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ORIGINAL ARTICLE

Parasympathetic Reactivity and Oxidative Stress among Participants Suffering from the Polycystic Ovarian Syndrome

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ABSTRACT

Background: Burden of PCOs is increasing throughout the world with a prevalence of 8% - 13% of females getting affected around the globe. Many studies have also reported autonomic dysfunction among participants with PCOs with poor response to the parasympathetic nervous system and increased response to the sympathetic nervous system in contrast to that in normal counterparts. This study will aim to assess the parasympathetic reactivity of the cardiac system and oxidative stress among participants suffering from PCOs in a tertiary care hospital in Pakistan. Females with PCOs will be compared to normal counterparts of similar age and weight.

Methodology: A cross-sectional study was conducted in the Department of Physiology of Jinnah Hospital, Lahore Pakistan from January 2021 to December 2021. Participants were recruited by purposive sampling following meeting inclusion and exclusion criteria. PCOs participants were matched with non-affected females with similar weight and age. The participants were assessed for oxidative stress by undergoing examination of serum catalase and MDA levels. Autonomic reactivity was assessed by recording ECG on taking deep breaths, on standing and following Valsalva maneuver. Both groups were compared for outcomes and measurement.

Results: The outcomes of this study showed that the group with PCOs females showed a significantly higher rate of heartbeat per minute, resting systolic and diastolic blood pressure in comparison to their normal counterparts. The serology reports showed PCOs affected group to have lower levels of catalase and increased levels of MDA in opposition to non-affected females. Furthermore, it was seen with serology and ECG measurement that E: I ratio, E-I difference, 30:15 ratio, and Valsalva ratio were all found to be positively associated with levels of plasma catalase, whereas all measurements were negatively associated with serum MDA levels in a group consisting of PCOs affected females.

Conclusion: This study concludes that a variation is seen in the parasympathetic stimulation among participants suffering from PCOs and this alteration of autonomic reactivity correlates to reduced response to parasympathetic inputs leading to a deficiency. The results of the study did not signify ay neuropathy which could be suggested by measurement of assessment of cardiac autonomic function. However, it cannot be overlooked that these measurements were different from that of normal counterparts. Lower catalase levels and increased levels of MDA among the PCOs group signify oxidative stress.

Keywords: Parasympathetic reactivity, Oxidative stress, Polycystic ovarian syndrome

INTRODUCTION

Polycystic ovarian syndrome (PCOs) is a disease in the female population that is associated with the malfunction of reproductive organs and hormones and consequently leading to conditions such as anovulation leading to infertility [1]. The disease is rapidly rising, and the burden is increasing throughout the world with a prevalence of 8% - 13% of females getting affected around the globe [2]. The disease is of significant concern as it presents with other important comorbidities such as insulin resistance, high blood pressure, dyslipidemia, and more frequently obesity [3]. These comorbidities pose a threat to the health of an individual and drastically reduce the quality of life among affected populations. With advances in medicine, our knowledge regarding PCOs has increased. Some pieces of literature have documented altered levels of sympathetic and parasympathetic function and body responses among PCOs positive population which has become the cause of cardiac pathology among affected participants [4]. Many studies have also reported autonomic dysfunction among participants with PCOs with poor response to the parasympathetic nervous system and increased response to the sympathetic nervous system in contrast to that in normal counterparts [5].

Sympathetic and parasympathetic functions have been assessed by conventional autonomic function tests that evaluated the response of the body to physiologic function [6]. The most commonly used function test is deep breaths during rest, assessment at standing, and the Valsalva maneuver. These tests allow assessment of expiration and inspiration ratios that allows evaluation of autonomic response to activities [7]. Further studies show a risk of oxidative stress among the affected population that can comprise the health and standard of living among females with PCOs [8]. Oxidative stress can be defined as an imbalance or alteration in equilibrium in the production of reactive oxygen species and antioxidants to neutralize these molecules [9]. When in the case of oxidative stress, the body is a threat of damage to many important molecules that are responsible for the regulation of bodily functions. This study will aim to assess the parasympathetic reactivity of the cardiac system and oxidative stress among participants suffering from PCOs in a tertiary care hospital in Pakistan. Females with PCOs will be compared to normal counterparts of similar age and weight.

