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Investigating Autonomic Nervous System in PCOS: Handgrip Strength, Heart RateVariability, and Valsalva Ratio Relationship.

Roohi Khan[1], (Dr.) Mohammad Hifzur Rehman[2], (Dr.) Suraiya Khanam[1], (Dr.) Khaleel Ahmed Manik[1], (Dr.) Gauhar Hussain[1].**

1. Department of Physiology, Integral Institute of Medical Sciences and Research, Integral University Lucknow, U.P.
2. Department of Physiology, Career Institute of Medical Sciences and Hospital, Lucknow, U.P.

[1]**Corresponding Author :- (Dr.) Khaleel Ahmed Manik (Khaleelahmedmanik774@gmail.com) Professor (Dr.) in the Department of Physiology, Integral Institute of Medical Sciences and Research, Integral University Lucknow, U.P.

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ABSTRACT

Recent studies reveal that polycystic ovary syndrome (PCOS) might be associated with cardiovascular autonomic dysfunction, but with inconsistent results.The aim of this study is to investigate autonomic nervous systems in PCOS women such as heart rate variability, valsalva maneuver and Handgrip strength. These tests are non-invasive tests. Heart rate variability, a spontaneous variation in the rhythm of the human heart from one beat to the next, occurs in a healthy state, used to measure both sympathetic and parasympathetic activity. Handgrip strength, refers to the maximum static force a hand can exert by squeezing a dynamometer, used to measure sympathetic activity. And the Valsalva ratio (VR) used to measure parasympathetic activity. PubMed, Google Scholar and SCOPUS were searched for studies comparing cardiovascular function between women with obese and non-obese PCOS. PCOS diagnosis relies on Rotterdam's criteria, necessitating the presence of two out of three indicators: polycystic ovaries, anovulatory cycles, or hyperandrogenism as the syndrome transitions from a reproductive ailment to a metabolic disorder, characterized by features such as insulin resistance, impaired glucose tolerance, type 2 diabetes mellitus (DM2), dyslipidemia, and cardiovascular risk factors. 19 studies were included to analyze. Some of the studies resulted in heightened cardiac vagal modulation and reduced sympathetic cardiac modulation among a group of women with PCOS but most of them have demonstrated cardiovascular autonomic dysfunction, characterized by diminished vagal tone and heightened sympathetic activity, but observed in obese individuals compared to non-obese ones. Consequently, obesePCOS patients are believed to face an elevated risk of developing cardiovascular problems. These findings highlight the significance of early screening and management of metabolic abnormalities in women with PCOS, considering the connection between cardiac health and impaired autonomic function.

KEYWORDS: Obese PCOS, non-obese PCOS, Autonomic Function Test, Valsalva maneuver, Handgrip strength, Heart Rate variability, and Hormonal Parameters

INTRODUCTION

Polycystic ovarian syndrome is a chronic endocrine disorder that affects women of reproductive age, often leading to menstrual irregularities, infertility, excess hair growth, acne, and obesity, among other symptoms.[1]

The World Health Organization (WHO) approximates that around 116 million women globally, constituting 3.4% of the female population, are affected by Polycystic Ovary Syndrome (PCOS). Prevalence rates of PCOS vary significantly worldwide, ranging from 2.2% to 26%. In India, it is estimated that approximately 10% of women are affected by PCOS; however, there is a lack of reliable official data on its prevalence in the country.[2] Obesity and PCOS have a mutually reinforcing relationship, with each condition exacerbating the other in an ongoing cycle. Studies report that 30–75% of women with PCOS are affected by obesity.[3]

PCOS diagnosis relies on Rotterdam's criteria, necessitating the presence of two out of three indicators: polycystic ovaries, anovulatory cycles, or hyperandrogenism.[3] Polycystic ovarian morphology is diagnosed through transvaginal ultrasonography, which should reveal either 12 or more follicles measuring 2-9 mm in diameter in each ovary or an increased ovarian volume (>10 mL) without a dominant follicle >10 mm.[4] The underlying mechanisms of PCOS are complex and not fully understood, though genetic and environmental factors likely contribute significantly to its development. Additionally, obesity and dysfunction in the hypothalamic pituitary-ovarian (HPO) axis may also play a role. Hyperandrogenism and insulin resistance are recognized as key factors in PCOS pathology, with approximately 60% to 80% of patients exhibiting hyperandrogenism and 50% to 80% showing signs of insulin resistance.[5]

