The Journal of Medical Research

Research Article

JMR 2023; 9(4):88-91
July- August
ISSN:2395-7565

www.medicinearticle.com
Received:07-07-2023
Accepted:16-08-2023
DOI: 10.31254/jmr.2023.9404

A Case-Control Study of the Carotid Intima Media Thickness as a Good Predictor of Subclinical Atherosclerosis in South Indian Women Diagnosed With Polycystic Ovarian Syndrome in a Tertiary Care Hospital

Lekhana Dayanand [1], Rohan PJ [2]

[1] Intern BGS Global Institute of Medical Sciences Bangalore, Karnataka, India

[2] MD (Radiodiagnosis) Assistant Professor Department of Radiodiagnosis BGS Global Institute of Medical Sciences Bangalore, Karnataka, India

Abstract

Background and Objective: Polycystic ovarian syndrome (PCOS) is a diverse condition whose likelihood of heightened cardiovascular disease (CVD) risk in the future is often disregarded. We need to predict the risk sooner due to the intrinsic propensity for CVD in Indians, increased prevalence in South Indians, and PCOS patients. The objectives are: 1. To elicit the presence of CVD risk factor in pcos patients 2. Considering CIMT (Carotid Intima Media Thickness) as a good predictor for CVD risk **Methods:** A total of 50 cases and 50 age and weight (+/-2 kg) matched controls were included in this study. We assessed the CIMT by the Doppler system with electrical linear transducer midfrequency of 10 MHz. **Results:** Women with PCOS had a greater CIMT (0.05 ± 0.01 cm in cases vs. 0.03 ± 0 cm in controls; $p < 0.001$). The CIMT of the cases is increased over their controls by 42.4% (014mm), $P \leq 0.001$. The r value of age and CIMT is more when compared to the r value of weight and CIMT in both cases and controls (Age and CIMT: cases: r= 0.431 & controls: r =0.312) (Weight and CIMT: cases: r = 0.164 & controls: r =0.233). **Conclusion:** In PCOS , CIMT is a good indicator of CVD risk. When opposed to an individual's weight, age shows a stronger positive correlation with CIMT. Hence, PCOS patients must get an early CIMT scan. CIMT must be a crucial component of PCOS management and CVD risk alleviation.

Keywords: Age, Cardiovascular disease, Carotid Intima Media Thickness, Polycystic ovarian syndrome, Risk, South India, Subclinical atherosclerosis.

***Corresponding author:**
Dr. Lekhana Dayanand
Intern BGS Global Institute of Medical Sciences Bangalore, Karnataka, India
Email: dlekhana@gmail.com

INTRODUCTION

Polycystic ovarian syndrome is a diverse condition that affects up to 10% of women of reproductive age[1] and is influenced by genetic and environmental factors [2]. Chronic anovulation, hyperandrogenism, and/or polycystic ovaries are all the symptoms of PCOS.

It has been designated as the ovarian manifestation of metabolic syndrome , 46% of women with PCOS were found to have this syndrome. Due to the presence of a cluster of metabolic disorders such as glucose intolerance, hypertension, obesity, dyslipidemia, insulin resistance and hyperinsulinemia, PCOS may represent a significantly unrecognised segment of the female population that is at heightened cardiovascular risk when compared with age matched controls. [3,6]

PCOS has been linked to a higher risk of atherosclerosis, with a calculated elevated risk (relative risk) of 7.4 for myocardial infarction. [4] Endothelial dysfunction [5], is considered an early sign of the atherogenic pathway that leads to overt CVD and insulin has been shown to have a direct hypertrophic effect on the vascular endothelium and smooth muscle cells in these patients. [7]

The increased CIMT is linked to decreased clearance of VLDL particles and chylomicrons. The breakdown of these large VLDL particles produces small, dense LDL that are poorly removed and highly atherogenic [8]

The intima media thickness (IMT) is a morphological measure of vascular damage. [9] In multiple regression analyses, PCOS was found to be the unique prognostic factor of variable IMT[10].Women with PCOS exhibited a significantly higher prevalence of carotid index of atheromatic plaques (7.2% versus 0.7%) than controls in a study.[11] Studies have found impaired carotid IMT in young women of normal weight who

were eulipidaemic, normotensive, and had PCOS, implying a PCOS-related premature structural vascular injury. [12]

