab Disord* 2015; 16: 365–371.
2. Hoeger KM, Dokras A, Piltonen T. Update on PCOS: Consequences, Challenges, and Guiding Treatment. *The Journal of Clinical Endocrinology & Metabolism* 2021; 106: e1071–e1083.
3. Moghetti P, Tosi F. Insulin resistance and PCOS: chicken or egg? *J Endocrinol Invest* 2021; 44: 233–244.
4. Magliano DJ, Sacre JW, Harding JL, et al. Young-onset type 2 diabetes mellitus — implications for morbidity and mortality. *Nat Rev Endocrinol* 2020; 16: 321–331.
5. Nolan CJ, Prentki M. Insulin resistance and insulin hypersecretion in the metabolic syndrome and type 2 diabetes: Time for a conceptual framework shift. *Diabetes and Vascular Disease Research* 2019; 16: 118–127.
6. Sampath Kumar A, Maiya AG, Shastry BA, et al. Exercise and insulin resistance in type 2 diabetes mellitus: A systematic review and meta-analysis. *Annals of Physical and Rehabilitation Medicine* 2019; 62: 98–103.
7. Miot HA. Tamanho da amostra em estudos clínicos e experimentais. *J vasc bras* 2011; 10: 275–278.
8. Moghetti P. Insulin Resistance and Polycystic Ovary Syndrome. *CPD* 2016; 22: 5526–5534.
9. Elicker Rosin B, Reinert Avilla Machado F, Martina da Rosa S, et al. Influência dos fatores “sobrepeso” e “sedentarismo” no aparecimento precoce de diabetes em mulheres com SOP. *Saud-Coletiv (Barueri)* 2021; 11: 4676–4685.
10. Abdelbasset WK. Resistance Exercise Versus Aerobic Exercise Combined with Metformin Therapy in the Treatment of type 2 Diabetes: A 12-Week Comparative Clinical Study. *EMIDDT* 2021; 21: 1531–1536.
11. Holman GD. Structure, function and regulation of mammalian glucose transporters of the SLC2 family. *Pflugers Arch - Eur J Physiol* 2020; 472: 1155–1175.
12. Kakoly NS, Khomami MB, Joham AE, Cooray SD, Misso ML, Norman RJ, et al. Ethnicity, obesity and the prevalence of impaired glucose tolerance and type 2 diabetes in PCOS: A systematic review and meta-regression. *Hum Reprod Update*. 2018 Jun 1;24(4):p.55–67.
13. Costa MF, Prado SD, Carvalho MC da VS. Orthorexia in social media: reflections between health and disease. *Saúde Soc.* [Internet]. 2022 May 16 [cited 2022 Jun 18];31(2):e210760pt. Available from: <https://www.revistas.usp.br/sausoc/article/view/197852>
14. Ahmadi S, Jamilian M., Karamali M., Tajabadi-Ebrahimi M., Jafari P, Taghizadeh M. et al. Probiotic supplementation and the effects on weight loss, glycemia and lipid profiles in women with polycystic ovary syndrome: a randomized, double-blind, placebo-controlled trial. *Hum Fertil (Camb)*. 2017; 20(4):254–61.
15. Darvishi S, Rafrat M, Asghari-Jafarabadi M, Farzadi L. Synbiotic supplementation improves metabolic factors and obesity values in women with polycystic ovary syndrome independent of affecting apelin levels: a randomized double-blind placebo-controlled clinical trial. *Int J Fertil Steril*. 2021; 15(1):51–9.
16. Green, M., Arora, K., Prakash, S. Microbial Medicine: Prebiotic and Probiotic Functional Foods to Target Obesity and Metabolic Syndrome. *Int. J. Mol. Sci.* 2020, 21 (8), 2890; <https://doi.org/10.3390/ijms21082890>