As the female's age advances, the syndrome transitions is from a reproductive ailment to a metabolic disorder, characterized by features such as insulin resistance, impaired glucose tolerance, type 2 diabetes mellitus (DM2), dyslipidemia, and cardiovascular risk factors.[6] Women, whether lean or overweight, are prone to exhibiting these metabolic characteristics, which are considered significant etiological factors in PCOS[7]. Cardiovascular disease ranks among the top causes of mortality in women. Certain studies have indicated the occurrence of cardiovascular risk factors in women with PCOS during early adulthood. Approximately 46.9 million individuals are believed to suffer from cardiovascular disease in India. [8]. In the Australian Longitudinal Study on Women's Health, which followed a community-based cohort, it wasfound that women who self-reported having PCOS had a higher incidence of hypertension compared to control women, regardless of BMI, within the age range of 28–33 years (5.1% versus 1.0%, respectively)[9]. In clinical settings, we encounter two categories of PCOS patients: one group who are obese and other groups who are non obese[3]. Patients exhibit variations in their hormonal parameters, and there is a notablecorrelation between the autonomic nervous system and cardiovascular mortality.[10]

The autonomic nervous system regulates numerous bodily functions. In individuals with good health, the sympathetic and parasympathetic nervous systems maintain equilibrium, termed sympathovagal balance, crucial for maintaining internal stability.[11] The sympathetic nervous system (SNS) and parasympathetic nervous system (PNS) have opposite functions, maintaining a dynamic equilibrium under normal conditions. Dysregulation in their interplay can result in various autonomic modulation-related disorders. [12] The gastrointestinal tract contains the enteric nervous system, which works in conjunction with the parasympathetic nervous system and sympathetic nervous system to controldigestion and absorption[13] The overall function of the body is chiefly regulated by the sympathetic and parasympathetic nervous systems. Neurotransmitters, namely acetylcholine (ACh) and norepinephrine

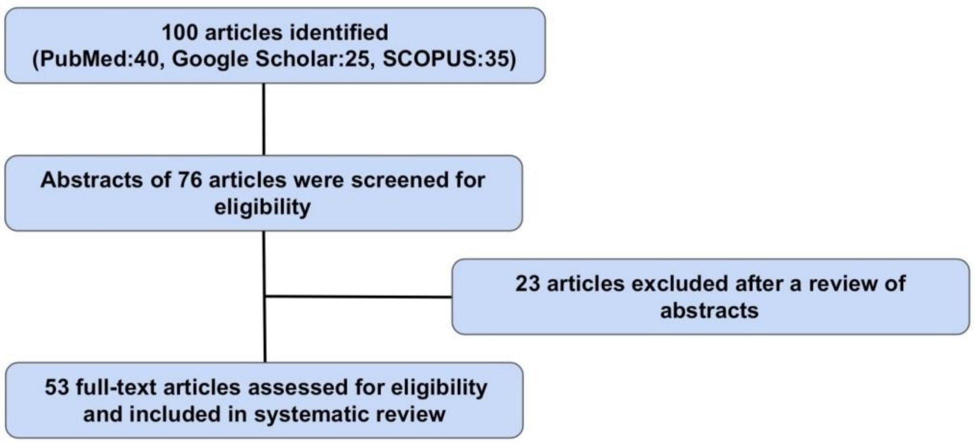
(NE), play vital roles in nerve function. Within the parasympathetic system, both pre- and postganglionic neurons release ACh. Presynaptic ACh primarily acts on nicotinic receptors in autonomic ganglia, while postsynaptic ACh affects muscarinic receptors in effector organs. In the sympathetic system, preganglionic neurons release ACh, whereas postganglionic neurons release NE, serving as the primary sympathetic neurotransmitter. NE acts on α and β adrenergic receptors in target organs.[14] Increasingly, studies have revealed that autonomic dysfunction plays a role in the progression of PCOS. [15,16] The function of the ovary is controlled not only by hormones but also by neural signals. Neural innervation includes the sympathetic superior ovarian nerve and the ovarian plexus nerve originating from the upper lumbar segment via visceral nerve fibers, as well as parasympathetic nerve input through the vagal nerve, which is regulated by the central nervous system (CNS).[17] Research indicates that women diagnosed with PCOS often exhibit compromised cardiac autonomic functions, specifically decreased activity of parasympathetic (vagal) [18] and increased activity of sympathetic nervous system.[19] Earlier studies, involving humans, have demonstrated that sympathetic nerve activity regulates ovarian steroid production, follicle growth, and the ovulation process[20.] Many women with PCOS experience heightened activity in their sympathetic nervous system, often without realizing it, which is linked to elevated androgen levels, anovulation, and menstrual irregularities, potentially contributing to the disorder's development.[18,19,21.] Sympathetic tone appears to be elevated generally, as indicated by a rise in resting heart rate, reduced heart rate variability, hypertension, heightened systolic blood pressure during exercise, slower heart rate recovery post-exercise, elevated muscle sympathetic nerve activity, and increased levels of adrenergic metabolites in the serum and urine.[20,21] Persistent overactivity of the sympathetic nervous system is linked to central obesity, and the obesity worsens this overactivity [24,25]. Studies have shown that females with PCOS may experience heightened sympathetic activity locally, including increased ovarian sympathetic nerve activity and expression of nerve growth factor. Additionally, there's an observed increase in sympathetic activity in adipose tissue, along with changes in adrenoceptor expression in both the ovaries and the periventricular nucleus of the hypothalamus.[26]