According to the World Health Organisation, India accounts for one-fifth of all CVD-related deaths worldwide, particularly among young people. According to the findings of the Global Burden of Disease study, India has an age-standardized CVD death rate which is much higher than the global average . CVDs strike Indians a decade before the rest of the world. [13]

In an ethnicity like ours, assessing risk factors for CVD at the earliest is of prime importance. When the assessment can be made out easily by a non invasive test using ultrasonography and measuring the intima thickness of the main arteries like the carotid artery , we are able to substantially decrease the risk of CVD in patients of PCOS who have an increased predisposition to atherosclerosis , by bringing to light their risk and prompting them to take necessary and essential steps to alleviate the detrimental effects of atheroma on cardiovascular health at the earliest.

Need for the study

The mortality rate associated with CAD is 20-50% higher among Asian Indians than in any other community globally [14].Furthermore, it is known that in comparison to North Indians, the prevalence of CAD in South Indians was 61.6% higher [15]. Cardiovascular problems, linked to metabolic dysfunction, are manifestly more common in PCOS patients. Therefore, proactive measures must be made, to quickly and accurately identify the approaching risk factors for CVD. The carotid intima media thickness (CIMT), is one such non-invasive approach. The outcome would motivate the patients to comprehend the role of risk factors in the burgeoning CVD epidemic and to implement efficient management methods for its prevention.

Owing to the inherent predisposition of CVD in Indians , increased prevalence of the same in South Indians and in PCOS patients , this study becomes essential in predicting cardiovascular events in the aforementioned group at the earliest and playing a crucial role in preventing the same.

Objectives

1. To elicit the presence of cardiovascular risk factor in the form of subclinical atherosclerosis in pcos patients
2. Considering CIMT as a good predictor for CVD risk in the form of subclinical atherosclerosis

METHODOLOGY

This case-control hospital-based study will be conducted in a medical college hospital situated in a metropolitan city, Bangalore for a period of two months after obtaining Institutional Ethics Committee approval.

On the basis of convenience sampling this study would enrol 50 patients aged 18-35 years from outpatient departments of Obstetrics andGynaecology who were diagnosed as PCOS according to Rotterdam criteria. We included 50age and weight matched (+/- 2kgs) normal healthy women as controls with normal menstrual cycles, with no evidence of hyperandrogenism , were selected from hospital staff. All study participants would be enrolled after receiving their written informed consent.

EXCLUSION CRITERIA: All patients who had secondary causes of hyperandrogenism such as hyperprolactinemia, late onset congenital adrenal hyperplasia, androgen-secreting tumor, Cushing's disease, hypothyroidism, end-stage liver or kidney disease, chronic cardiovascular disease, hematologic disease, pregnancy, hypertension, and diabetes mellitus were excluded.

Physical examination was performed, including measurement of weight and blood pressure .Weight was measured with the subject wearing light clothing without shoes. Blood pressure was measured manually with a sphygmomanometer.

CIMT was measured by B mode ultrasound using linear probe at frequency of 10 MHz. The CIMT of the posterior wall of common carotid arteries (1 cm proximal to the origin of the bulb) was measured at the end of the diastole. Average CIMT was taken as the mean of 6 readings, 3 on each side.

The intima media thickness was measured in the far wall of the artery at sites identified as diffuse and continuous projections with the greatest distance between the luminal-intimal interface and media adventitial interface but without atherosclerotic plaques. Localized lesions >2 mm thickness were considered to be atherosclerotic plaques. CIMT was assessed by single observer who was blinded for the diagnosis.

With the formula (0.009 x age in years)+0.116mm, Homma and colleagues discovered that the normal intima-media thickness in the CCA—as assessed in areas free of plaque—increases linearly with age, from a mean of 0.48mm at age 40 to 1.02mm at age 100. [16]

Using this formula, we would calculate the normal intima media thickness for the respective ages of the cases and controls. Later we would be measuring the CIMT sonographically ,and would compare the measured CIMT values to the calculated ones to estimate the true increase in CIMT values in consideration of the age related variance amongst the cases and controls.