METHODOLOGY

A cross-sectional study was conducted in the department of Physiology of Jinnah Hospital, Lahore Pakistan from January 2021 to December 2021. The goal of the study was to assess the correlation between cardiac parasympathetic activities resulting in oxidative stress among newly diagnosed PCO participants. Recruited participants were selected from patients coming to the outpatient department of endocrinology in tertiary care hospitals by purposive sampling. Ethical approval for the study was taken by respective authorities. Participants were recruited after meeting inclusion and exclusion criteria. The inclusion criteria included females recently diagnosed with PCOs ranging in age between 20 years to 35 years. All recruited participants were made part of the study if their BMI was more than normal ranges and were considered obese. A group of control participants who were not suffering from PCOs and were similar to the study case was recruited after matching the age and weight of the case participants. Exclusion criteria included females who were pregnant, breastfeeding, and on hormone therapy, or were diagnosed with other comorbidities that may influence the outcomes of this study such as cardiac diseases. A verbal explanation of the study was given to participants followed by the

undertaking of written consent. Failure to give consent led to termination from the study population.

Participant Examination: Recruited participants underwent extensive clinical and laboratory examinations. Blood samples were taken for assessment of plasma catalase and malondialdehyde (MDA). Other laboratory assessments included fasting blood glucose levels, creatinine levels in serum, and levels of serum TSH and ALT. Plasma levels were taken within the physiology laboratory and plasma samples were stored for 28 days following the taking of the samples. These samples were subjected to spectrometry for evaluation of catalase and MDA. Participants who were recruited for the study were kept on Nil per Oral from a night before and were taken off from any hypnotic or sedative regimens. Patients were subjected to extensive history assessment stress and general physical examination followed by calculation of BMI and waist circumference. Participants were assessed for resting blood pressure and pulse rate measurement. A resting ECG was performed after 20 minutes of relaxation of all participants. Participants' response to deep breaths while resting in terms of heart rate was calculated by ECG monitoring with participants taking deep breaths with 6 breaths per minute. Following ECG performed at resting position, participants were asked to stand to assess ECG changes, the third ECG reading was taken as participants were asked to blow in a tube connected to a manometer with a dial that was predetermined on 40 mmHg pressure. Participants were asked to blow in the tube for 15 minutes and ECG was performed after completion of the maneuver. The three readings of ECG at rest, standing, and after the Valsalva maneuver was recorded for both case and control groups. Following assessment of ECG of participants on rest, heart rate response during the first ECG reading was evaluated by calculating the E: I ratio. E: I ratio can be defined as the ratio between the longest interval between two RR intervals during exhalation to the shortest RR interval during inspiration. The second calculation for assessing heart rate response to deep breaths was made by subtracting the two values (I – E). For a response to standing up, a ratio of longest RR interval at 30th beat by shortest RR interval at 15th beat was calculated (30:15). Assessment of heart rate response to Valsalva maneuver, Valsalva ratio was calculated.

RESULTS

Both the groups of case and control were similar in age, BMI, and waist to hip circumference ratio. On the assessment of blood pressure of participants, it was seen the group with PCOs females showed a significantly higher rate of heart beat per minute, resting systolic and diastolic blood pressure in comparison to normal counterparts. The serology reports showed PCOs affected group to have lower levels of catalase and increased levels of MDA in opposition to non-affected females. When assessing ECG findings, it was observed that the group suffering from PCOs was found to have lower values of the E: I ratio, the difference between E and I, and the 30:15 ratio.

Table 1:

characteristics	PCOs positive group	PCOs negative group
Age in years	26.9 ± 5.02 (20 – 35)	26.7 ± 4.2 (22 – 32)
BMI (kg/m2)	29.3 ± 3.5 (26 - 37.2)	27.83 ± 2.50 (24.38 – 34.58)
Waist hip ratio	0.9 ± 0.06 (0.75 - 1)	0.84 ± 0.05 (0.76 - 0.92)
Heart rate on rest	89.1 ± 8.9 (75 - 102.4)	80.08 ± 11.22 (61 - 97.7)
Systolic blood pressure on rest (mm/Hg)	122.1 ± 7.6 (110 – 134)	117.14 ± 6.98 (102 – 131)
Diastolic blood pressure on rest (mm/Hg)	80.2 ± 4.8 (70 – 87)	76.11 ± 5.42 (66 – 86)
Serum catalase levels (U/ml)	173 ± 64.9 (59 – 283)	228.60 ± 80.28 (103 – 390)
Serum MDA levels (ng/ml)	541.9 ± 223.4 (101.3 - 952.5)	202.43 ± 91.16 (83.04 - 477.89)

It was seen with serology and ECG measurement that E: I ratio, E-I difference, 30:15 ratio, and Valsalva ratio were all found to be positively associated with levels of plasma catalase, whereas all measurements were negatively associated with serum MDA levels in a group consisting of PCOs affected females. The variation between two groups for various ECG measurements is depicted in the following table.