Heart rate variability (HRV), a spontaneous variation in the rhythm of the human heart from one beat to the next, occurs in a healthy state. This variability is regulated by the autonomic nervous system, whichis constantly influenced by both internal and external stimuli.[27] Heart rate variability, a spontaneous variation in the rhythm of the human heart from one beat to the next, occurs in a healthy state. This variability is regulated by the autonomic nervous system, which is constantly influenced by both internal and external stimuli.[11] While patients with PCOS exhibit significant metabolic abnormalities, some studies have indicated minor impairment in HRV among these women[28]**.** Handgrip strength, measured noninvasively, refers to the maximum static force a hand can exert by squeezing a dynamometer. [29] This tool has been used to forecast general bodily strength and functional capabilities across various demographics, while also gathering data on nutritional status, muscle mass, physical function, and overall health.[30-32] Demographic information and socioeconomic factors, like age, gender, income and employment influence both hand grip strength (HGS) and skeletal muscle strength. Additionally, lifestyle choices, health behaviors, and overall health, including any existing medical conditions, play a role, [33] as well as several physical factors, such as muscle mass, body mass index (BMI),[30] hand dimensions [34] and androgens [35] are also relevant. Few studies have investigated HGS in women with PCOS, and the results are conflicting. [36]

The Valsalva ratio (VR) indeed provides valuable insights into the function of the cardiovascular autonomic nervous system (ANS), encompassing both parasympathetic and sympathetic activity, along with vascular sympathetic nervous system activity. It's a comprehensive test for assessing overall ANS function. [37]

MATERIAL AND METHODS

In conducting this review, we utilized electronic searches of literature databases such as Google Scholar PubMed and SCOPUS, employing keywords including 'obese PCOS,' 'non-obese PCOS,' 'Autonomic Function Test,' 'Valsalva maneuver,' 'Handgrip strength,' 'Heart Rate variability,' and 'Hormonal Parameters.' Additionally, we examined the bibliographies of relevant articles to supplement our search. In total, 53 articles were identified for inclusion in this review."



DISCUSSION

This study has examined the correlation between autonomic status and hormonal fluctuations in both obese and non-obese patients with polycystic ovarian syndrome (PCOS). Kayastha F.R. et al,[38] demonstrated that the average BMI was 22.45 in the lean PCOS group and 30.91 in the obese PCOS group, mirroring findings by Makhija et al [39] and Ali et el[40]. Gupta P et al[41] and numerous other studies have also observed elevated waist-to-hip ratios (WHR) in obese women with PCOS. It was observed that central obesity is more prevalent in obese women with PCOS compared to lean counterparts.