Statistical Analysis

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean $\pm$ SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5% level of significance. Student t test has been used to find the significance of study parameters on continuous scale between two groups on metric parameters. Leven`s test for homogeneity of variance has been performed to assess the homogeneity of variance. Chi-square test has been used to find the significance of study parameters on categorical scale between two or more groups. Pearson correlation between study variables is performed to find the degree of relationship. The Statistical software namely SPSS 22.0, and R environment ver.3.2.2 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc**.**

RESULTS

The age and weight distribution of the samples are shown in Table 1 and 2 respectively. The samples are age matched and the p value for the weight is 0.878 which is not significant.

The blood pressure data is depicted in Table 3. Neither the cases nor the controls had hypertension.

The mean of the calculated normal CIMT for age in both the cases and controls is 0.33±0.03 mm, with P=1.000, is not significant. Table 4 depicts the normal CIMT for age in mm- frequency distribution.

The mean of the scanned readings of the CIMT in the cases is 0.05±0.01mm on both sides , is significant with p value <0.001 and that of the controls is 0.03±0 mm on both sides, is significant with p value <0.001. This shows that the CIMT is increased in the cases when compared to the controls. The distribution is denoted in Table 5.

The average of 6 readings of the CIMT showed that , 41 (82%) of the study group and only 5 (10%) of the control group had CIMT value of >0.40mm , 9(18%) of the study group and 33(66%) of the control group had CIMT value between 0.31-0.40, and none of the study

group population had a CIMT value up to 0.30mm but 11(22%) of the control group had it, as indicated in Table 6.

It is found that with P value ≤0.001, the CIMT value of the PCOS patient is increased over their age and weight matched controls by 42.4% (014mm), which is significant.

Both age and weight variables when compared with CIMT show a positive relation. But the r value of age and CIMT is more when compared to the r value of weight and CIMT in both cases and controls (Age and CIMT: cases: r= 0.431 & controls: r =0.312) (Weight and CIMT : cases: r = 0.164 & controls: r =0.233), age plays a very important factor in determining the CIMT when compared to the weight, as depicted in Table 7.

Table 1: Age in years –frequency distribution in two groups of patients studied

Age in Years	STUDY GROUP	CONTROL GROUP	Total
<20	4(8%)	4(8%)	8(8%)
20-30	43(86%)	43(86%)	86(86%)
>30	3(6%)	3(6%)	6(6%)
Total	50(100%)	50(100%)	100(100%)
Mean ± SD	24.06±3.76	24.06±3.76	24.06±3.74

Samples are age matched with P=1.000, student t test

Table 2: Weight (kg)- frequency distribution in two groups of patients studied

Weight (kg)	STUDY GROUP	CONTROL GROUP	Total
<60	14(28%)	14(28%)	28(28%)
60-80	34(68%)	33(66%)	67(67%)
>80	2(4%)	3(6%)	5(5%)
Total	50(100%)	50(100%)	100(100%)
Mean ± SD	63.08±8.38	63.34±8.47	63.21±8.38

P=0.878, Not Significant, Student t Test

Table 3: Comparison Of Blood Pressures In Two Groups Of Patients Studied

Variables	STUDY GROUP	CONTROL GROUP	Total	P Value
Systolic BP	119.68±3.37	117.76±3.35	118.72±3.48	0.005**
Diastolic BP	74.08±4.48	73.08±4.28	73.58±4.39	0.257

Table 4: Normal CIMT for age in mm-frequency distribution in two groups of patients studied

Normal CIMT for age in mm	STUDY GROUP	CONTROL GROUP	Total
UPTO 0.30	6(12%)	6(12%)	12(12%)
0.31-0.40	42(84%)	42(84%)	84(84%)
>0.40	2(4%)	2(4%)	4(4%)
Total	50(100%)	50(100%)	100(100%)
Mean ± SD	0.33±0.03	0.33±0.03	0.33±0.03

P=1.000, Not Significant, Student t Test

Table 5: Readings- Cimt –Comparison In Two Groups Of Patients Studied

CIMT	STUDY GROUP	CONTROL GROUP	Total	P Value
R1 (cm)	0.05±0.01	0.03±0	0.04±0.01	<0.001**
R2 (cm)	0.05±0.01	0.03±0	0.04±0.01	<0.001**
R3 (cm)	0.05±0.01	0.03±0	0.04±0.01	<0.001**
L1 (cm)	0.05±0.01	0.03±0	0.04±0.01	<0.001**
L2 (cm)	0.05±0.01	0.03±0	0.04±0.01	<0.001**
L3 (cm)	0.05±0.01	0.03±0	0.04±0.01	<0.001**

