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POLYCYSTIC OVARIAN SYNDROME - CURRENT CHALLENGES

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Abstract: Polycystic ovary syndrome (PCOS) is a complex endocrinological condition that affects around 5% to 10% of women of childbearing age, with impacts that go beyond the reproductive system. Characterized by hyperandrogenism, anovulation and the presence of multiple ovarian cysts, PCOS often coexists with Metabolic Syndrome, increasing the risk of complications such as insulin resistance, obesity, dyslipidemia, type 2 diabetes and cardiovascular disease. Recent research reveals that the metabolic and hormonal symptoms of PCOS can appear early, affecting health in a comprehensive way. Scholars point out that obesity and reduced baroreflex sensitivity are aggravating factors. In addition, there is growing evidence that biomarkers such as asprosin level and Achilles tendon thickness can help diagnose and understand the associated cardiovascular risks. In the field of treatments, new approaches are being explored. In addition to traditional treatments such as metformin and contraceptives, research points to the potential of stem cell therapies and the use of natural compounds such as Nigella sativa and melatonin to relieve symptoms. GLP-1 agonists, such as liraglutide, have also shown efficacy in follicular development and in reducing insulin resistance, offering promising alternatives. Advances in therapeutic and diagnostic strategies indicate a promising future for the management of PCOS. However, the condition requires a multidisciplinary and personalized approach that addresses both symptoms and metabolic comorbidities. By deepening research into the mechanisms and interventions for PCOS, it is hoped to promote a better quality of life for affected women.
Keywords: Polycystic Ovary Syndrome; Hyperandrogenism; Metabolic Syndrome; Insulin Resistance; Anovulation.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is one of the most common endocrinopathies among women of reproductive age, affecting around 5% to 10% of this population. Characterized by hormonal changes that include hyperandrogenism, anovulation and the presence of multiple ovarian cysts, PCOS is often associated with a series of metabolic and cardiovascular complications that go far beyond the reproductive system. The condition is often accompanied by insulin resistance, obesity, dyslipidemia and an increased risk of developing type 2 diabetes and heart disease, conditions that constitute what is known as Metabolic Syndrome.

In recent years, research into PCOS has advanced on several fronts, exploring everything from early identification of the syndrome to the development of new biomarkers and innovative therapies for its treatment. Recent studies have focused on the interrelationship between PCOS and metabolic complications, as well as new therapeutic possibilities that go beyond conventional treatments, such as the use of stem cells, hormone supplements and emerging pharmacological interventions.

This discussion aims to present an analysis of these studies, highlighting the risk factors, the metabolic implications of PCOS and the most promising treatments. By better understanding the mechanisms and impact of this syndrome, it is hoped to contribute to a more effective and personalized approach, capable of mitigating its effects and improving the quality of life of affected women.

METHODOLOGY

RESEARCH CHARACTERIZATION

The aim of this study was to associate Polycystic Ovary Syndrome (PCOS) with metabolic and structural consequences in women's bodies, as well as to bring to light new treatments that have already been consolidated or are still being studied.

SCIENTIFIC LITERATURE SEARCH

A literature review was carried out on the subject of Polycystic Ovary Syndrome (PCOS).

The searches were carried out in the following databases: Portal Regional da BVS (Regional Portal of the Virtual Health Library) and Scielo (Scientific Electronic Library Online). Articles were read and selected in English, Portuguese and Spanish, published in the last 6 years (2019-2024), according to the criteria available in each database.

The descriptors used were: Polycystic Ovary Syndrome and Metabolic Syndrome in the VHL Portal, using the Boolean operator OR between the descriptors and AND between polycystic ovary syndrome, *fulltext* and 2019-2024. In Scielo, all articles from 2019 to 2024 were read and selected.

Articles selected for title reading	
Databases	No. of articles
SCIELO	17
VHL PORTAL	50
Total	67

Table 1 - Selected articles

After reading titles / selected for reading abstracts	
Databases	No. of articles
SCIELO	11
VHL PORTAL	44
Total	55

Table 2 - Articles selected for reading

After reading the abstracts/selected for reading in full	
Databases	Number of articles
SCIELO	08
VHL PORTAL	24
Total	32

Table 3 - Articles selected for full text

INCLUSION AND EXCLUSION CRITERIA

The following were included: studies available in full in the databases; in the last 6 (six) years; in Portuguese, English and Spanish.

The following were excluded: articles in other languages, in other periods, incomplete, restricted, paid for or not in line with the study's objective.

DISCUSSION

The discussion on Polycystic Ovarian Syndrome (PCOS) and its association with metabolic syndromes and advances in treatments reflects the complexity of this multifaceted condition, which impacts on women's reproductive, metabolic and cardiovascular health.

