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Association of Polycystic ovaries with intima media thickness of common carotid artery polycystic ovarian syndrome

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ABSTRACT Polycystic ovary syndrome, or PCOS, is the most common endocrine disorder in women of reproductive age. The syndrome is named after the characteristic of the cysts, which may form on the ovaries, though it is important to note that this is a sign and not the underlying cause of the disorder. The objective of this study was to check the CIMT in PCOs patients by comparing with healthy women that either atherosclerosis more commonly occurs in PCOs patients or in healthy women. A comparative analytical study was conducted at the University Ultrasound Clinic Green Town, Lahore for duration of 7 months. 300 females of reproductive age were included in this study. 152 women with polycystic ovarian syndrome and 148 healthy controls. The mean age of participants in the study was 28 + 6.2 years with a range of 19 – 43 years. Mean carotid intima-media thickness in women with PCOS was 0.6 + 0.15 mm and 0.3 in healthy controls. Out of 300 study participants, 130 (43.3 %) were non-obese and 170 (56.7 %) were obese. According to the current study, Women with PCOS are more likely to have symptoms of early systemic atherosclerosis at a young age, as seen by their higher carotid IMT measurements.

1. INTRODUCTION

PCOS is the most prevalent female endocrine condition in the developed world, including Pakistan. It is a complex and extremely disputed reproductive endocrine illness in young girls with highly contentious pathogenesis (Norman et al., 2007). As diagnostic criteria, the National Institutes of Health (NIH) guidelines from 1990 comprised hyperandrogenism, oligo-ovulation, and the exclusion of other illnesses that mimicked PCOS. On ultrasonography, however, 20 to 25 % of routinely ovulating women had PCOS. Although aberrant ovarian morphology is associated with PCOS, it is not required for diagnosis. Furthermore, new research has demonstrated that ovarian architecture is no longer a necessary diagnostic criterion for PCOS (Artini et al., 2010). However, the Endocrine Society recommends that PCOS be diagnosed if an adult woman has two of the following symptoms: increased androgen production, anovulation, and pearl-sized cysts in the ovaries (Legro et al., 2013). PCOS is more common in South Asian women, particularly in Pakistani women (52 %) (Akram & Roohi, 2015), than in the White population (20- 25 % in the UK). The rising prevalence is due to genetic, environmental, and intermarriage factors. Furthermore, oligomenorrhea is common among the families of women with PCOS. Metabolic abnormalities such as abdominal obesity, dyslipidaemia, decreased glucose tolerance, type II diabetes mellitus (DM), arterial hypertension, and metabolic syndrome are further clinical symptoms of PCOS (Azziz, 2007; Moran et al., 2010; Bajuk Studen & Pfeifer, 2018). These features are known potential causes for early atherosclerosis (Moran et al., 2010), which increases the likelihood of developing cardiovascular disease (Legro , 2003). In fact, there is a twofold increase in the risk of coronary heart disease or stroke (De Groot et al., 2016). PCOS individuals had a greater frequency of coronary artery and aortic calcification (Talbott et al., 2004).The measurement of common carotid artery intima-media thickness (CIMT) using brightness mode ultrasonography (B-mode) is a reliable biomarker of early systemic atherosclerosis (Pignoli et al., 1986; Poredos, 2004; Lorenz et al., 2007). This sensitive and non-invasive approach can thus be used to screen for atherosclerosis and measure cardiovascular risk. CIMT has been linked to an elevated risk of coronary heart disease (Chambless et al., 1997) and allows for the prediction of future cardiovascular events including stroke and myocardial infarction. (Poredos, 2004; Lorenz et al., 2007; Chambless et al., 1997).There is proof that CIMT is higher in women with PCOS Luque-Ramírez et al. (2018); Meyer et al. (2012) specifically beyond the age of forty Talbott et al. (2000); Guzick et al. (1996) However, CIMT increases can be detected at a young age, such as adolescence (Vural et al., 2005), despite contradictory data (Meyer et al., 2012; Kim et al., 2013). Previous research has also found a link between CIMT and lipid pro-

Table 1. Mean comparison Carotid IMT in females with and without PCOS

	PCOS Status	N	Mean	Std. Deviation	Std. Error Mean	P-Value
Carotid Intima Media Thickness in mm	Yes	152	.6126	.15130	.01227	0.00
	No	148	.3050	.09581	.00788	

file, as well as a link between hyperinsulinemia (Saha et al., 2018), and endogenous androgen, albeit the results have been mixed. Indeed, hyperandrogenism is thought to promote CIMT via its proatherogenic impact (Luque-Ramírez et al., 2018). The objective of this study was to check the thickness of carotid artery in PCOs patients by comparing with healthy women that either atherosclerosis more commonly occurs in PCOs patients or in healthy women.