The dysfunction of the hypothalamic-pituitary-ovarian axis is believed to play a role in the development of PCOS. Elevated estrogen levels produced by the ovaries disrupt normal feedback mechanisms, resulting in an increase in LH levels, consequently elevating the LH/FSH ratio in women with PCOS compared to those without PCOS. Typically, the LH/FSH ratio is raised in PCOS patients. While most studies indicate higher LH levels and LH to FSH ratios in PCOS women compared to controls, the absence of these markers does not necessarily exclude a diagnosis of PCOS. Gupta P[42] and Kayastha F.R.[39] found no distinction in BMI's correlation with LH/FSH ratio among women with PCOS. Conversely, Liou T.H et al, [43] observed that obese PCOS patients exhibited decreased LH levels and LH to FSH ratio compared to non-obese counterparts.

In a study conducted by Sangeetha M.C. et al[44] 21.42% of individuals in the non-obese group and 23.38% in the obese group exhibited high serum TSH levels. However, this disparity was not deemed statistically significant. Notably, 23.02% of women with PCOS were found to have serum TSH levels ≥ 4.2 µIU/ml, contrasting with the findings of Ramanand et al[45], who reported a thyroid dysfunction prevalence of 15%.

Various research investigations have established a connection between PCOS and autonomic function tests (AFTs). Because vagal discharge primarily regulates resting heart rate, those with PCOS might undergo decreased vagal tone, resulting in a modified sympathovagal balance during periods of rest. Prasad A and Azad M K et al[27] categorized the study group of 27 women diagnosed with PCOS into two groups based on BMI: Group I with BMI > 25 and Group II with BMI < 25. A comparison of heart rates in beats per minute between the two groups revealed highly significant results ($p < 0.001$), with mean heart rates ± standard deviation reported. Similar findings were obtained by Rajalakshmi et al[46] in their study. Also in the study of Prasad A and Azad M K[27], observed a correlation between obesity, PCOSin women, BMI, and WHR, alongside an increase in LFnu and LF/HF ratio indicating sympathovagal imbalance. Conversely, Sa et al[47]. discovered that 16 weeks of aerobic exercise led to enhanced cardiac vagal modulation, reduced sympathetic cardiac modulation in 15 women with PCOS, reflected in increased RMSSD, HF, and HFnu powers, and decreased LF and LFnu powers. Saranya et al[18] observed arise in DBP during IHG, mirroring findings by Sharma V et al[5] which is also indicating significantly elevated DBP in PCOS patients during Isometric hand grip exercise. Additionally, Kogure G.S et al[48] demonstrated that the PCOS group exhibited higher Hand grip strength compared to the non-PCOS group. Conversely, Pattnaik S et al[49] demonstrated that overweight patients with PCOS did not exhibit a significant difference compared to the control group. Hashim Z H et al[50] found no statistically significant differences in the valsalva ratio between obese and non-obese women with PCOS and their respective control groups, mirroring the findings of Shrivastava R et al[51]**.** However, in contrast, Sukhera et al[52] Akhter A et al[53] and Sharma V et al[5] observed lower vagal activity in PCOS patients compared to controlswhen investigating parasympathetic reactivity through Valsalva ratios.

CONCLUSION

To conclude, there is evidence suggesting that women diagnosed with PCOS may experience cardiovascular autonomic dysfunction. Several research studies, including those by Rajalakshmi et al[46], Prasad A and Azad M K[27] Akhter A et al,[53] and Sharma V et al[5] have demonstrated cardiovascular autonomic dysfunction, characterized by diminished vagal tone and heightened sympathetic activity, leading to a disrupted sympathovagal balance at rest. But Sa J C et al[47] discovered that engaging in aerobic exercise for 16 weeks resulted in heightened cardiac vagal modulation and reduced sympathetic cardiac modulation among a group of 15 women with PCOS. Hashim Z H et al[50] demonstrated that women diagnosed with PCOS display changes in autonomic function, with a more pronounced sympathoexcitation observed in obese individuals compared to non-obese ones. Consequently, obese PCOS patients are believed to face an elevated risk of developing cardiovascular problems. These findings highlight the significance of early screening and management of metabolic abnormalities in women with PCOS, considering the connection between cardiac health and impaired autonomic function.