PCOS is characterized by menstrual irregularities, hyperandrogenism and the presence of polycystic ovaries. Studies such as those by Hachul et al. (2019) show that obesity and hyperandrogenism exacerbate sleep disorders in PCOS, highlighting the impact of hormonal changes on general well-being. In addition, Lana et al. (2020) indicate that metabolic impairments can appear in the early stages of reproductive life, intensifying the risk of cardiovascular and metabolic diseases.

PCOS is often associated with Metabolic Syndrome (MS), a set of conditions such as hypertension, abdominal obesity and insulin resistance. Tavares and Barros (2019) document that the prevalence of MetS varies according to the PCOS phenotype, suggesting the need for personalized treatment strategies.

Recent research also addresses the need for new biomarkers and diagnostic methods.

RESULTS

STUDY	OBJECTIVE	SAMPLE/POPULATION	RESULTS	CONCLUSION
1- HACHUL, H. et al., 2019	To evaluate the sleep of women with PCOS, with and without hyperandrogenism, compared to a healthy control group, as well as to study the effects of hyperandrogenism and obesity on sleep parameters.	44 volunteers were recruited to take part in the study.	Women with PCOS had lower subjective sleep quality, an increased incidence of of snoring e higher risk for obstructive syndrome, based on the on the questionnaire. Furthermore, after o adjustment for body body mass index, women with PCOS had shorter REM sleep time than those in the control group. Among women with PCOS, those with hyperandrogenism hyperandrogenism had differences in any variable. Women with obstructive apnea syndrome were diagnosed in the PCOS group.	The results indicate that PCOS affects the subjective and objective qualities of sleep due to the reduction in REM sleep time in women diagnosed with the syndrome. Obesity affected sleep-related parameters, but hyperandrogenism had no effect. Obstructive apnea syndrome was only diagnosed in women with PCOS.
2-LANA, M. P. et al, 2020	Determine if women with PCOS have a higher risk of Metabolic Syndrome or some degree of metabolic impairment.	96 women diagnosed with PCOS (Rotterdam consensus criteria)	Forty by percent of women with a BMI <25 kg/m2; 85,4% with blood pressure <130/85 mm Hg; 22.9% had HDL cholesterol >50 mg/dl, 57.3% had triglycerides <150 mg/dl, 63.5% had fasting blood glucose <100 mg/dl. According to the ATP criteria III to SM, 8,33% had no criteria, 19.79% had one criterion, 15.63% had two criteria, 41.67% had three criteria, 13.54% had four criteria, 1.05% had all five criteria.	Considering the high prevalence of MS or some altered metabolic component in patients with PCOS at the time of diagnosis, their screening regular is necessary to reduce mortality and morbidity in these women.
3-LAVOR, C. B. H.; VIANA JÚNIOR, A. B.; MEDEIROS, F. DAS C., 2022	Evaluate a association between PCOS and metabolic syndrome (MS), adding liver assessment by elastography and ultrasound for correlation with non-alcoholic fatty liver disease (NAFLD). liver disease (NAFLD).	The following were included 100 women, 50 with PCOS and 50 controls, matched by age by age (18-35 years) and body mass index index (BMI), restricted to patients who were overweight and obesity grade 1, at the Maternity School Assis Chateaubrian, Federal University of Ceará, Brazil. University, Brazil.	Patients with PCOS presented a risk 4 times greater risk of having MetS, odds ratio (range of confidence of 95%) = 4.14, from than those in the control group. Women with PCOS had a higher average abdominal circumference (100.9±9.08 cm vs 94,96±6,99 cm) e triglycerides (162±54.63 mg/dL vs 137.54±36.91mg/ dL) e lower average of cholesterol HDL (45.66±6.88 mg/dL vs 49,78±7,05 mg/dL),	Women with PCOS had a 4 times higher frequency of MetS, with no statistical difference in the proportion There was no change in liver stiffness between the groups. in elastography. The results can be extended only to populations with overweight and grade 1 obesity, with or without PCOS.
4-MANIQUE, M. E. S.; FERREIRA, A. M. A. P., 2022	Summarize the existing evidence on PCOS in adolescence, particularly its diagnostic criteria and therapeutic options	This is a literature review article	The diagnostic criteria include irregular menstrual cycles according to with time post-menarche e evidence of hyperandrogenism clinical and/or biochemical after excluding other causes. Polycystic of the ovaries should not be used as a diagnostic criterion. Treatment should be directed at the manifestations and/or comorbidities, even in the absence of a definitive diagnosis. are the first-line treatment. treatment. Combined oral contraceptives, metformin or anti-androgens may also be considered as adjuvants.	PCOS screening in adolescence is fundamental, because it allows early intervention symptoms symptoms and comorbidities present, leading to better reproductive and metabolic results in the long term.