2. METHOD

It was a comparative analytic study on the relationship between polycystic ovaries and intima-media thickness of the common carotid artery. The current study included 300 females of reproductive age using a straightforward sampling approach. 152 of them had PCOS, whereas the remaining 148 were healthy people. The study lasted four months and was conducted at The University Ultrasound Clinic in Green Town, Lahore. Toshiba Xario300 Doppler ultrasonography with convex and linear probes (3MHz to 5MHz) (7-10 MHz). Standard sonographic criteria were used to scan the patients with the transabdominal and trans-linear transducers. The existence of polycystic ovarian syndrome was determined, and the intima media wall thickness of the Common Carotid artery was examined. The University of Lahore's Ethical Committee granted ethical approval. The Clinic administration gave their approval for the data collecting. All information and data gathered were kept strictly secret. Throughout the trial, participants remained anonymous. All of the study's protocols were thoroughly described to the volunteers. They were also allowed to withdraw at any moment during the research procedure. The patient or the patient's legal representative signed informed consent. Data collection sheets were used to collect data, which was then tabulated and analysed using SPSS version 25 and Microsoft Excel. In the study, quantitative characteristics such as age and carotid intima-media thickness were described in mean ± standard deviation.

3. RESULTS & DISCUSSION

3.1 Results

e examined 300 women of reproductive age, 148 healthy women with no known gynaecological condition, and 152 women with PCOS. The mean age of participants was 28.2 years with a range of 19 – 43 years. Of 300 participants 130 (43.3 %) were non-obese and 170 (56.7 %) were obese. Out of 170 obese females, 94 (55.3 %) women had PCOS, and 76 (44.7 %) females were normal. Mean Carotid intima-media thickness in women with PCOS was 0.6 + 0.15 mm. Mean Carotid intima-media thickness in normal females was 0.3 + .09 mm. By applying Levine's Test and T-test CIMT thickness in PCOS and healthy controls was found to be statistically significant p <0.05 at the 95 % level of confidence. According to cross-tabulation between PCOS status and BMI out of 148 controls, 72 (48.6 %) participants were non-obese and 76 (51.4 %) were obese. Out of 152 PCOS participants, 58 (38.2 %) were non-obese and 94 (61.8 %) were obese. 300 Participants were enrolled in this study out of them, 130 (43.3 %) were non-obese and 170 (56.7 %) were obese in table 1 and table 2.

Table 2. PCOS in obese and non-obese females

		Obesity			
		Non-Obese	Obese	Total	P-Value
PCOS	No	72 (48%)	76 (51,4%)	148 (100%)	
	Yes	58 (38,2%)	94 (61,8%)	152 (100%)	
	Total	130 (43.3%)	170 (56,7%)	300 (100%)	