REFERENCES

1. Rao M, Broughton KS, LeMieux MJ. Cross-sectional study on the knowledge and prevalence of PCOS at a Multiethnic University. Progr Prev Med. 2020;5(2).

2. Carmina E, Azziz R. Diagnosis, phenotype, and prevalence of polycystic ovary syndrome. Fertil Steril. 2018;86:S7-8.

3. Sachdeva G, Gainder S, Suri V, Sachdeva N, Chopra S. Obese and Non-obese Polycystic Ovarian Syndrome: Comparison of Clinical, Metabolic, Hormonal Parameters, and their Differential Response to Clomiphene. Indian J Endocrinol Metab. 2019;23(2):1-6.

4. Setji T L, Brown A J. Polycystic Ovary Syndrome: Update on Diagnosis And Treatment. The American Journal of Medicine.October 2014;127(10):912-919.

5. Vanshika V, Jyotsna S, Premlata M ,Amita.The Comparison of Cardiac Autonomic Functions in Patients with Polycystic Ovarian Syndrome and Healthy Controls. International Journal of Pharmaceutical and Clinical Research 2023; 15(4); 435-440.

6. Teede HJ, Misso ML and Costello MF. Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome. Hum Reprod 2018; 33: 1602–1618.

7. Fatima N et al. Study of Drugs prescribed and adverse drug reaction in polycystic ovarian syndrome and menstrual disorder in Gynaecology Department at Integral Institute of Medical Sciences and Research, Lucknow, India.Int. J. Adv. Res.; 11(08): 848-858.

8. Bano R, Swami D, and Ahmad N. Study of Association of Anthropometric Parameters of Obesity and Blood Pressure in Hypertensive Subjects in A Tertiary Care Hospital. Indian Journal of Applied Research. October 2016; 6(10): 55 and 56.

9. Joham AE, Boyle JA and Zoungas S. Hypertension in reproductive-aged women with polycystic ovary syndrome and association with obesity. Am J Hypertens 2015; 28: 847–851.

10. Vijaykumar N, Badiger S P, Sharankumar Tm, Nallulwar S C, Cardiovascular Autonomic Functional Modulation in Polycystic Ovarian Syndrome – A Cross Sectional Study. Indian J Clin Anat Physiol 2016;3(1):27-29

11. Pal GK. Sympathetic and Parasympathetic Systems. In: Textbook of Medical Physiology. Ahuja Publications, New Delhi. 2010; 2009- 216.

12. Ondicova K, Mravec B. Multilevel interactions between the sympathetic and parasympathetic nervoussystems: A minireview. Endocr Regul. 2010;44(2):69–75.

13. Gibbons CH. Basics of autonomic nervous system function. In: Handb Clin Neurol. 2019;160:407–18. doi:10.1016/B978-0-444-64032-1.00027-8.

14. Wehrwein EA, Orer HS, Barman SM. Overview of the anatomy, physiology, and pharmacology of the autonomic nervous system. Compr Physiol. 2016;6(3):1239-1278. doi:10.1002/cphy.c150037

15. Velusami D, Sivasubramanian S. Sympathovagal imbalance and neurophysiologic cognitive assessment using evoked potentials in polycystic ovary syndrome in young adolescents—a cross-sectional study. J Basic Clin Physiol Pharmacol. 2018;30(2):233-237.

16. Li W, Chen Y, Xu L. Association of sympathetic nervous system activity with polycystic ovarian syndrome. Clin Exp Obstet Gynecol. 2014;41(5):499-506.

17. Mónica Brauer M, Smith PG. Estrogen and female reproductive tract innervation: Cellular and molecular mechanisms of autonomic neuroplasticity. Auton Neurosci. 2015;187:1–17.

18. Saranya K, Pal GK, Habeebullah S. Assessment of cardiovascular autonomic function in patients with polycystic ovary syndrome. J Obstet Gynaecol Res 2014;40:192–9.

19. Lambert EA, Teede H, Sari CI. Sympathetic activation and endothelial dysfunction in polycystic ovary syndrome are not explained by either obesity or insulin resistance. Clin Endocrinol 2015;83:812–9.