5-PHILBOIS, S. V. et al., 2019	Investigating the changes in autonomic modulation and SBR in women with PCOS with PCOS, as well as to evaluate whether these alterations are due to PCOS or to an increase in body fat	Thirty volunteers with normal weight [body index (BMI) <25 kg/m2] without PCOS (control group) and 60 volunteers with PCOS, divided into into normal (BMI < 25 kg/m2, N = 30) and obese women (BMI > 30 kg/m2, N = 30).	Compared to the normal weight groups, there were no differences in the autonomic parameters. The comparison between the PCOS groups showed that both groups did not differ in the analysis of APV. However however, the obese SOP group showed lower of SBR and HRV in oscillations of low and high frequencies, in units absolute.	Obesity has had little influence on a heart rate heart rate variability (HRV) in women with PCOS, but it can affect spontaneous SBR.
6- MIRZOHRE H, S. T.; PANAHI, P.; HEIDARI, F., 2024	Evaluate cardiac autonomic function by analyzing a heart rate heart rate variability (HRV) in women with PCOS.	Systematic review	Combined analyses indicated a notable decrease in HRV among individuals with PCOS compared the control group. Subgroup analysis revealed significant changes of HRV in PCOS cases with normal weight e overweight. No significant changes in VFC was observed in obese PCOS cases.	Evidence suggests decreased HRV in individuals with PCOS in compared to the control group without PCOS.
7-TAVARES, A.; BARROS, R. C. R., 2019	Evaluate a prevalence of metabolic syndrome in phenotypes polycystic syndrome.	111 women aged between 18 and 39 diagnosed with PCOS according to the Rotterdam criteria, and grouped into four phenotypes: A: ovulatory dysfunction + hyperandrogenism + polycystic ovaries; B: ovulatory dysfunction + hyperandrogenism; C: hyperandrogenism smo + polycystic ovaries; D: ovulatory dysfunction + polycystic ovaries.	The prevalence of metabolic syndrome found in this sample was 33.6%, e there was no statistically significant difference ($p < 0.05$) between the four phenotypes. However, o phenotype D showed an average glucose level significantly higher after fasting (93.6 mg/dL) e two hours after ingestion of a solution containing 75g of anhydrous glucose (120 mg/dL), as well as o lowest average of cholesterol HDL (44.7 mg/dl). The women in this group showed a high prevalence of abdominal circumference ≥ 80 cm (68.2%), as well as the highest average of abdominal circumference (90.1 cm). Among women with an abdominal circumference ≥ 80 cm, phenotype A increased the chance of by approximately 6 times the chance of developing metabolic syndrome in relation to phenotype C.	The four phenotypes of ovarian syndrome phenotypes showed similar rates of prevalence of metabolic syndrome; abdominal obesity played a a relevant role in the development of metabolic alterations, regardless of phenotype.
8-WEN, X; WANG, L.; BAI, E., 2024	Investigate the metabolic characteristics of different phenotypes in women with PCOS of reproductive age.	442 women with PCOS were recruited in this cross-sectional study. The women were divided into three groups: the chronic ovulatory dysfunction and hyperandrogenism group (OD-HA group, n = 138), the chronic ovulatory dysfunction and polycystic ovarian morphology (group OD- PCOM, n = 161) and the hyperandrogenic group e polycystic ovarian morphology (group HA- PCOM, n = 143).	The body mass index (BMI), waist circumference e waist-to-hip ratio (WHR) of women from the OD-HA group and the HA- PCOM group were significantly higher than those of the women from the OD-PCOM group ($p < 0.05$). Serum insulin concentration and evaluation of the homeostasis model of insulin resistance homeostasis model at 2 h and 3 h after oral glucose powder in women in the of the OD--HA group and the HA- PCOM group were higher than those of the OD-PCOM group ($p < 0.05$).Cholesterol total serum (TC), triglycerides (TG) and low-density lipoprotein cholesterol (LDL-C) in women of the OD-HA group and the HA- PCOM group were higher than those in women from the OD-PCOM group ($p < 0.05$).	The phenotypes of OD--HA e HA- PCOM in women with PCOS were vulnerable to metabolic disorders compared to with OD-PCOM. Thus, metabolic metabolic disorders in women with PCOS, especially those with the HA phenotype, should receive more attention to reduce long-term complications.