Table 6: Average of 6 readings in mm-CIMT- COMPARISON IN TWO GROUPS STUDIED

Average of 6 readings in CIMT mm	STUDY GROUP	CONTROL GROUP	Total
UPTO 0.30	0(0%)	11(22%)	11(11%)
0.31-0.40	9(18%)	33(66%)	42(42%)
>0.40	41(82%)	5(10%)	46(46%)
Total	50(100%)	50(100%)	100(100%)
Mean ± SD	0.47±0.09	0.33±0.06	0.4±0.1

P≤0.001**, 42.4% (014mm) INCREASE OVER CONTROL , Significant, Student t Test

Table 7: Pearson Correlation

Variables	STUDY GROUP		CONTROL GROUP	
	r value	P Value	r value	P Value
Age VS Average of 6 readings in CIMT(mm)	0.431	0.002**	0.312	0.028*
Weight VS Average of 6 readings in CIMT (mm)	0.164	0.256	0.233	0.103

Significant figures

+ Suggestive significance (P value: 0.05<P<0.10)

* Moderately significant (P value:0.01<P ≤ 0.05)

** Strongly significant (P value : P≤0.01)

DISCUSSION

Our work demonstrates that, young women with PCOS have increased subclinical atherosclerosis as indicated by higher CIMT measured by B-mode Ultrasonography. It also shines light on the fact that weight of the patient has a less positive relation to CIMT when compared to the age.

According to Meyer et al.'s systematic review and meta-analysis, women with PCOS are more likely to develop early atherosclerosis. [17] Results from earlier studies on PCOS patients' CIMT and FMD (Flow mediated dilatation) have been inconsistent. When compared to matched controls, Orio et al. discovered considerably lower FMD and greater CIMT in a sample of thin, normotensive, and non-dyslipidemic PCOS women. [18] Karoli et al. observed similar findings when they compared 50 women with controls who were of a similar age and discovered increased CIMT in cases. [19]

Epidemiological evidence also shows that women with PCOS have a higher chance of developing CVD. In comparison to women with regular cycles, Solomen et al. showed that women with a history of irregular menstrual cycles had an adjusted relative risk for CVD of 1.53 (95% CI 1.24-1.90). [20] It is also known that South Indians had a 61.6% greater prevalence of CAD than North Indians.[15] It is alarming to know

that Myocardial infarction risk rises by 15% and stroke risk rises by 18% with every 0.10 increase in CIMT [21].

Attributing to the increased prevalence of CVD in South Indians and in PCOS patients, this study becomes essential in predicting cardiovascular events in the aforementioned group at the earliest by utilizing a method which is economical , non invasive and robust – like the CIMT.

Only a prospective research can determine whether these patients with increased CIMT are indeed at risk for CVD in the long run. But having known that an increased CIMT does have a bearing on CVD in PCOS patients , CIMT monitoring in PCOS patients becomes necessary for motivating the patients to comprehend the role of risk factors in the burgeoning CVD epidemic and to implement efficient management methods for its prevention.

Having used only a non invasive modality like CIMT to determine the impending risk of CVD and counselling the patients to take steps to alleviate the risk is the strength of our study. The fact that we did not assess the FMD , hormonal assay of the patients and did not follow up the patients to see their lifestyle modifications leading to a change in CIMT are limitations of our study.

CONCLUSION

This study shows a greater CIMT in PCOS patients when compared to the age and weight matched controls, thereby proving that CIMT is a good predictor of CVD risk in the form of subclinical atherosclerosis. The study also shows that age has a more positive relation to CIMT when compared to the weight of individuals. Hence, it becomes necessary for an earlier CIMT scan in PCOS patients, as CIMT, keeps increasing with age. The study makes it imperative to include CIMT as an integral part of PCOS care and CVD risk alleviation.