20. Luna SL, Neuman S, Aguilera J, Brown DI, Lara HE. In vivo beta-adrenergic blockade by propranolol prevents isoproterenol-induced polycystic ovary in adult rats. Horm Metab Res. 2012;44:676.
21. Dag ZO, Alpha M, Turkel Y, Isik Y. Autonomic dysfunction in patients with polycystic ovary syndrome. Taiwan J Obstet Gynecol. 2015;54(4):381-384. doi:10.1016/j.tjog.2015.03.002
22. Serravalle G, Dimitriadis K, Dell'Oro R, Grassi G. How to assess sympathetic nervous system activity in clinical practice. Curr Clin Pharmacol. 2013;8(3):182-188.
23. Lansdowne A, Rees DA. The sympathetic nervous system in polycystic ovary syndrome: a novel therapeutic target? Clin Endocrinol (Oxf). 2012;77(6):791-801.
24. Canale MP, Manca di Villahermosa S, Martino G. Obesity-related metabolic syndrome: mechanisms of sympathetic overactivity. Int J Endocrinol. 2013;2013:865965. doi: 10.1155/2013/865965.
25. Thorp AA, Schlaich MP. Relevance of sympathetic nervous system activation in obesity and metabolic syndrome. J Diabetes Res. 2015;2015:341583. doi:10.1155/2015/341583
26. Nohara K, Waraich RS, Liu S, et al. Developmental androgen excess programs sympathetic tone and adipose tissue dysfunction and predisposes to a cardiometabolic syndrome in female mice. Am J Physiol Endocrinol Metab. 2013;304(12):E1321-1330.
27. Prasad A, Azad MK. A Study of Heart Rate Variability and Lipid Profile in Women with Polycystic Ovary Syndrome. Int J Fam Med Prim Care. 2021;2(4):1048.
28. Di Domenico K, Wiltgen D, Nickel FJ, Magalhães JA, Moraes RS, Spritzer PM. Cardiac autonomic modulation in polycystic ovary syndrome: does the phenotype matter? Fertil Steril. 2013;99:286-292.
29. Kim CR, Jeon YJ, Kim MC, Jeong T, Koo WR. Reference values for hand grip strength in the South Korean population. PLoS One. 2018;13(4):e0195485. doi: 10.1371/journal.pone.0195485.
30. Perna FM, Coa K, Troiano RP, et al. Muscular grip strength estimates of the U.S. population from the National Health and Nutrition Examination Survey 2011–2012. J Strength Cond Res. 2016;30(03):867–874. doi:10.1519/JSC.0000000000001104.
31. Liao KH. Hand grip strength in low, medium, and high body mass index males and females. Middle East J Rehabil Health. 2016;3(01):e53229. DOI: 10.17795/mejrh-33860.
32. Scharff M, Wiepjes CM, Klaver M, Schreiner T, T'Sjoen G, den Heijer M. Change in grip strength in trans people and its association with lean body mass and bone density. Endocr Connect. 2019;8(07):1020–1028. DOI: 10.1530/EC-19-0196
33. Yorke AM, Curtis AB, Shoemaker M, Vangsnes E. Grip strength values stratified by age, gender, and chronic disease status in adults aged 50 years and older. J Geriatr Phys Ther. 2015;38(03):115–121. doi: 10.1519/JPT.0000000000000037.
34. Alahmari KA, Kakaraparthi VN, Reddy RS, Silvian PS, Ahmad I, Rengaramanujam K. Percentage difference of hand dimensions and their correlation with hand grip and pinch strength among schoolchildren in Saudi Arabia. Niger J Clin Pract. 2019;22(10):1356–1364. doi: 10.4103/njcp.njcp_121_19.
35. Chiu HT, Shih MT, Chen WL. Examining the association between grip strength and testosterone. Aging Male. 2019;1–8. DOI: 10.1080/13685538.2019.1632282.
36. Kogure GS, Silva RC, Picchi Ramos FK, et al. Women with polycystic ovary syndrome have greater muscle strength irrespective of body composition. Gynecol Endocrinol. 2015;31(03):237–242. DOI: 10.3109/09513590.2014.982083.
37. Novak P. Quantitative Autonomic Testing. J Vis Exp. 2011;(53):2502.