9-LUO, Y. et al., 2024	Identification of possible diagnostic genes for atherosclerosis in women with PCOS	O database database Gene Expression Omnibus database provided four sets sets of SOP data and two AS datasets for this study.	The SOP group identified 53 genes and the AS group identified 175 genes by crossing DEGs and WGCNA key modules. Next, 18 genes from two groups were analyzed by algorithm algorithm. Death-associated protein kinase kinase 1 (DAPK1) was recognized as an essential gene. The results of immune infiltration and single gene GSEA suggest that DAPK1 is associated with with immune responses mediated by T cells.	Association between AS e SOP e identified DAPK1 as a diagnostic biomarker for AS in PCOS.
10-JIANG, J.; GAO, S; ZHANG, Y., 2019	Investigating the therapeutic effects of dimethyldiguanide associated with with citrate citrate clomiphene no treatment of PCOS.	79 patients with POCS and 35 healthy women were included, and endometrial biopsies were obtained.	O combined treatment improved a cervical mucus score, the rate of rate follicular development, ovulation rate single follicle, endometrial thickness, the positive rate of three lines lines and the level of FSH.	The therapeutic effect of combined treatment is better than clomiphene citrate alone in treatment of PCOS.
11- LOMBARDI, L. A. et al, 2019	Evaluate the ovarian effects effects of melatonin (Mel) in rats with polycystic syndrome (PCOS) before and after the induction of estro- permanent.	Thirty-two female rats with regular estrous cycles were equally divided into four into four groups: 1) GCtrl - estrus phase. 2) GSOP - permanent phase. 3) GMel1 - treated by 60 days with Honey (0,4 mg/kg) during a induction permanent and 4) GMel2 - pussy with SOP e treated with honey.	The GSOP showed no of corpora lutea and several ovarian cysts, as well as numerous interstitial cells. A presence of corpora lutea and an increase of primary eantral follicles were observed in the in the groups treated with Mel, which also showed a decrease in the number of cysts and in area occupied by the interstitial cells. The results were more evident in GMel1 than in GMel2.	The administration of melatonin prevents the state of permanent oestrus in rats with PCOS. This effect is more efficient when melatonin is administered after induction of the state permanent.
12- ZHAO, M. et al., 2024	Currently, several clinical trials have been carried out with the GLP-1 receptor agonist liraglutide in treatment of polycystic ovary syndrome (PCOS). In However, the effect of liraglutide on follicle development and its specific mechanism remain unclear. are still unclear.	O RNA sequencing was used to explore the molecular characteristics of granulosa cells of PCOS patients treated with liraglutide.	Liraglutide inhibited secretion of inflammatory factors in cells granulosa of PCOS, among which CXCL10 was the most significant. Liraglutide inhibited the secretion of of CXCL10 via the JAK signaling pathway in PCOS granulosa cells and may improve the disorders of follicular development induced by dehydroepiandrost erone (DHEA), which are reverted by CXCL10 supplementation.	This study suggests that liraglutide inhibits the secretion of CXCL10 in granulosa cells by the signalling signaling JAK signaling pathway, thus improving homeostasis homeostasis between the oocyte and the the granulosa cells before physiological ovulation and, ultimately improving follicular development e ovulation in PCOS, which provides further evidence for the clinical application of liraglutide in treatment of ovulatory disorders in PCOS.
13- SARVESTA NI, M. et al, 2024	The mesenchymal stem cells derived from from placenta (PDMSCs) are derived from the placenta and have advantages over other sources of MSCs in terms availability, safety and immunomodulation.	Twenty female Wistar rats were assigned to a four groups (n = 5), including control, sham, SOP and SOP groups + PDMSCs.	O number of corpus luteal and primordial follicles, primary, secondary and antral was significantly higher in the SOP+PDMSCs group in compared to the group GROUP. However however, the number of cystic follicles decreased significantly in the group SOP+PDMSCs. LH and testosterone levels also decreased, while the levels of FSH levels increased in the PCOS+PDMSCs group. The levels levels of fasting blood glucose, fasting insulin and resistance and insulin resistance in the PCOS+PDMSCs group. In addition, the profile improved and AST E ALT decreased.	The results of this study suggest that PDMSCs are an option potential of treatment for PCOS because they can effectively restore a folliculogenesis and correct hormonal imbalances, lipid profiles and liver dysfunction in a rat model of PCOS. However, more research is needed to establish safety e efficacy of PDMSCs in the treatment of PCOS.

