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A Study of Heart Rate Variability and Lipid Profile in Women with Polycystic Ovary Syndrome

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Abstract

Background: Polycystic ovarian syndrome (PCOS) is a chronic, diverse endocrine disease that affects mostly women of reproductive age. It is commonly associated with menstrual dysfunction, infertility, hirsutism, acne and obesity among other symptoms**.**

Material and methods: This descriptive Crossectional study was conducted in Jannayak Karpoori Thakur Medical College and Hospital, Madhepura, Bihar from Jan 2021 to Jun 2021. A sample size of 90 women of age group 15-39 years were recruited for this study. Based on the BMI and the clinical diagnosis of PCOS, the study group was divided into three groups. Women who were diagnosed as PCOS with BMI>25 as Group I (n=30); Women who were diagnosed as PCOS with BMI<25 as Group II (n=30); and age-sex matched clinically normal healthy women with BMI<25 as Group III (controls, n=30).

Results: The mean age ± standard deviation between groups results not significant as p value > 0.05. In addition, the mean height, mean weight and mean BMI ± standard deviation was for group I, II & III respectively and results was highly significant as p value < 0.001. Similar results also seen for Systolic & diastolic BP, heart rate & lipid profile respectively.

Conclusion: Heart rate variability test in PCOS women indicate that there is a sympathovagal imbalance in the form of increased sympathetic activity and parasympathetic withdrawal. In obese women with PCOS, correlated with BMI and WHR, and increase in LF nu, LF/HF ratio a marker of sympathovagal imbalance playing a major role increasing the cardiovascular risks and other comorbidities

Keywords: PCOS, BMI, Lipid profile, Heart rate variability

Introduction

Polycystic ovarian syndrome (PCOS) is a chronic, diverse endocrine disease that affects mostly women of reproductive age. It is commonly associated with menstrual dysfunction, infertility, hirsutism, acne, and obesity, among other symptoms. Until now, three groups have offered the diagnostic criteria for PCOS: the National Institutes of Health/National Institute of Child Health and Human Disease (NIH/NICHD), the European Society for Human Reproduction and Embryology/American Society for Reproductive Medicine (ESHRE/ASRM) or the 'Rotterdam Criteria'; and the Androgen Excess and PCOS Society. Chronic oligo/anovulation, clinical and/or biochemical hyperandrogenism, and polycystic ovarian morphology on transvaginal ultrasound are all included in all three groups, as well as different combinations of these disorders [1].

World Health Organization (WHO) estimates that PCOS has affected 116 million women (3.4%) worldwide in 2012. PCOS prevalence estimates vary widely throughout the world, ranging from 2.2

percent to as high as 26 percent. Experts estimate that 10% of women in India are affected by PCOS; however, there is no reliable official data on the prevalence of PCOS in India [2].

PCOS has a complicated and unknown pathogenesis. Environmental and genetic variables have a significant influence in pathogenesis. PCOS is caused by a disruption in the hypothalamic-pituitary-ovarian axis, along with obesity. In 60 percent to 80 percent of women with PCOS, hyperandrogenism is present, and insulin resistance is present in 50 percent to 80 percent. The pathophysiology of PCOS is influenced by hyperandrogenism and insulin resistance [3].

WHO defines obesity as "A condition with excessive fat accumulation in the body to an extent that health and well being are adversely affected." The definition of Obesity is limited to Body mass index. Body mass index (BMI) is an internationally accepted tool widely used to assess the obesity [4]. Body mass index (BMI) > 25 kg/m2 is present in at least 35-50% of women with PCOS. Infertility rate is 40% higher in women with whose BMI is > 30kg/m2 than those whose BMI is <30 kg/m2 [4].

Increased sympathetic activity is linked to factors that contribute to PCOS. Chronic stress, obesity, and insulin resistance, which results in increased adrenergic drive and decreased vagal activity, cause autonomic dysfunction. In a healthy state human heart does not beat at a regular rate and there occurs a variation from one beat to the next beat. This variation, which is spontaneous, is known as Heart rate Variability. The autonomic nervous system regulates the heart rate and this system is under constant influence of both external and internal stimuli. Autonomic dysfunctions leads to metabolic and cardiovascular disorders, leading to compromise in blood pressure and heart rate which results in cardiovascular mortality. In patients with PCOS few studies have reported cardiovascular autonomic involvement in the form of decreased heart rate variability and increase in sympathetic tone. Reduced HRV predicts increased cardiac mortality [5-6].

