Original Article

Sonographic Evaluation of Carotid Intima Media Thickness in Premenopausal and Postmenopausal Diabetic Females

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Abstract

Objective: To evaluate and compare carotid intima-media thickness (CIMT) between premenopausal and postmenopausal diabetic females using sonographic imaging.
Study design: It was a cross-sectional study.
Place and duration of study: The study was conducted at Saeed Medicare, Gojra, and Samar Diagnostic Lab, Lahore, from August to December 2024.
Material and Methods: This study was carried out on 128 diabetic females, equally divided into premenopausal and postmenopausal groups, aged 40 and above. A stratified purposive sampling method was used to select participants. CIMT measurements were taken using high-resolution ultrasonography, and clinical data including age, BMI, blood glucose levels, and blood pressure were recorded. Data analysis in SPSS version 27 included independent samples t-tests to compare mean CIMT and multiple linear regression to identify key predictors. Effect sizes (Cohen's d, R^2), 95% confidence intervals, and ANOVA within regression were reported, with $p < 0.05$ considered statistically significant.
Results: A total of 128 participants were included, comprising 64 postmenopausal and 64 premenopausal diabetic females. The mean carotid intima-media thickness (CIMT) was significantly higher in postmenopausal females (1.013 ± 0.17 mm) compared to premenopausal females (0.666 ± 0.17 mm). Blood glucose levels were also elevated in postmenopausal females (239.62 ± 81.08 mg/dL) compared to premenopausal participants (156.25 ± 47.45 mg/dL). Regression analysis identified postmenopausal status (B = 0.709, $p < 0.001$) and blood glucose levels (B = 0.001, $p < 0.001$) as significant predictors of increased CIMT, collectively explaining 58.6% of the variation in CIMT ($R^2 = 0.586$). Other factors, including BMI, age, and blood pressure, did not show a statistically significant association with CIMT.
Conclusion: The study concludes that postmenopausal diabetic women are at significantly elevated risk for cardiovascular complications due to increased carotid intima-media thickness (CIMT) and higher blood glucose levels compared to premenopausal women. Given that postmenopausal status and hyperglycemia explain a significant proportion of CIMT variation, early vascular screening and strict glycemic control should be prioritized in postmenopausal diabetic women to mitigate cardiovascular risk.
Keywords: Carotid intima-media thickness, Premenopausal, Postmenopausal, Diabetic Females, Sonography, Cardiovascular risk

1. Introduction

Despite substantial progress in cardiovascular disease (CVD) management, it remains the leading cause of morbidity and mortality worldwide. The World Health Organization reports that CVD accounts for approximately 17.9 million deaths annually, representing nearly 31% of global mortality.(1) CVD encompasses a range of disorders affecting the heart and blood vessels, including atherosclerosis, a condition marked by lipid accumulation and arterial inflammation that can lead to myocardial infarction and stroke.(2)

Carotid intima-media thickness (CIMT) is a well-established marker of subclinical atherosclerosis and future cardiovascular risk. It is non-invasively measured using ultrasound, making it a cost-effective tool for early detection.(3) Increased CIMT is associated with traditional risk factors such as hypertension, diabetes, obesity, and metabolic syndrome, all of which contribute to atherosclerotic progression and vascular remodeling.(4)

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Diabetes and Cardiovascular Risk

Diabetes mellitus (DM) is a major metabolic disorder that significantly increases CVD risk. Currently, hypertension and DM contribute to 48% and 3.5% of CVD-related deaths, respectively.[5] Chronic hyperglycemia promotes endothelial dysfunction, arterial stiffness, and systemic inflammation, accelerating the development of atherosclerosis.[6] Studies indicate that diabetic patients have significantly higher CIMT compared to non-diabetic individuals, reinforcing the impact of metabolic disturbances on vascular health.[7]

