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Comparison of Anthropometric Profile and Heart Rate Variability Parameters between Women with Polycystic Ovarian Disease and Apparently Healthy Women

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Abstract: ***Background: Polycystic ovary syndrome (PCOS) patients reflect features like increased insulin resistance and adiposity, which can be results as autonomic dysfunction. Objective: To compare heart rate variability (HRV) between women with polycystic ovarian syndrome (PCOS) and apparently healthy women. To study the anthropometric profile of PCOS patients. Methods: 30 women with PCOS aged 20 to 40 years (as per Rotterdam criteria) were enrolled as cases and 30 age-matched women having normal ovulatory cycles were enrolled as controls. HRV was recorded. The following frequency-domain parameters were assessed: Low Frequency (LF), LF nu, HF nu, LF/HF ratio. Results: Mean BMI of PCOS women was 25.39±2.69 kg/m^2. A total of 18 (60%) had BMI >25 kg/m^2. Cases had significantly higher BMI, blood pressure as compared to control. Majority of cases (66.7%) had SBP/DBP >130/85 mmHg as compared to only 6 (20%) of controls (p<0.001). For different frequency domain parameters, mean LF%, LF(nu) and LF/HF were significantly higher in cases as compared to controls. For all the other mean value was significantly lower in cases as compared to that of controls (p<0.05) Conclusions: This study indicated that autonomic nervous system is affected by PCOS status of women.***

Keywords: PCOS, Heart rate variability, Anthropometric profile, HF, LF, VLF

1. Introduction

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder.[1]Nearly 5-10% of women of reproductive age group affected by PCOS. It is now recognized as a common, heterogeneous, heritable disorder affecting women throughout their lifetime.PCOS is also known as hyperandrogenic an ovulation (HA).Some of the consequences associated with this disorder are menstrual dysfunction and infertility in reproductive aged women. Hirsutism, hyperandrogenism, severe acne and irregular menstrual cycle are some of the clinical features.[3] Though recognized as an ovarian disorder, it is not limited only to ovulation abnormalities. It has been recognized as a major cardiovascular and metabolic risk factor. It is believed that insulin resistance and as a result of it, hyperinsulinemia affects the normal cardiometabolic profile.[4]Cardiovascular mortality has a significant relationship with autonomic dysfunction.

Polycystic ovaries develop when the ovaries are stimulated to produce excessive amounts of male hormones (androgens), particularly testosterone, by either the release of excessive luteinizing hormone by the anterior pituitary gland, high levels of insulin in the blood (hyperinsulinaemia) in women whose ovaries are sensitive to this stimulus or reduced levels of sex-hormone binding globulin (SHBG) resulting in increased free androgens.[5]

The syndrome acquired its name due to the common sign on ultrasound examination of multiple ovarian cysts which represent immature follicles. The follicles have developed from primordial follicles but the development has stopped at an early antral stage due to the disturbed ovarian function. The follicles may be oriented along the ovarian periphery appearing as a 'string of pearls' on ultrasound examination. [6]. Hyperinsulinemia increases GnRH pulse frequency, LH over FSH dominance, increased ovarian androgen production, decreased follicular maturation and decreased SHBG binding. All these factors contribute to the development of PCOS.[7],[8]

Heart Rate Variability: is the beat-to-beat variation in heart rate. In this method, the autonomic nervous function is estimated indirectly. The high-frequency component is reflects vagal activity and low-frequency component is reflective of sympathetic activity. The ratio of two (LF/HF) shows sympatho vagal balance. The heart rate variability studies have been found useful clinically and low HRV has been found to be associated with an increased mortality risk among patients with heart failure and after myocardial infarction.[9]

2. Materials and Methods

A Case and control study conducted in Department of Physiology, in collaboration with Department of Obstetrics and Gynaecology, after receiving approval from the Institutional Ethics Committee, King George's Medical

University, Lucknow. The study duration of one year (August 2019 to July 2020).

Total 60 subjects were enrolled in the study after obtaining written informed consent. Heart rate variability analysis of the subjects/patients was done on A D instrument HRV(2.0) machine in premises of autonomic laboratory Physiology department. All Women of reproductive age (20-40 year) group diagnosed with PCOS according to ROTTERDAM criteria visiting the Obstetrics and Gynaecology Department of KGMU, Lucknow were included in PCOS group. The control group consisted of women with regular menstrual cycles and without clinical and/or biochemical signs of PCOS were included in the study. Pregnant women, Subjects suffering from Diabetes mellitus, hypertension, dyslipidaemia, History of substance abuse and those receiving medications that could affects the ANS at the time of study were excluded in the study.