Therefore, in this present study, the Heart rate variability of PCOS women is assessed, which indicates autonomic dysfunction earlier are assessed, compared, and correlated with that of controls of normal BMI.

Material and methods: This descriptive Crossectional study was conducted in Jannayak Karpoori Thakur Medical College and Hospital, Madhepura, Bihar from Jan 2021 to Jun 2021. A sample size of 90 women of age group 15-39 years were recruited for this study. Based on the BMI and the clinical diagnosis of PCOS, the study group was divided into three groups. Women who were diagnosed as PCOS with BMI>25 as Group I (n=30); Women who were diagnosed as PCOS with BMI<25 as Group II (n=30); and age-sex matched clinically normal healthy women with BMI<25 as Group III (controls, n=30).

Inclusion criteria: Sixty women (15-39 years) who were clinically diagnosed of PCOS for more than six months were recruited based on Rotterdam criteria (those who fulfilled 2 out of 3 criteria): Oligo/anovulation, Hyperandrogenism

1. Clinical (hirsutism or male pattern alopecia)
2. Or biochemical (raised Free Androgen Index or free testosterone)
3. Polycystic ovaries (12 or more follicles on USG volume >10ml)

Exclusion criteria: Women who were diagnosed of Pregnancy, Women who were on oral contraceptive pills, ovulation induction drugs, Steroids, anti-diabetics, anti-androgens and other hormonal drugs, Women who were diagnosed of hypothyroidism, any benign uterine or ovarian conditions, any hepatic or renal or cardiac illness.

Selection of Controls: Thirty clinically normal and healthy women (15-39 years) with BMI 18.5-24.99 were recruited as control group.

Data analysis: For descriptive analyses, numbers and percentages were used to express categorical variables. Means with standard deviations were used to express continuous variables. The Kruskal-Wallis test was used for the ordinal variables and the one-way analysis of variance (ANOVA) test for continuous variables. Post hoc analysis was performed using the Bonferroni method. A p-value of <0.05 was considered statistically significant.

Methodology: The study was started after clear explanation and demonstration of the procedure to all the participants. A written informed consent was obtained from the study group and they were asked to fill up a pro-forma consisting of their socio-

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demographic details and clinical history. A thorough clinical examination was done, following which the BMI of each participant was calculated with their weight (kgs) and height (m) as measured, using Quetelets index [BMI = weight(Kg)/Height(m2). Their waist hip ratio (WHR) was calculated by the ratio between the waist circumference to the hip circumference. [WHR = Waist circumference/Hip circumference]. Their waist circumference which was measured in centimeters at the level of umbilicus or midway between lower ribcage and pubic symphysis; and their hip circumference which was measured as widest circumference at the level of greater trochanter. Waist circumference more than or equal to 88cm was considered as obesity whereas WHR more than 0.9 for females was considered as obesity. Vital parameters such as pulse rate, blood pressure, temperature and respiratory rate for every participant was noted.

Procedure of recording HRV

After clarification of the procedure, every participant was instructed to follow few mandatory requirements:

1. Must have a good sleep (8-10 hours) the day before the recording
2. Breakfast should be taken 2 hours prior to the recording.
3. Caffiene and Nicotine should be avoided 2 hours before the recording.
4. Abstinence of alcohol for one week prior to the recording.
5. Must accompany with his/her spouse or family member.
6. Must empty bladder prior to the recording

The HRV recording was done in a calm air conditioned room, with the temperature maintained at an optimum level of 25-28°C in a subdued lighting. All electronic gadgets were kept away from the recording site. The electrical/electronic devices in the room was checked to avoid volume conduction in the recording. Then the participant was made to lie quietly in the supine position with eyes open and to relax for about 10- 15 minutes.

Electrode placement: The area where the electrodes to be placed was cleaned thoroughly with spirit. One electrode as the ground electrode was placed over the right lower limb above the medial malleolus. Three limb electrodes were used in this test, where each electrode was placed over the left lower limb above the medial malleolus, over the wrist of right and left upper limb respectively. They are then connected to the ECG recorder attached to the Medicaid 8 channel Physiopac. The difference in the electrical signal between the left lower limb and left upper limb is the lead II which is mainly considered for the analysis of the HRV recording.

Resting Heart rate variability:

The total period of rest was increased to 30 minutes. During this resting period, ECG was acquired for 5 minutes (320 seconds), by a continuous recording, which is required for short term ECG analysis. The ECG data was screened for any artifact. After editing it, the results were fed to HRV analysis software.