Menopause and Atherosclerosis

The transition from reproductive to post-reproductive life, known as menopause, represents a critical phase in female cardiovascular health.[8] Premenopausal women exhibit a lower risk of cardiovascular disease compared to men of the same age, likely due to estrogen's protective effects on vascular function.[9] However, after menopause, the incidence of CVD sharply rises, surpassing that observed in men.[10]

Estrogen deficiency post-menopause contributes to increased arterial stiffness, lipid abnormalities, and endothelial dysfunction, leading to CIMT thickening and higher cardiovascular risk.[11] Studies indicate that postmenopausal women with diabetes have a disproportionately higher risk of CIMT progression, reinforcing the interplay between metabolic and hormonal changes.[12]

CIMT in the Pakistani Population

While extensive research has examined CIMT in Western and Asian populations, there is limited data from Pakistan. A study conducted in Lahore, Pakistan, demonstrated that diabetic and hypertensive individuals had significantly higher CIMT values than healthy controls, emphasizing the need for localized research on vascular risk in postmenopausal women.[13] Additionally, South Asian populations, including Pakistanis, have a higher genetic predisposition to metabolic syndrome, insulin resistance, and early-onset cardiovascular disease, necessitating region-specific investigations.[14]

Given the synergistic effects of menopause and diabetes on vascular health, understanding their impact on CIMT progression is crucial. This study aims to evaluate and compare CIMT in premenopausal and postmenopausal diabetic females in Pakistan using sonographic imaging. Additionally, it seeks to assess the impact of metabolic factors—including age, body mass index (BMI), blood glucose levels, and blood pressure—on CIMT. Identifying the strongest predictors of CIMT progression will provide valuable clinical insights for cardiovascular risk stratification in diabetic women undergoing menopause.

Furthermore, this study addresses a critical gap in Pakistani data by incorporating regional findings and population-specific risk factors, contributing to better preventive strategies for cardiovascular complications in postmenopausal diabetic females.

2. Materials & Methods

A cross-sectional study was conducted at Saeed Medicare, Gojra, and Samar Diagnostic Lab, Lahore, from August to December 2024, involving 128 diabetic females (64 premenopausal and 64 postmenopausal). Participants were selected using stratified purposive sampling to ensure equal representation of both groups.

Females were included if they were aged 40 years or older, diagnosed with Type 1 or Type 2 diabetes. Premenopausal women were included if they had regular menstrual cycles, while postmenopausal women were included if they had no menstruation for at least one year. Exclusion criteria included hormone therapy, advanced renal disease, malignancy, pregnancy, cardiovascular conditions, and prior carotid surgeries.

The estimated sample size for the study is calculated as follows: The effect size (d) is set at 0.5, which represents a medium effect. The alpha level (α) is typically set at 0.05, which corresponds to a maximum probability of a Type I error of 0.1. The desired power

(1-β) is usually set at 0.8 or 0.9. The standard deviation (σ) is estimated to be 0.1 mm. Using the Fisher formula, $n = (Z\alpha/2 + Z1\text{-}\beta)^2 / (\sigma^2 / d^2)$, where Zα/2 and Z1-β are the Z-scores corresponding to the desired alpha and power levels, respectively. Plugging in the values, $n = (1.96 + 0.842)^2 / (0.1^2 / 0.5^2) = 7.84^2 / 0.04 = 61.47$, which is approximately 62 participants per group. To account for potential dropouts or missing data, it is recommended to add 10-20% to the total sample size. Therefore, the total sample size for the study is estimated to be 128 participants.

Ethical approval was obtained from the institutional review board, and written informed consent was obtained from all participants. To maintain confidentiality, participant data was anonymized and stored securely in password-protected digital files.