3.2 Discussion

The study of early vascular disease in polycystic ovary females with elevated IMT using noninvasive testing found that these individuals were more susceptible to atherosclerosis than healthy controls (Talbott et al., 2000; Orio et al., 2004). Other studies have found that elevated IMT, as a noninvasive measure, is an important predictor of cardiovascular and cerebrovascular events and correlates well with traditional cardiovascular risk factors such as increasing age, obesity, and unfavorable lipid profiles, all of which are common in PCOS (Simon et al., 2002; Woldeamanuel et al., 2019; Wang et al., 2022). Previous studies have shown that women with PCOS are twice as likely as those who are not afflicted to develop metabolic syndrome (Moradi & Akbarzadeh, 2010). Obesity, hypertension, and cholesterol issues are other common causes of metabolic syndrome(Fonseca, 2004). Obesity was identified in both the control and study groups in our investigation, however, the Carotid intima-media wall thickness was statistically significant in both groups. (Allameh et al., 2013) were analogous to ours in that there was no significant difference in BMI between the two groups, despite the fact that numerous criteria for metabolic syndromes, such as waist size in PCOS patients, were larger than normal. Meyer et al. (2012) did a retrospective analysis in 2012, assessing 36 articles involving 1,123 instances of PCOS women and 923 healthy women, and discovered that Carotid intima-media thickness was considerably larger in women with polycystic ovarian syndrome than in healthy women (Meyer et al., 2012). This was consistent with our findings that Carotid intima-media thickness was considerably greater in PCOS than in controls. In a study similar to this one, (Luque-Ramírez et al., 2018). discovered that carotid IMT in PCOS women was significantly higher than in the healthy group. Furthermore, Teng et al. (2013) investigated young Chinese-Taiwanese women, including patients with polycystic ovaries and healthy women, and discovered that,

while the frequency of atherosclerotic risk factors was higher in women with PCOS, there was no evidence of elevated IMT in young women with PCOS. These findings conflicted with the current study's findings of a significant increase in Intima-media thickness in women with polycystic ovarian syndrome compared to controls. As previously described, measuring CIMT with B-mode ultrasonography is a viable biomarker of asymptomatic atherosclerosis and allows for cardiovascular risk assessment (Poredos, 2004; Lorenz et al., 2007). There is evidence that women with polycystic ovaries have higher Carotid Intima-media thickness than healthy controls Meyer et al. (2012); Luque-Ramírez et al. (2018); Garg et al. (2014) with reported mean Carotid IMT differs ranging from 0.06 mm (Heutling, 2008) to 0.14 mm (Vural et al., 2005; Orio et al., 2004). In a recent study conducted by Jabbour et al. (2020), Carotid IMT was found to be 0.12 mm. In our study mean + SD of CIMT in study group was found to be 0.6+ 0.15 mm and 0.3 + 0.09 mm in control group. This therefore consistent with the literature, as are our observed CIMT values within each group of interest, given that prior research show a mean CIMT range from 0.4 to 0.7 mm in PCOS and from 0.3 to 0.7 mm in controls 32.Despite some differences in the literature review, as discussed above, it seems that the thickness of the carotid artery in PCOS patients is higher, and as a result, people with the disease are at elevated risk for premature atherosclerosis, and thus PCOS women with CVD risk factors require care and monitoring.

4. CONCLUSION

TBased on the current study, females with PCOS are more prone to develop early systemic atherosclerosis symptoms, as seen by increased Carotid IMT readings. Furthermore, given that illness duration appears to have a predictive impact on the degree of CIMT elevation, our findings show that early exposure to poor cardiac risk factors in the setting of this condition may have long-term ramifications for the venous system.

References

Akram, M., and Roohi, N. (2015). Endocrine Correlates of Polycystic Ovary Syndrome in Pakistani Women. *J Coll Physicians Surg Pak*, 5(1). 22–26.

Allameh, Z., Rouholamin, S., Adibi, A., Mehdipour, M., Adeli, M. (2013). Does Carotid Intima-media Thickness have Relationship with Polycystic Ovary Syndrome?. *Int J Prev Med*, 4(11). 1266-1270.

Artini, P. G., Di Berardino, O. M., Simi, G., Papini, F., Ruggiero, M., Monteleone, P., et al. (2010). Best Methods for Identification and Treatment of PCOS. *Minerva Ginecol*, 62. 33-48.

Azziz, R. (2007). Evaluation for Insulin Resistance and Comorbidities Related to Insulin Resistance in Polycystic Ovary Syndrome. In: Diamanti-Kandarakis E, Nestler JE, Panidis D, Pasquali R, editors. *Insulin Resistance and Polycystic Ovarian Syndrome—Pathogenesis*, Evaluation and Treatment. Humana Press Inc. p. 1–13

Bajuk Studen, K., Pfeifer, M. (2018). Cardiometabolic Risk in Polycystic Ovary Syndrome. *Endocr Connect*, 7(7). 238–251.