Financial support & Sponsorhip: NIL

Conflicts of interest: NIL

REFERENCES

1. Ibbotson, S. H. (n.d.). DAVIDSON'S PRINCIPLES AND PRACTICE OF MEDICINE (23rd ed., Vol. 1). Elsevier.
2. Diamanti-Kandarakis E,,Kandarakis H,, Legro RS.. The role of genes and environment in the etiology of PCOS. *Endocrine.* 2006;30:19–26.
3. Glueck CJ, Papanna R, Wang P, Goldenberg N, Sieve-Smith L. Incidence and treatment of metabolic syndrome in newly referred women with confirmed polycystic ovarian syndrome. *Metabolism.* 2003;52:908–15.
4. Dahlgren E,,Janson PO,, Johansson S,. et al. Polycystic ovary syndrome and risk for myocardial infarction. Evaluated from a risk factor model based on a prospective population study of women. *ActaObstetGynecol Scand.* 1992;71:599–604.
5. Ross R.. The pathogenesis of atherosclerosis: a perspective for the 1990s. *Nature.* 1993;362:801–9.
6. Lobo RA,,Carmina E.. The importance of diagnosing the polycystic ovary syndrome. *Ann Intern Med.* 2000;132:989-93.
7. Arcaro G,,Cretti A,, Balzano S,. et al. Insulin causes endothelial dysfunction in humans: sites and mechanisms. *Circulation.* 2002;105:576-82.
8. Krauss RM, Siri PW. Metabolic abnormalities: triglyceride and low-density lipoprotein. *EndocrinolMetabClin N Am.* 2004;**33**:405–415.
9. O–Leary DH,,Polak JF,, Kronmal RA,. et al. Carotid-artery intima and media thickness as a risk factor for myocardial infarction and stroke in older adults. Cardiovascular Health Study Collaborative Research Group. *N Engl J Med.* 1999;340:14–22.
10. Guzick DS,,Talbott EO,, Sutton-Tyrrell K,. et al. Carotid atherosclerosis in women with polycystic ovary syndrome: initial results from a case-control study. *Am J Obstet Gynecol.* 1996;174:1224–9.
11. Talbott EO,,Guzick DS,, Sutton-Tyrrell K,. et al. Evidence for association between polycystic ovary syndrome and premature carotid atherosclerosis in middle-aged women. *ArteriosclerThrombVasc Biol.* 2000;20:2414–21.
12. Orio F Jr,,Palomba S,, Cascella T,. et al. Early impairment of endothelial structure and function in young normal-weight women with polycystic ovary syndrome. *J ClinEndocrinolMetab.* 2004;89:4588–93.
13. Prabhakaran D., Jeemon P., Roy A. Cardiovascular diseases in India. *Circulation.* 2016;133:1605–1620.
14. Sreeniwas Kumar A, Sinha N. Cardiovascular disease in India: A 360 degree overview. *Med J Armed Forces India*. 2020;76(1):1-3. doi:10.1016/j.mjafi.2019.12.005
15. Begom R, Singh RB. Prevalence of coronary artery disease and its risk factors in the urban population of South and North India. *ActaCardiol*. 1995;50(3):227-240.
16. Pellerito, J., &Polak, J.F. (2012). Introduction to Vascular Ultrasonography. Elsevier Heath Sciences.
17. Meyer ML, Malek AM, Wild RA, Korytkowski MT, Talbott EO. Carotid artery intima-media thickness in polycystic ovary syndrome: A systematic review and meta-analysis. Hum Reprod Update 2011;18:112-26.
18. OrioJr F, Palomba S, Cascella T, et al. Early impairment ofendothelial structure and function in young normal-weight women with polycystic ovary syndrome. J ClinEndocrinolMetab 2004;89:4588–93.
19. Karoli R, Fatima J, Siddiqi Z, et al. Study of early atherosclerotic markers inwomen with polycystic ovary syndrome. Indian JEndocrinolMetab 2012;16:1004–8.
20. Solomon CG, Hu FB, Dunaif A, et al. Long or highly irregular menstrual cycles as a marker for risk of type 2 diabetes mellitus. JAMA 2001;286:2421–6.
21. Lorenz MW, Markus HS, Bots ML, et al. Prediction of clinicalcardiovascular events with carotid intima-media thickness: asystematic review and meta-analysis. Circulation 2007;115:459–67.