2.1 Methodology

Anthropometry and general examination was performed. Following which weight, height, waist and hip circumference of the participants was taken and body mass index was calculated. Following which blood pressure measurements were taken using a sphygmomanometer.

Thereafter, all the patients were subjected to heart rate variability studies using the AD Machine in Autonomic nervous system Laboratory of the Department of Physiology, kGMU.

2.2 Procedure for Heart Rate Variability Studies

HRV was recorded using a ECG Machine (AD Instruments, India). The participant were placed in the supine position for 5 minutes in a silent room. Before recording it 10 min rest is mandatory

2.3 Statistical analysis

Data analysis was done using SPSS Version 21.0 statistical analysis software. Independent samples 't'-test, chi-square test and ANOVA were used to compare the data. A 'p' value less than 0.05 was considered as statistically significant.

3. Results

The age of cases and normal healthy controls was found to be comparable. PCOS cases had significantly higher body weight, BMI, SBP and DBP. (Table 1)

Significantly higher proportion of PCOS females as compared to controls had BMI >25.0 kg/m^2 (60.0% vs. 0.0%) but none of them more than 30 and high SBP/DBP (66.7% vs. 20.0%).

The above frequency domain HRV parameters except LF (nu) and LF/HF ratio of PCOS females were lower than that of Controls. (Table 2)

Out of 60 females enrolled in the study 42 had BMI <25 kg/m^2 and rest 18 had BMI ≥25 kg/m^2. On comparing the HRV parameters all the above parameters were higher in lower BMI i.e. <25 kg/m^2 (LF (nu) and LF/HF Ratio). Significant differences between low BMI and high BMI (≥25 kg/m^2) were found. (Table 3)

Association of blood pressure with none of the above HRV parameters [except LF (nu)] was found to be statistically significant for non-PCOS women alone. (Table 4)

LF (nu) was found to be significantly higher among those with high range of blood pressure as compared to those with low range of blood pressure

PCOS had a definitive impact on Heart rate variability, though cardiometabolic factors as well as anthropometry have their own incidental effect on HRV, however, in present study, they were dominated by presence of PCOS and did not show an independent effect. HRV is blunted in patients with PCOS as compared to non PCOS group, shows the sympathetic hyperactivity.

4. Discussion

In present study, though, all the PCOS women were in non-obese category yet their body weight, body mass index was significantly higher as compared to that of controls. As such, PCOS has a strong link with obesity and despite our effort to include non-obese PCOS women in the study, a number of PCOS women were in overweight category. PCOS women in present study also had significantly higher systolic and diastolic blood pressure values (within normotensive range) as compared to controls. These findings suggest that within same age range, PCOS women tend to have a higher body weight/obesity as well as increased cardiometabolic risk though not manifested in form of a disorder. Di Domenico *et al.* (2013) conducted a study that enrolled 30 anovulatory women with PCOS, 16 women with ovulatory PCOS and 23 age- matched women with normal cycles. Mean age was 22.80 ± 5.80 years in patients with classic PCOS, 19.81 ± 6.43 years in ovulatory PCOS, and 22.65 ± 5.89 years in controls. Under mental stress, patients with classic PCOS showed lower HRV response when compared with the control group. Saranya *et al.* (2014)**Error! Bookmark not defined.**enrolled 31 newly diagnosed PCOS cases and compared them with 30 age-matched controls for short term HRV and conventional autonomic function tests (AFT). PCOS patients had significantly higher BMI, WHR, BHR, SBP, DBP and RPP as compared to that of controls. Mean LF/HF ratio was significantly higher in cases as compared to that in controls

Cases had significantly higher body weight, height and BMI as compared to controls. Mean BMI of cases was 25.93±2.69 kg/m^2 as compared to 20.88±1.66 kg/m^2 for controls. A total of 18 (60%) of PCOS women had BMI >25 kg/m^2 as compared to none in control group.

Cases had significantly higher systolic blood pressure as compared to controls. Proportion of those with SBP/DBP >130/85 was 20 (66.7%) in cases as compared to 6 (20%) in controls.