The analogue to the digital conversion of the resting ECG signal was analyzed under power spectrum using Fast Fourier Transformation (FFT) analysis. SDNN, Mean HR, normalized Low frequency (LF nu), normalized High frequency (HF nu), LF/HF ratio were all estimated.

Results: Out of 90 subjects recruited in this study, based on their BMI they were categorized into Group-I: as 30 subjects with clinically diagnosed PCOS of BMI>25kg/m2, Group-II: as 30 subjects with clinically diagnosed PCOS of BMI<25kg/m2 and Group-III: as 30 clinically healthy normal individuals. All subjects were tested for heart rate variability and serum adiponectin levels to study the impact of PCOD illness on the test variables.

Table 1: Comparison of age, height, weight and BMI among the three studied groups by one-way ANOVA

Variable	Group I (n=30)	Group II (n=30)	Group III (n=30)	p Value
Age in years	25.32 ± 5.22	24.57 ± 4.78	23.91 ± 4.17	< 0.518^{NS}

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Height (cm)	156.50 ± 4.12	160.39 ± 5.90	158.35 ± 6.31	0.028^{S}
Weight (Kg)	74.53 ± 7.60	62.24 ± 9.04	54.52 ± 7.44	$<0.001^{HS}$
BMI	30.89 ± 3.93	23.32 ± 2.92	21.34 ± 3.56	$< 0.001^{HS}$

Table 1 shows comparison between all three groups with respect to age, height in cm, weight in kg and Body mass index in kg/m2. The mean age ± standard deviation was 25.32 ± 5.22, 24.57 ± 4.78 and 23.91 ± 4.17 for group I, II & III respectively. That shows results not significant as p value > 0.05. In addition, the mean height ± standard deviation was 156.50 ± 4.12, 160.39 ± 5.90 and 158.35 ± 6.31 for group I, II & III respectively and results was significant as p value < 0.05. Similarly, the mean weight ± standard deviation was 74.53 ± 7.60, 62.24 ± 9.04 and 54.52 ± 7.44 for group I, II & III respectively and results was highly significant as p value < 0.001. For the BMI also, the mean ± standard deviation was 30.89 ± 3.93, 23.32 ± 2.92 and 21.34 ± 3.56 for group I, II & III respectively and results was highly significant as p value < 0.001.

Table 2: Comparison of waist, hip and waist-hip ratio among the three studied groups by one-way ANOVA

Variable	Group I (n=30)	Group II (n=30)	Group III (n=30)	p Value
Waist (cms)	103.26 ± 4.96	75.32 ± 4.99	74.35 ± 5.16	$<0.001^{HS}$
Hip (cms)	105.66 ± 5.68	96.54 ± 5.46	92.27± 6.11	$<0.001^{HS}$
WHR	0.97 ± 0.02	0.74 ± 0.03	0.78 ± 0.03	$<0.001^{HS}$

Table 2 shows comparison between all three groups with respect to waist in cm, hip in cm and waist and hip ratio. The mean waist in cm ± standard deviation was 103.26 ± 4.96, 75.32 ± 4.99 and 74.35 ± 5.16 for group I, II & III respectively. That shows results was highly significant as p value < 0.001. In addition, the mean hip in cm ± standard deviation was 105.66 ± 5.68, 96.54 ± 5.46 and 92.97 ± 6.11 for group I, II & III respectively and results was highly significant as p value < 0.001. Similarly, the mean WHR ± standard deviation was 0.97 ± 0.02, 0.74 ± 0.03 and 0.78 ± 0.03 for group I, II & III respectively and results was highly significant as p value < 0.001.

Table 3: Comparison of systolic and diastolic blood pressure among the three studied groups by one-way ANOVA

Variable	Group I (n=30)	Group II (n=30)	Group III (n=30)	p Value
Systolic Blood Pressure (mm/Hg)	119.13 ± 8.16	112.11 ± 7.49	113.94 ± 8.16	0.003^{S}
Diastolic Blood Pressure (mm/Hg)	78.43 ± 7.19	73.42 ± 6.49	75.19 ± 7.55	0.025^{S}

NS=Not significant (p>0.05); S=Significant (p<0.05, p<0.01); HS= highly significant (p<0.001).