38. Kayastha FR, Aparnathi R, Padasala R, Kanani K. Comparative study of clinical and endocrine profile between lean and obese patients of polycystic ovary syndrome. Int J Reprod Contracept Obstet Gynecol. 2023 Sep;12(9):2768-2771.

39. Makhija N, Tayade S, Toshniwal S, Tilva H. Clinicometabolic profile in lean versus obese polycystic ovarian syndrome women. Cureus. 2023;15(4):e37809.

40. Ali EA, Ahmed AL, Satha M, Khateeb AL. The association between serum nesfatin-1 level and BMI in Iraqi patients with polycystic ovary syndrome (PCOS). Health Res Policy Syst. 2021;15:1490-5.

41. Gupta P, Agrawal S, Agarwal A, Pandey A, Kumar N, Ali W. Comparison of endocrine and metabolic profile of obese and lean PCOS women with infertility. Int J Infertil Fet Med. 2022;13(3):125-8.

42.Akshaya S, Bhattacharya R. Comparative study of clinical profile of lean and obese polycystic ovary syndrome women. Int J Reprod Contracept Obstet Gynecol. 2016;5:2530-3.

43. Liou TH, Yang JH, Hsieh CH, Lee CY, Hsu CS, Hsu MI. Clinical and biochemical presentations of polycystic ovary syndrome among obese and nonobese women. Fertil Steril. 2009;92(6):1960-5.

44. Sangeetha MC, Suman Shivanagouda Patil, Nalini Arunkumar. A comparative study of thyroid stimulating hormone among lean and obese women with polycystic ovarian syndrome. Int J Reprod Contracept Obstet Gynecol. 2019 Dec;8(12):4711-4715.

45. Ramanand SJ, Ghongane B B, Ramanand J B, Patwardhan M H, Ghanghas R R, Jain S S. Clinical characteristics of polycystic ovary syndrome in Indian women. Indian J Endocrinol Metab. 2013;17(1):138-145.

46. Rajalakshmi R, VijayaVageesh Y, Nataraj SM, Srinath CG. Heart rate variability in Indian obese young adults. Pak J Physiol. 2012;8(1):39-44.

47. Sa JC, Costa EC, da Silva E, Tamburus NY, Porta A, Medeiros LF, Lemos TM, Soares EM, Azevedo GD. Aerobic exercise improves cardiac autonomic modulation in women with polycystic ovary syndrome. Int J Cardiol. 2016;202:356-361.

48. Kogure GS, Ribeiro VB, Gennaro FGO, Ferriani RA, Miranda-Furtado CL, Reis RM. Physical performance regarding handgrip strength in women with polycystic ovary syndrome. Rev Bras Ginecol Obstet. 2021;42(12):811-819.

49. Pattnaik S, Gupta S, Saxena U, Matlani M, Kapoor R. Comparison of autonomic function tests and high-sensitivity C-reactive protein in overweight patients of polycystic ovarian syndrome and overweight controls. Indian J Physiol Pharmacol. 2020;64(4):303-308.

50. Hashim Z H, Hamdan F B, Al-Salihi A R. Autonomic dysfunction in women with polycystic ovary syndrome. Iran J Reprod Med. 2015 Jan;13(1):27-34.

51. Shrivastava R, Pathak T, Shrivastava P, Patel S, Chouhan S, Singh R, Parashar R, Mishra S.Assessment of cardiac autonomic function in women with polycystic ovary syndrome through Ewing's battery, heart rate variability analysis, and Composite Autonomic Symptom Score-31 scale. Cureus. 2023 Sep 19;15(9):e45580. doi: 10.7759/cureus.45580.

52. Sukhera S, Ilyas J, Iqbal S, Mastoor M, Zaman Q. Parasympathetic Reactivity and Oxidative Stress among Participants Suffering from Polycystic Ovarian Syndrome. Pakistan Journal of Medical & Health Sciences. 2022 Jul 23;16(05):1126.

53. Akhter A, Ferdousi S, Sultana S, Mostafa M. Relationship between parasympathetic reactivity and oxidative stress in polycystic ovary syndrome. Journal of Bangladesh Society of Physiologist. 2020;14(2):48–55.