Clinical and metabolic data were recorded, including:

- Blood glucose levels measured via glucometer.
- Body mass index (BMI) calculated as weight (kg) divided by height (m^2).
- Blood pressure measured using a mercury sphygmomanometer, with three readings taken five minutes apart.
- Carotid intima-media thickness (CIMT) assessed bilaterally using a high-resolution ultrasound system (Toshiba Aplio Mx, Toshiba Xario) with a 6–15 MHz linear transducer. Measurements were taken 1–2 cm proximal to the carotid bulb, and three readings were recorded per side, with the mean value calculated to ensure accuracy.

A structured questionnaire was used to collect demographic, medical, menstrual, and family history data. The questionnaire included sections on:

- Personal history: Age, marital status, weight, and height.
- Medical history: Diabetes type and duration, history of cardiovascular disease, hypertension, and cholesterol levels.
- Menstrual history: Menopausal status, time since menopause, and history of hormone replacement therapy.
- Lifestyle factors: Smoking status, physical activity, and prior sonographic evaluations.

The questionnaire was adapted from established epidemiological studies and reviewed by a panel of experts, including a sonologist, an endocrinologist, and a research methodologist, to ensure content validity. While a separate pilot study was not conducted, the questionnaire was based on previously validated frameworks in cardiovascular and diabetes research, minimizing the need for additional independent testing. Expert review and informal pretesting were conducted to enhance clarity and consistency.

Statistical analyses were conducted using SPSS version 27 to evaluate differences in carotid intima-media thickness (CIMT) and identify its key predictors. Descriptive statistics summarized the clinical and demographic characteristics of participants. An independent samples t-test was used to compare mean CIMT between premenopausal and postmenopausal diabetic females. To assess the influence of multiple factors on CIMT, multiple linear regression analysis was performed, identifying menopausal status and blood glucose levels as significant predictors. The model's explanatory power was evaluated using R^2 and adjusted R^2 values, while ANOVA within the regression model tested the overall significance of predictors. Additionally, effect sizes (Cohen's d for t-tests, R^2 for regression) and 95% confidence intervals were reported to enhance the robustness of findings. A p-value < 0.05 was considered statistically significant for all analyses.

3. Results

The SPSS (Statistical Package for the Social Sciences program version 27) was used to analyze the effects of menopausal state and other metabolic factors on vasculature in diabetic women.

Table 1: compares key health parameters between premenopausal and postmenopausal diabetic females, including age, BMI, blood glucose levels, duration of diabetes, blood pressure, type of diabetes, and carotid intima-media thickness (CIMT). Postmenopausal women are significantly older (mean age: 61.67 years) and have had diabetes for a longer duration (mean: 12.56 years) compared to premenopausal women (mean age: 44.52 years, diabetes duration: 4.61 years). Blood glucose levels are also notably higher in postmenopausal women (mean: 239.62 mg/dL) than in premenopausal women (mean: 156.25 mg/dL). Both groups have similar BMI values, around 26. Blood pressure, both systolic and diastolic, is slightly elevated in postmenopausal women. While premenopausal women exhibit a mix of Type 1 and Type 2 diabetes, all postmenopausal women have Type 2 diabetes. Importantly, CIMT, an indicator of arterial wall thickness, is significantly higher in postmenopausal women (mean: 1.013 mm) compared to premenopausal women (mean: 0.6656 mm), suggesting a greater risk of atherosclerosis in older diabetic females.

Table 1: Comparison of key health parameters between premenopausal and postmenopausal diabetic women