Chambless, L. E., Heiss, G., Folsom, A. R., Rosamond, W., Szklo, M., Sharrett, A. R., et al. (1997). Association of Coronary Heart Disease Incidence with Carotid Arterial wall Thickness and Major Risk Factors: the Atherosclerosis Risk in Communities (ARIC) Study, 1987–1993. *Am J Epidemiol*, 146(6):483–494.

De Groot, P. C. M., Dekkers, O. M., Romijn, J. A., Dieben, S. W. M., Helmerhorst, F. M. (2017). PCOS, Coronary Heart Disease, Stroke and the Influence of Obesity: A Systematic Review and Meta-Analysis. *Hum Reprod Update*, 17(4):495–500.

Fonseca, V. (2004). Effect of Intensive Treatmenton Vascular and Other Complications of Diabetes Mellitus. *Clinical Cornerstone*, 6(2). 40-47.

Garg, N., Dharmalingam, M., Prabhu, V., Murthy, N. S. (2016). Carotid Intimo-medial Thickness: A Predictor for Cardiovascular Disorder in Patients with Polycystic Ovarian Syndrome in the South Indian population. *Indian J Endocrinol Metab*, 20(5):662–666.

Guzick, D. S., Talbott, E. O., Sutton-Tyrrell, K., Herzog, H.C., Kuller, L. H., Wolfson, S. K. (1996) Carotid Atherosclerosis in Women with Polycystic Ovary Syndrome: Initial Results from A Case-control Study. *Am J Obstet Gynecol*, 174(4):1224–1232.

Heutling, D., Schulz, H., Nickel, I., Kleinstein, J., Kaltwasser, P., Westphal, S., et al. (2008). Asymmetrical Dimethylargi Nine, Inflammatory and Metabolic Parameters in Women with Polycystic Ovary Syndrome Before and After Metformin Treatment. *J Clin Endocrinol Metab*, 93(1). 82–90.

Jabbour, R., Ott, J., Eppel, W., Frigo, P. (2020). Carotid intima-media thickness in Polycystic Ovary Syndrome and its Association with Hormone and Lipid Profiles. *PLoS One*. 24. 15(4).

Kim, J. J. , Choi, Y. M., Kang, J. H., Hwang, K. R., Chae, S. J., Kim, S. M., et al. (2013). Carotid Intima-Media Thickness in Mainly Non-obese Women with Polycystic Ovary Syndrome and Age-Matched Controls. *Obstet Gynecol Sci*. 56 (4). 249–255.

Legro, R. S., Arsalanian, S. A., Ehrman, D. A., Hoeger, K. M., Murad, M. H., Pasquall R., et al. (2013). Diagnosis and treatment of polycystic ovary syndrome: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*. 98. 4565-4592.

Legro, R. S. (2003). Polycystic Ovary Syndrome and Cardiovascular Disease: A Premature Association? *Endocr Rev*, 24(3). 302–312.

Lorenz, M. W., Markus, H. S., Bots, M. L., Rosvall, M., Sitzer, M. (2007). Prediction of Clinical Cardiovascular Events with Carotid Intima-Media Thickness: A Systematic Review and Meta-Analysis. *Circulation*, 115(4):459–467.

Luque-Ramírez, M., Mendieta-Azcona, C., Alvarez-Blasco, F., & Escobar-Morreale, H. F. (2007). Androgen Excess is Associated with the Increased Carotid intima-media Thickness Observed in Young Women with Polycystic Ovary Syndrome. *Human Reproduction*, 22(12). 3197–3203. https://doi.org/10.1093/humrep/dem324

Meyer, M. L., Malek, A. M., Wild, R. A., Korytkowski, M. T., Talbott, E. O. (2012) Carotid Artery Intima-media Thickness in Polycystic Ovary Syndrome: A Systematic Review And Meta-analysis. *Hum Reprod Update*, 18(2):112–126.

Moradi, F., & Akbarzadeh, M. (2010). Investigation of the Prevalence of Metabolic Syndrome in PCMS Women. *Koomesh* Q, 11. 221-229.

Moran, L. J., Misso M. L., Wild R. A., Norman, R. J. (2010). Impaired Glucose Tolerance, Type 2 diabetes and metabolic syndrome in polycystic ovary syndrome: A Systematic Review and Meta-Analysis. *Hum Reprod Update*. 16(4). 347–363.