Table 3 shows comparison between all three groups with respect to systolic blood pressure and diastolic blood pressure in mmhg. The mean systolic blood pressure in mmhg ± standard deviation was 119.13 ± 8.16, 112.11 ± 7.49 and 113.94 ± 8.16 for group I, II & III respectively. That shows results was significant as p value 0.003. In addition, the mean Diastolic Blood Pressure in mmhg ± standard deviation was 78.43 ± 7.19, 73.42 ± 6.49 and 75.19 ± 7.55 for group I, II & III respectively and results was significant as p value 0.025.

Table 4: Comparison of heart rate and SDNN among the three studied groups by one-way ANOVA

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Variable	Group I (n=30)	Group II (n=30)	Group III (n=30)	p Value
Heart Rate (bpm)	81.67 ± 5.16	73.29 ± 4.89	75.49 ± 5.64	<0.001^{HS}
SDNN (ms)	54.17 ± 8.42	63.52 ± 13.46	76.29 ± 12.44	<0.001^{HS}

NS=Not significant (p>0.05); S=Significant (p<0.05, p<0.01); HS= highly significant (p<0.001)

SDNN - is the standard deviation of all Normal-to-Normal intervals that are simple variable and expressed in milliseconds.

Table 4 shows comparison between all three groups with respect to heart rate in beats per minute and SDNN in millisecond. The mean heart rate in beats per minute ± standard deviation was 81.67 ± 5.16, 73.29 ± 4.89 and 75.49 ± 5.64 for group I, II & III respectively. That shows results was highly significant as p value < 0.001. In addition, the mean SDNN in millisecond ± standard deviation was 54.17 ± 8.42, 63.52 ± 13.46 and 76.29 ± 12.44 for group I, II & III respectively and results was highly significant as p value < 0.001.

Table 5: Comparison of LF (normalized units), HF (normalized units), LF/HF ratio in HRV analysis among the three studied groups by one-way ANOVA

Variable	Group I (n=30)	Group II (n=30)	Group III (n=30)	p Value
LF (nu)	61.49 ± 7.89	48.24 ± 8.26	42.17 ± 7.65	<0.001^{HS}
HF (nu)	40.16 ± 8.42	52.41 ± 12.10	57.16 ± 9.47	<0.001^{HS}
LF/HF	1.43 ± 0.49	0.94 ± 0.53	0.88 ± 0.34	<0.001^{HS}

NS=Not significant (p>0.05); S=Significant (p<0.05, p<0.01); HS= highly significant (p<0.001).

[LF= Low frequency, HF = High frequency, nu= normalized unit]

Table 4 shows comparison between all three groups with respect to mean value of Frequency domain variables. The mean LF ± standard deviation was 61.49 ± 7.89, 48.24 ± 8.26 and 42.17 ± 7.65 for group I, II & III respectively. That shows results was highly significant as p value < 0.001. In addition, the mean HF ± standard deviation was 40.16 ± 8.42, 52.41 ± 12.10 and 57.16 ± 9.47 for group I, II & III respectively and results was highly significant as p value < 0.001. Similarly, the mean LF/HF ± standard deviation was 1.43 ± 0.49, 0.94 ± 0.53 and 0.88 ± 0.34 for group I, II & III respectively and results was highly significant as p value < 0.001.

Table 6: Comparison of lipid profile among the three studied groups by one-way ANOVA

Variable	Group I (n=30)	Group II (n=30)	Group III (n=30)	p Value
TG	296.49 ± 17.09	231.34 ± 18.86	142.71 ± 7.35	<0.001^{HS}
LDL-C	161.23 ± 15.02	155.24 ± 12.88	115.24 ± 9.73	<0.001^{HS}
HDL-C	45.21 ± 6.34	62.21 ± 5.65	68.34 ± 9.57	<0.001^{HS}
TC	236.32 ± 25.68	210.35 ± 28.68	156.65 ± 15.68	<0.001^{HS}

NS=Not significant (p>0.05); S=Significant (p<0.05, p<0.01); HS= highly significant (p<0.001).

Table 6 shows comparison between all three groups with respect to mean value of TG, LDL-C, HDL-C and TC. The mean TG ± standard deviation was 296.49 ± 17.09, 231.34 ± 18.86 and 142.71 ± 7.35 for group I, II & III respectively. That shows results was highly significant as p value < 0.001. In addition, the mean LDL-C ± standard deviation was 161.23 ± 15.02, 155.24 ± 12.88 and 115.24 ± 9.73 for group I, II & III respectively and results was highly significant as p value < 0.001. Similarly, the mean HDL-C ± standard deviation was 45.21 ± 6.34, 62.21 ± 5.65 and 68.34 ± 9.57 for group I, II & III respectively and results was highly significant as p

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value < 0.001. At last, mean TC ± standard deviation was 236.32 ± 25.68, 210.35 ± 28.68 and 156.65 ± 15.68 for group I, II & III respectively and results was highly significant as p value < 0.001.