Table 2:

Characteristics	Patients affected by PCOs	Control participants
E: I ratio	1.2 ± 0.08 (1.2 - 1.4)	1.29 ± 0.12 (1.12 - 1.6)
E-I diff (beats/min)	16.3 ± 5.05 (10.5 - 29)	20 ± 7 (10.2 - 39)
Valsalva ratio	1.3 ± 0.17 (1.10 - 1.7)	1.3 ± 0.17 (1.11 - 1.8)
30:15 ratio	1.7 ± 0.16 (1.0 – 1.7)	1.3 ± 0.1 (1.1 - 1.7)

DISCUSSION

The outcomes of this study showed that the group with PCOs females showed a significantly higher rate of heartbeat per minute, resting systolic and diastolic blood pressure in comparison to their normal counterparts. The serology reports showed PCOs affected group to have lower levels of catalase and increased levels of MDA in opposition to non-affected females. Furthermore, it was seen with serology and ECG measurement that E: I ratio, E-I difference, 30:15 ratio, and Valsalva ratio were all found to be positively associated with levels of plasma catalase, whereas all measurements were negatively associated with serum MDA levels in a group consisting of PCOs affected females. This segment of this research will compare and contrast the findings of pre-existing literary evidence on a similar subject.

A study conducted by Saranya et al. assessed the response of the parasympathetic nervous system to the cardiac system of females suffering from PCOs. The study included 62 participants with 31 participants diagnosed with PCOs making the case, whereas demographically similar participants without PCOs made a group of control participants. the outcomes of the study showed that participants had a higher BMI, and waist-to-hip ratio. The participants also showed increased levels of resting systolic and diastolic blood pressures and higher resting heart rates in comparison to the control group [10]. The outcomes of this study are similar to the results of this clinical research presenting increased cardiac activity among participants suffering from PCOs. Other research that was found to have outcomes in accordance with this paper is [11], [12]. The advance in medicine teaches us that resting heart rate is a function of vagal stimulation and resting blood pressure is a function of the sympathetic nervous system, by reaching a conclusion of increased resting heart rate and blood pressure among participants suffering from PCOs, is concluded that an increased vagal stimulation and an altered sympathetic tone is seen among participants with PCOs [13].

Moreover, this study showed that assessment of parasympathetic activity among PCO participants as measured by various activities on ECG was significantly lower among the PCOs group in comparison to normal counterparts, however, the outcomes for Valsalva maneuver were not significantly different between the two groups. Studies that found a similar relationship in the E: I ratio between two groups are as follows [14], [15]. The findings of a lower Valsalva ratio among both groups of affected PCOs females and non-affected obese females were also supported by other studies [16]. All these findings suggest that females affected by PCOs are found to have lower vagal or parasympathetic stimulation when contrasted against the control group of the study population.

When evaluating the level of oxidative stress among participants, it was seen that participants with PCOs showed lesser levels of catalase in serum. Many studies exist which are in accordance with our findings and are as follows [17], [18], and [19]. Therefore, it can be concluded that PCOs do not influence the levels of antioxidants within the body. The finding of increased levels of MDA was also reported by pre-existing literature and the outcomes of the study in accordance with the outcomes of this clinical research are as follows [20], [21].

This study concludes that a variation is seen in the parasympathetic stimulation among participants suffering from PCOs and this alteration of autonomic reactivity correlates to reduced response to parasympathetic inputs leading to a deficiency. The results of the study did not signify ay neuropathy which could be suggested by measurement of assessment of cardiac autonomic function. However, it cannot be overlooked that these measurements were different from that of normal counterparts. Lower catalase levels and increased levels of MDA among the PCOs group signify oxidative stress.

CONCLUSION

This study concludes that a variation is seen in the parasympathetic stimulation among participants suffering from PCOs and this alteration of autonomic reactivity correlates to reduced response to parasympathetic inputs leading to a deficiency. The results of the study did not signify ay neuropathy which could be suggested by measurement of assessment of cardiac autonomic function. However, it cannot be overlooked that these measurements were different from that of normal counterparts. Lower catalase levels and increased levels of MDA among the PCOs group signify oxidative stress.

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