14- OZTURK, H. A., 2024	Investigate the thickness of the calcaneal tendon (ATT) and the levels of asprosin in patients with PCOS and to evaluate the relationship of these parameters, which may related to cardiometabolic diseases.	45 patients sex female with PCOS e 30 healthy women of a similar age.	Serum levels of DHEAS, total testosterone, AMH and asprosin, HOMA-IR value, LF/FSH ratio and ATT values were higher in patients with PCOS. In the univariate analysis, the parameters associated with ATT were detected as asprosin, DHEAS and AMH. In the linear regression analysis, the levels of asprosin e DHEAS were found associated with ATT.	ATT values and serum asprosin levels were found to be significantly increased in patients with PCOS, and there is a very close positive relationship between ATT and serum levels of asprosin. For this reason, it was thought that measuring ATT could be a cheap, simple and cheap, simple and non-invasive monitoring invasive that could be used in monitoring routine cardiometabolic assessment of patients with PCOS.
15- ZHANG, R. et al., 2024	Clarifying the potential mechanism of Decoction of YJKL no PCOS treatment based on network pharmacology and verification of experiments.	The network pharmacology and experimental validation approach was used to investigate the bioactive ingredients, critical targets and potential mechanisms of the against PCOS.	Five main targets were screened, Threonine kinase 1 (AKT1), Tumor cell antigen p53 (TP53), Tumor necrosis factor necrosis factor (TNF), Albumin (ALB) and Vascular endothelial growth factor A (VEGFA). A analysis KEGG showed that treatment with YJKL for PCOS includes the AGE- RAGE signaling pathway in diabetic complications, the TNF signaling pathway and the HIF-1 signaling pathway. The molecular docking results showed that the compounds have greater affinity with the targets.	Based on an approach pharmacology systematic network and experimental verification, our results have comprehensively illustrated the active ingredients, potential targets and molecular mechanism of YJKL for application in PCOS and help illustrate o mechanism of action on a comprehensive level.
16- YU, J. H. et al., 2024	To retrospectively investigate the treatment status of of patients with PCOS who visited a domestic tertiary hospital to analyze patterns of use and the safety of medicines.	212 patients diagnosed with PCOS between July 2014 e September 2022, excluding patients under the age of 13 e those who were not medications were included. 105 adolescents (49.5%) and 107 adults (50.5%).	During the period, 114 patients (53.8%) were prescribed of medroxyprogester medroxyprogester acetate (MPA), 66 (31,1%) received oral contraceptives (ethinylestradiol + drospirenone prescribed for 52 (24,5%)) e 17 (8%) were simultaneously prescribed of MPA e contraceptives oral.	MPA alone and ethinylestradiol with drospirenone were the most prescribed drugs
17- MANSOORI, M. et al., 2024	Investigating the potential therapeutic use of stem cells derived from menstrual blood (MenSCs) and their exosomes in mitigating mitochondrial dysfunction and oxidative stress in cells of granulosa of PCOS.	Using a mouse model of SOP induced by letrozole, granulosa granulosa cells were collected and cultured.	Treatment with MenSCs and their exosomes demonstrated significant improvements in mitochondrial biogenesis, oxidative stress levels e production of estrogen in cells of granulosa of PCOS. Subsequent analyses showed of MenSCs about the exosomes, attributed à their sustained secretion of bioactive factors. MenSCs and exosomes activated pathways related mitochondrial biogenesis and defense antioxidant	This study offers insights about o role of mitochondria of cells cells granulosa in the pathogenesis of PCOS and proposes MenSCs and exosomes as a potential strategy for to mitigate mitochondrial dysfunction and oxidative stress in PCOS.

18- TAY, C. T. et al., 2024	Systematic review and meta-analysis on the risk of clinical events of cardiovascular disease (CVD) in women with PCOS to inform the International PCOS Guideline Evidence-Based Guideline 2023.	Twenty studies involving 1.06 million women (369,317 with PCOS e 692.963 without SOP).	A SOP was associated higher risk of composite CVD , composite ischemic heart disease , myocardial infarction myocardial and stroke. The relationship with cardiovascular mortality was less clear Meta-analyses of RRIs support these findings.	This review provides evidence and highlights the importance to recognize PCOS as a significant risk factor for CVD morbidity. significant risk factor for CVD morbidity. A International 2023 International Evidence-Based PCOS Guideline now recommends awareness of the increased risk of CVD and a comprehensive risk assessment in PCOS to help mitigate the burden of CVD in this common condition and high risk.
19- CHANG, K.-J., 2024	Provide an in-depth examination of the etiology, pathophysiology, diagnosis and treatment of PCOS, focusing on its molecular and cellular aspects.	This study is a review (no sample).	Genome genome wide association association studies (GWASs) have identified several genes candidates related to steroidogenesis and insulin signaling. Environmental factors, such as endocrine disrupting chemicals and lifestyle choices, also exacerbate PCOS traits. In addition of lifestyle changes lifestyle changes and surgical intervention, pharmacological treatments such as anti-androgens, metformin, thiazolidinediones, aromatase inhibitor aromatase inhibitor, ovulation drugs, as well as combined oral contraceptives with or without cyproterone are great options for resuming regularity menstrual.	A complete understanding of the molecular and SOP cell phones is crucial for the development of public health policies and effective treatment strategies. In addition, several unknown aspects of PCOS warrant further investigation.
20- TALMO, M. S. A. et al., 2024	To explore the association between maternal PCOS and newborn anthropometry and the modifying effects of maternal body mass index, PCOS phenotype and gestational diabetes.	This cohort study followed women from the first half of pregnancy until delivery e combined data from 3 clinical trials of pregnant women with PCOS e a reference population made up of participants from the Norwegian Mother, Father, and Child Cohort (MoBa).	390 pregnant women with PCOS and 68,708 women in group of reference. Offspring in the SOP had lower birth weight, birth length e head circumference than the descendants of the group reference. The group also had a lower weight index and placental weight , higher ratio BWPW and greater restriction.	In this cohort of mother-baby pairs, maternal PCOS status was associated with lower birth weight, shorter birth length and smaller head circumference in the offspring. This growth restriction was more pronounced when adjusting for BMI, providing insights into the association between PCOS and body mass index. The study contributed to a understanding of how PCOS affects offspring.