Norman, R. J., Dewailly, D., Legro, R. S., Hickey, T. E. (2007). *Polycystic Ovary Syndrome*. Lancet. 370. 685.

Orio, F., Palomba, S., Cascella, T., De Simone, B., Di Biase, S., Russo, T., et al. (2004). Early Impairment of Endothelial Structure and Function in Young Normal-Weight Women with Polycystic Ovary Syndrome. *J Clin Endocrinol Metab*, 89(9). 4588–93.

Pignoli P., Tremoli, E., Poli, A., Oreste, P., Paoletti, R. (1986). Intimal Plus Medial Thickness of the Arterial Wall: a Direct Measurement with Ultrasound Imaging. *Circulation*, 74 (6):1399–1406.

Poredos, P. (2004). Intima-Media Thickness: Indicator of Cardiovascular Risk and Measure of the Extent of Atherosclerosis. *Vasc Med*, 9(1). 46–54.

Saha, S., Sarkar, C., Biswas, S. C., Karim, R. (2008). Correlation between Serum Lipid Profile and Carotid intima-media Thickness in Polycystic Ovarian Syndrome. *Indian J Clin Biochem*, 23(3):262–266.

Simon, A., Gariepy, J., Chironi, G., Megnien, J. L., Levenson, J. (2002). Intima–media Thickness: A New Tool for Diagnosis and Treatment of Cardiovascular Risk. *Journal of Hypertension*, 20(2). 159-169.

Talbott E. O., Guzick, D. S., Sutton-Tyrrell, K., McHugh-Pemu, K. P., Zborowski, J. V., Remsberg, K. E., et al. (2000). Evidence for Association between Polycystic Ovary Syndrome and Premature Carotid Atherosclerosis in Middle-Aged Women. *Arterioscler Thromb Vasc Biol*. 20(11). 2414–3421.

Talbott, E. O., Zborowski, J. V., Rager, J. R., Boudreaux, M. Y., Edmundowicz, D. A., Guzick, D. S. (2004). Evidence for an Association between Metabolic Cardiovascular Syndrome and Coronary and Aortic Calcification among Women with Polycystic Ovary Syndrome. *J Clin Endocrinol Metab*, 89(11). 5454–5461.

Teng, H. W., Chien, Y. W., Hsu, M. I., Chen, C. I. (2013). The Relationship between Carotid Intima-Media Thickness and Endogenous Androgens in Young Women with Polycystic Ovary Syndrome in Taiwan. *Gynecological Endocrinology*, 9(3):238-2341.

van der Meer, I. M., Iglesias del Sol, A., Hak, A. E., Bots, M. L., Hofman, A., Witteman, J. C.M. (2003). Risk Factors for Progression of Atherosclerosis Measured at Multiple Sites in the Arterial Tree: the Rotterdam Study. *Stroke*, 34(10):2374–2379.

Vural, B., Caliskan, E., Turkoz, E., Kilic, T., Demirci, A. (2005). Evaluation of Metabolic Syndrome Frequency and Premature Carotid Atherosclerosis in Young Women with Polycystic Ovary Syndrome. *Hum Reprod*, 20(9). 2409–3413.

Wang T. J., Nam B.H., Wilson, P.W., Wolf, P.A., Levy, D., Polak, J.F., D'Agostino, R.B., O'Donnell, C. J. (2022). Association of C-reactive Protein with Carotid Atherosclerosis in Men and Women: the Framingham Heart Study. *Arteriosclerosis, Thrombosis, and Vascular biology*. 22(10). 1662-1667.

Yildiz, B. O, Yarali, H., Oguz, H., Bayraktar, M. (2003). Glucose Intolerance, Insulin Resistance, and Hyperandrogenemia in First Degree Relatives of Women with Polycystic Ovary Syndrome. *J Clin Endocrinol Metab*, 88.2031-2036.

Zimarino, M., Cappelletti, L., Venarucci, V., Gallina, S., Scarpignato, M., Acciai, N., Calafiore, A. M., Barsotti, A., De Caterina, R. (2001). Age-Dependence Of Risk Factors for Carotid Stenosis: An Observational Study Among Candidates for Coronary Arteriography. *Atherosclerosis*. 159(1):165-173.