For frequency-domain HRV parameters, LF (nu) and LF/HF values were found to be significantly higher in cases as compared to that in controls.

On evaluation of effect of BMI on HRV parameters, in overall evaluation. It was seen that HF (nu) significantly higher in lower BMI (<25 kg/m^2) as compared to that in higher BMI (≥25 kg/m^2). PCOS had a definitive impact on Heart rate variability. HRV is blunted in patients with PCOS as compared to non PCOS group, shows the sympathetic hyperactivity.

5. Conclusion

The findings of present study showed that Anthropometry and HRV parameters findings in case and control group were significantly different. It was further shown that cardiovascular risk factors like obesity and blood pressure modulate these effects. Owing to strict exclusion criteria, the role of cardiometabolic risk factors in modulation of these heart-rate variability changes could not be elucidated in detail, however, insulin resistance in PCOS women alters the cardiometabolic equilibrium which eventually leads to heart rate variability.

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Table 1: Comparison ofAnthropometric and Blood Pressure Profile of Cases and Controls

SN	Characteristic	Cases (n=30)	Controls (n=30)	Statistical significance
1.	Mean body weight±SD (kg)	61.51±6.23	54.30±5.15	't'=3.572; p=0.001*
2.	Mean height±SD (cm)	156.00±4.43	161.22±6.67	't'=7.813; p<0.001*
3.	Mean BMI±SD (kg/m^2)	25.39±2.69	20.88±1.66	χ^2=25.714; p<0.001*
4.	No. of women with BMI>25 kg/m^2	18 (60.0%)	0	't'=5.937; p<0.001*
5.	Mean SBP±SD (mmHg)	127.10±6.69	116.00±7.75	't'=3.963; p<0.001*
6.	Mean DBP±SD (mmHg)	85.80±5.97	78.73±7.75	χ^2=13.303; p<0.001*
7.	No. of women with SBP/DBP >130/85mmHg	20 (66.7%)	6(20.0%)	

Table 2: Comparison of Frequency-Domain HRV parameters between cases and controls

SN	Characteristic	Cases (n=30)		Controls (n=30)		Statistical significance	
		Mean	SD	Mean	SD	't'	'p'
1.	LF (nu)	66.15	9.71	35.99	9.87	11.925	<0.001*
2.	HF (nu)	33.50	8.83	59.70	6.64	12.988	<0.001*
3.	LF/HF	2.34	1.64	0.62	0.17	5.687	<0.001*

Table 3: Evaluation of effect of Higher BMI on Frequency Domain parameters

(a) Overall Study Population (n=60)

SN	Characteristic	BMI <25 kg/m^2 (n=42)		BMI≥25 kg/m^2 (n=18)		Statistical significance	
		Mean	SD	Mean	SD	't'	'p'
	Frequency Domain						
1.	LF (nu)	43.85	15.71	67.91	10.28	-5.957	<0.001*
2.	HF (nu)	53.02	12.66	31.60	9.34	6.451	<0.001*
3.	LF/HF	0.97	0.68	2.65	2.02	-4.839	<0.001*

Table 4(a): Comparison of HRV Parameters of those with low and high range of blood pressure (SBP/DBP >130/85) : PCOS Women (30)

SN	Characteristic	SBP/DBP <130/85 mmHg (n=10)		SBP/DBP >130/85 mmHg (n=20)		Statistical significance	
		Mean	SD	Mean	SD	't'	'p'
	Frequency Domain						
1.	LF (nu)	66.05	10.15	66.20	9.76	0.037	0.970
2.	HF (nu)	34.18	9.21	33.16	8.86	0.293	0.772
3.	LF/HF	2.14	0.95	2.43	1.92	0.450	0.656

Table 4 (b): Control group (n=30)

SN	Characteristic	SBP/DBP ≤130/85 mmHg (n=24)		SBP/DBP >130/85 mmHg (n=6)		Statistical significance	
		Mean	SD	Mean	SD	't'	'p'
	Frequency Domain						
1.	LF (nu)	34.02	9.05	43.86	9.80	2.345	0.026*
2.	HF (nu)	60.48	6.87	56.56	4.87	1.310	0.201
3.	LF/HF	0.60	0.16	0.70	0.17	1.419	0.167