Discussion:

The purpose of the present study was to evaluate the Heart Rate Variability and to assess the serum Adiponectin levels in women with polycystic ovarian syndrome. The study group included ninety women in the age group of 15-39 years with 30 women with PCOS & BMI ≥ 25 (Group I) , 30 women with PCOS & BMI ≤ 25 (Group II) and 30 age matched controls with BMI 18.5- 24.9 (Group III).

There was a marked difference in the weight of the study groups. There was a significant increase in the BMI of Group I when compared to Group II and Group III with P value of <0.001 which was very highly significant. There was no significant difference in age between the Groups with a P value of 0.518. The waist hip ratio of Group I was increased significantly when compared to Group II and Group III with P value of <0.001 which was very highly significant. Also having high significant difference in the Waist hip ratio between Groups with a P value < 0.001. Waist to hip ratio is a direct indicator of abdominal obesity that is visceral fat. A greater Waist to hip ratio is independently associated with a significantly increased risk of coronary heart disease.

Similarly Bharathi RV et al [7] a cross – sectional survey study done on 502 young women (between 18 and 24 years) from Chennai and collectively 566 girls from Thiruvallur and Dindugal districts to represent urban and rural population respectively. They found significant results between two groups of urban and rural population with respect to BMI.

Present study also found that in all groups lipid profile i.e. total cholesterol, triglyceride, low density lipoprotein and high density lipoprotein, results were highly significant with p value < 0.001.

Similarly Giallauria F et al [8] included Two-hundred forty-three young PCOS patients without known risk factors for cardiovascular risk were enrolled. All patients underwent hormonal and metabolic profile, white blood cells (WBCs) count and C-reactive protein (CRP). Also compared TG, LDL-C, HDL-C & TC, shown significant results between studied groups.

Özkeçeci G et al [9] Twenty-three patients with PCOS (mean age 22.8±3.9 years) and 25 healthy female volunteers who were matched for age and body mass index (BMI) (mean age 23.5±6.2 years) were enrolled in this as case-control study. Twenty-four hour ambulatory electrocardiogram recordings of all participants were taken using Pathfinder software. Triangular index measure of HRV was negatively correlated with high density lipoprotein cholesterol levels (r=-0.47, p<0.05), while age and BMI were significantly correlated with TO (r=0.31 and 0.47, respectively; p<0.05 for all). There was a significant decrease of SDNN in present study in Group I (obese with PCOS) than Group II & Group III with a P value of <0.001. Ozkecei Get al [9] has shown similar results in his study.

Comparison between all three groups with respect to heart rate in beats per minute. The mean heart rate in beats per minute ± standard deviation shown results in studied groups were highly significant as p value < 0.001. Rajalakshmi R et al [10] has got similar results in her study.

There is a significant alteration in Heart rate variability in the form of increased sympathetic and decreased parasympathetic activity in obese women with PCOS than non obese women with PCOS and controls. Since 50 % of PCOS patients are either overweight or obese, obesity could be a significant contributing factor in deterioration of cardiac autonomic functions in patients with PCOS. Similarly Sieminska L et al [11] also found comparable results with the present study.

Conclusion:

Heart rate variability test in PCOS women indicate that there is a sympathovagal imbalance in the form of increased sympathetic activity and parasympathetic withdrawal. Chronic activation of sympathetic nervous system makes them more prone for adverse cardiovascular events at an early age. In obese women with PCOS, correlated with BMI and WHR, and increase in LF nu, LF/HF ratio a marker of sympathovagal imbalance playing a major role increasing the cardiovascular risks and other comorbidities.

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PCOS women also related with total cholesterol, low density lipoprotein, high density lipoprotein and triglyceride levels. In all groups they show significant relationship with p value < 0.05. That indicates BMI > 25 kg/m^2 showing bad lipid profile than BMI <25 kg/m^2 and to healthy controls.

Limitations of Study:

1. Lack of obese control group without PCOS.
2. Small size of study group
3. Measuring catecholamines and their metabolites would be a better indicator of autonomic functions than HRV

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