21- UYSAL, E. et al., 2024	Apply new anthropometric indices [body body adiposity index (BFI), visceral visceral adiposity index (VIA), product of lipid accumulation (PAL), body body roundness index (CRI), body shape index (BFI)] and new atherogenic indices [Castelli-I Castelli--I index, Castelli-II index index, plasma atherogenic risk (IPA), atherogenic coefficient (AC), combined index (LCI), triglyceride/ col sterol ratio of high high (TG/HDL-C), in patients with SOP.	A retrospective analysis was conducted on 248 women diagnosed with PCOS.	Significant correlations were found between fasting fasting e several anthropometric indices, such as body mass index (BMI) mass index (BMI), waist-to-height ratio (WHtR) e IAB, indicating a link between adiposity and glucose metabolism in PCOS. Atherogenic indices such as the Castelli risk index, AIP e AC showed positive correlations with glucose and insulin insulin levels, reinforcing their role in cardiovascular risk assessment. New indices such as METS-IR and TyG have shown strong correlations with profiles profiles glucose and insulin.	The study highlights the importance of using a range of anthropometric and atherogenic for comprehensive metabolic assessment in women with PCOS. Indices such as METS-IR e TyG offer valuable insights on insulin sensitivity e cardiovascular risk, potentially assisting better management e prognosis of PCOS.
22- SHEN, D. et al., 2024	To evaluate the correlation between PCOS and infertility.	Using the latest data from the database Global Burden of Disease 2019 database.	Between 1990-2019, was observed an upward trend in age-standardized prevalence by age of PCOS-related female infertility infertility in China. The ARIMA predicted a relatively rapid upward trend in prevalence standardized by age of infertility related infertility in China from 2020-2030.	A standardized prevalence by age of PCOS-related female infertility in China increased between 1990-2019. The ARIMA predicted that the age-standardized prevalence by age of this disease may continue increase in next decade. This study could increase attention the public , improve a awareness of women's health and have a certain significance to reduce infertility in PCOS.
23- ZHANG, J. et al, 2019	Comprehensive assessment of the global, regional e national SOP in incidence, prevalence and years lived with disability (ADLs) based on the Global Burden of Disease (GBD) Study 2019.	Article is a review - data on the incidence, prevalence and DLYs of PCOS from 1990 a 2019 were obtained from study GBD 2019.	The number of PCOS incidences in one year increased from 1.4 million in 1990 to 2.1 million in 2019 (54.3%). The incidence and prevalence was negatively correlated with the HDI. The 10-19 age group had the highest counts of incidence of PCOS globally. In addition, the ARIMA and BAPC model showed the trend increasing burden of PCOS.	To promote better o early diagnosis and early treatment, o consensus and the diagnostic criteria should be formulated according to the characteristics of different ethnic groups or regions. É emphasize early screening e actively developing targeted drugs for PCOS.
24- MELIANI- RODRÍGUEZ , A. et al., 2024	Evaluate a association between coffee e the presence of a diagnosis of PCOS in women in Murcia, Spain.	121 PCOS patients and 155 controls	The higher the coffee consumption, the lower a probability of having SOP in the multivariable analysis (p - trend = 0,034). Women with PCOS were less likely to drink a cup of cup compared to those who never had drank coffee.	The consumption of at least one cup of coffee a day may be associated with a reduction in PCOS symptoms.
25- WANG, F. et al., 2024	Analyze a effectiveness of metformin on carotid intima-media thickness (CIMT) and carotid artery by flow (FMD) in	Review - A total of 12 studies with 248 patients were included	The IMCE was lower in the group (after metformin) compared to the baseline group. FMD was also higher in the group of outcome. No statistically significant differences was observed in nitroglycerin-mediated dilation (NMD) between the two groups.	Metformin may have a beneficial effect on CIMT and FMD, but not on NMD, suggesting that metformin may help to reduce events. cardiovascular in patients with PCOS. Notably, the clinical efficacy of metformin can be influenced by regional differences and study types.

26- YIFU, P., 2024	Explore the potential benefits of NAC in treatment of polycystic ovary syndrome (PCOS). Specifically investigate how a NAC offers protection against PCOS.	Review	A most studies suggest that NAC, whether used alone or in combination with other drugs, has the potential to neutralize oxidative stress, utilize its anti-inflammatory and anti-apoptotic properties and offer benefits in treatment of SOP.	Biological biological effects of NAC indicate its potential usefulness as a supplementary or therapeutic approach to the treatment of PCOS. As a result, further research is needed to explore its potential in the treatment of PCOS.
27- MAHMOUDIAN, A. et al., 2024	Investigating o effect of Nigella sativa supplementation on PCOS symptoms e its severity in adolescents.	O randomized clinical trial was conducted on 114 adolescents with PCOS. Data from 103 participants (control group = 53, intervention group = 50) were analyzed. The average of the participants was 17.0.	The mean difference in the changes in hirsutism score ($p < 0.001$), right ovarian volume ($p = 0.002$) and ($p = 0.010$), serum LH ($p < 0.001$) and testosterone ($p = 0.001$) were significantly higher in the intervention group compared the control group. The frequency of oligomenorrhea, menometrorrhagia and amenorrhea was significantly reduced after the study in the intervention group compared to the control group (p s < 0,001).	Short-term supplementation with Nigella sativa may be effective in reducing ovarian volume and improving hormonal balance and menstrual irregularities in adolescents with PCOS. Further research and long-term studies are necessary to validate the Potential therapeutic effects of Nigella sativa in adolescents with PCOS.
28- AVELINO, C. M. S. F.; DE ARAÚJO, R. F. F., 2024	Identify o impact of the imbalance redox in clinical evolution of patients with PCOS and carry out a qualitative and quantitative projection of the benefits of vitamin D supplementation.	Review 136 articles recovered, 6 intervention studies were included (445 women)	A vitamin D effectively reduced the levels of malondialdehyde (P=0.002) e total testosterone (P=0.0004) e increased the levels of total antioxidant capacity (P=0.01). The levels of sex hormone binding globulin and androgen index free were identified and the results were not statistically significant.	Vitamin D is a promising alternative for the PCOS treatment with positive influence on oxidative, metabolic and endocrine of this syndrome.
29- AZHAR, A.; ALAM, S. M.; REHMAN, R.,2024	Explore a relationship between vitamin D and lipid profile in women with PCOS and infertile women without PCOS.	A total of 180 infertile women with 120 PCOS and 60 no SOP were enrolled. Lipid profile and BMI of the patients were acquired from from table, e vitamin D was estimated by enzyme-linked immunosorbent assay (ELISA)	Women with PCOS showed significantly low levels of vitamin D ($p < 0.001$). The levels of total cholesterol, low density lipoprotein, very low density lipoprotein e triglycerides were increased, and cholesterol of high-density lipoprotein was lower compared to group without PCOS ($p < 0.001$).	The study provides a link between women with PCOS and abnormalities in the profile . Reduced levels of vitamin D in women with PCOS were associated with a abnormal profile characterized by increased in cholesterol , triglycerides e low-density which can lead to metabolic abnormalities.
30- STAŃCZAK, N. A.; GRYWALSKA, E.; DUDZIŃSKA , E., 2024	Review current knowledge about SOP e the treatment treatment options for patients with the disease.	Standard review of publications in the field diagnosis and treatment of PCOS	Diet should be the of first choice. Only if if dietary intervention does not bring results, the doctor considers pharmacotherapy. Sleep sleep, physical activity and stress are also are important. Recently, acupuncture and herbal medicine, a stimulation of the vagus nerve have been used in the treatment and regulation of hormone levels.	Proper diet, physical activity - lifestyle changes are crucial in the treatment of PCOS. Supplements and pharmaceutical products support the treatment. It is mandatory to examine environmental factors and lifestyle, because they not only contribute to the occurrence of the disease, but also influence its progression.

31-BAHRI HOMAMI, M. al. 2024	Update our previous systematic review, meta-analysis and meta-regression to determine the prevalence of pregnancy complications in women with and without PCOS and explore whether pregnancy outcomes in women with and without PCOS are affected by age, body mass index (BMI), ART design or high-quality study design	Systematic review and meta-analysis included 104 studies e 106.690 pregnancies in women with and without PCOS from onset to July 13, 2022. 2022. 17.384 women with PCOS and 89,306 women without PCOS. Fifty and two studies were carried out in Asia, 26 in Europe, 21 in America, two in Australia and New Zealand and two in Africa.	Six studies reported results in women who took metformin after conception, and one study reported results in in women who conceived after bariatric surgery. Thirty e three studies reported results in pregnancies pregnancies, e four reported outcomes in pregnancies with gestational diabetes in women with and without PCOS. Twenty-seven studies compared women with and without PCOS in terms of age e 14 compared age and BMI. A lower age (-0.68 years; -0.93, -0.44) and the highest BMI (1.68 kg/m^2; 1.35, 2.00) remained significant in women with SOP.	Women with PCOS are younger and have a higher body mass index (BMI) (BMI) around the time of conception and have greater weight gestational gestational weight gain. The chances of miscarriage, gestational mellitus, gestational hypertension, pre eclampsia e caesarean section are higher in women with PCOS.
32- WANG, L. et al., 2024	To assess the prevalence and factors associated with depression among adolescent girls with PCOS in order to identify early and intervention in order to reduce the impact of depression on these adolescents.	Observational study with 335 adolescent girls with PCOS	The prevalence of of depression was 36.12% among adolescent girls with PCOS. The factors found were: support social perceived (95% CI 0.921 ~ 0,965%, p = 0.000), sleep quality (95% CI 1.134 ~ 1,324%, p = 0.000), belief disease (95% CI, 1.040 ~ 1,102%, p = 0.000), hirsutism (95% CI, 1.292 ~ 4.392%, p = 0.005) and LH/FSH ≥ 2 (95% CI, 1,939 ~ 6,369%, p = 0,000).	The symptoms of depression are a major problem among adolescent girls with PCOS in China. A approach with social support, health education structured for the disease and assessment of status psychological of PCOS girls with hirsutism (e) or LH/FSH ≥ 2 over time is important for minimize the symptoms of depression and improve psychological health among adolescent girls with SOP.

Luo et al. (2024) explore diagnostic genes associated with atherosclerosis in women with PCOS, highlighting the increased cardiovascular risk. This risk is supported by the research of Philbois et al. (2019), who identified a reduction in baroreflex sensitivity, possibly linked to increased body fat.

Other emerging biomarkers, such as asprosin level and Achilles tendon thickness (Ozturk and Arici, 2024), have also been linked to PCOS, reflecting their potential to identify specific aspects of the syndrome and its complications.

In the field of treatments, the approach continues to evolve beyond the traditional use of contraceptives and metformin. Research by Jiang et al. (2019) suggests that the combination of dimethylbiguanide (metformin) with clomiphene citrate has beneficial therapeutic effects, especially in controlling symptoms of insulin resistance and inducing ovulation.

In addition, innovative studies on stem cell therapies, such as the use of placenta-derived mesenchymal cells (Sarvestani et al., 2024), offer hope for restoring ovarian function and improving the metabolic profile. The use of Nigella sativa (Mahmoudian et al., 2024) and melatonin (Lombardi et al., 2019) are also investigated as possible natural interventions that could alleviate the symptoms of PCOS.

Another promising treatment includes the use of the GLP-1 agonist liraglutide, as documented by Zhao et al. (2024), which showed improvements in follicular development by inhibiting the secretion of CXCL10. This advance is particularly relevant considering the insulin resistance and ovulation problems commonly associated with PCOS.

A growing trend is the use of nutritional supplements, such as vitamin D, whose effectiveness in reducing oxidative stress in women with PCOS was observed by Avelino

and Araújo (2024). Coffee consumption, studied by Meliani-Rodríguez et al. (2024), has also been evaluated, suggesting a potentially protective effect against PCOS, although more evidence is needed.

Finally, the importance of psychological support also stands out, since adolescents with PCOS have a high prevalence of depressive symptoms (Wang et al., 2024), highlighting the need for a multidisciplinary approach to managing the syndrome.

Research into PCOS and its relationship with metabolic syndromes has advanced on several fronts, from understanding molecular mechanisms to developing innovative therapies. However, research is still needed to consolidate individualized treatments and define effective preventive strategies. PCOS is not just a hormonal disorder, but a condition with a global impact on health that requires a personalized, long-term approach.

CONCLUSION

In conclusion, Polycystic Ovary Syndrome (PCOS) has emerged as a complex and multifactorial condition, whose impacts go beyond reproductive health, also affecting the metabolism and the cardiovascular system. Evidence points to a direct relationship between PCOS, Metabolic Syndrome and an increased risk of complications such as type 2 diabetes and cardiovascular disease. These findings reinforce the need for early diagnosis and personalized treatment approaches that take into account both hormonal variables and associated metabolic comorbidities.

Advances in therapeutic strategies, such as the use of new medications, stem cell therapies, nutritional supplements and hormonal interventions, indicate a promising path towards relieving symptoms and improving the quality of life of women with PCOS. However, recent findings highlight the importance of a multidisciplinary approach that includes not only medical treatments, but also psychological support and lifestyle guidance.

The continuous development of biomarkers and studies focused on genetics and inflammatory responses promises to improve diagnostic accuracy and the effectiveness of treatments. However, it is essential that more research is carried out to solidify these interventions and provide evidence-based support for these new therapeutic options. Ultimately, the proper management of PCOS requires a comprehensive and personalized approach, seeking to treat both symptoms and associated conditions to ensure patients' holistic well-being.

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