	Premenopausal Diabetic females				Postmenopausal Diabetic females			
	Min.	Max.	Mean	Std. Deviation	Min.	Max.	Mean	Std. Deviation
Age	40	49	44.52	2.800	47	75	61.67	8.075
Weight (kg)	50	90	70.6	12.551	51	89	71.19	10.938
Height (cm)	150	180	164.98	9.377	150	180	166.30	9.588
Body Mass Index	16.36	39.11	26.02	5.685	16.89	36.79	26.0306	5.14597
Blood Glucose Level	101	291	156.25	47.448	120	429	239.62	81.081
Years Having Diabetes	1	11	4.61	2.826	5	24	12.56	4.500
Systolic blood pressure	120	141	128.0	6.998	120	189	130.8	10.664
Diastolic blood pressure	80	90	82.45	4.012	70	116	83.9	6.4722
Type of Diabetes	1	2	1.97	0.175	2	2	2.00	0.000
Right Carotid Intima Media Thickness (mm)	0.4	1.0	0.656	0.1689	0.7	1.3	1.013	0.1723
Left Carotid Intima Media Thickness (mm)	0.4	1.0	0.673	0.1748	0.7	1.4	1.009	0.1734
Mean Carotid Intima Media Thickness (mm)	0.40	0.95	0.6656	0.16853	0.75	1.35	1.0131	0.16641

Table 2: Comparison of Mean Carotid Intima-Media Thickness (CIMT) Between Premenopausal and Postmenopausal Diabetic Women Using Independent Samples t-Test

Group of the Participant		Group Statistics			Independent Samples Test	
		N	Mean	t	df	Sig. (2-tailed)
Mean Carotid Intima Media Thickness (mm)	Premenopausal Diabetic Women	64	.6656	-11.738	126	<.001
	Postmenopausal Diabetic Females	64	1.0131	-11.738	125.980	<.001

The study analyzed carotid intima-media thickness (IMT) in 128 diabetic females, with 64 premenopausal and 64 postmenopausal participants. The Group Statistics table shows that the mean IMT in postmenopausal diabetic females was significantly higher (1.0131 mm) compared to premenopausal females (0.6656 mm). The standard deviations for both groups were similar (0.16853 mm and 0.16641 mm, respectively), indicating consistent variability across the groups.

The Independent Samples t-Test confirms that this difference is statistically significant. The p-value for the t-test is <0.001, meaning the observed difference is highly unlikely to be due to chance. The mean difference between the groups is -0.34750 mm, with a 95% confidence interval of -0.40609 to -0.28891 mm, suggesting a strong and reliable difference. Levene's test for equality of variances (p = 0.869) indicates that the assumption of equal variances is valid, so the "Equal variances assumed" row is used.

The Effect Size Analysis shows that the magnitude of the difference between the two groups is large, with a Cohen's d of approximately -2.07. This indicates a substantial clinical significance of the findings. The results suggest that postmenopausal diabetic females have significantly greater carotid IMT than their premenopausal counterparts. This may point to increased cardiovascular risk in postmenopausal diabetic women, highlighting the importance of targeted screening and interventions.

Figure 1: Bar chart showing mean CIMT values with error bars for premenopausal and postmenopausal groups

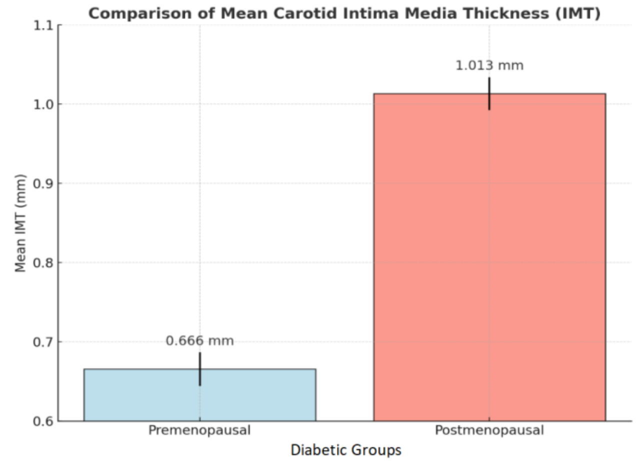

Figure 1 describe that visually represents the significant difference in mean carotid intima media thickness (IMT) between premenopausal and postmenopausal diabetic females. Postmenopausal females exhibit a higher mean IMT (1.013 mm) compared to premenopausal females (0.666 mm), aligning with the statistical results. This highlights the increased cardiovascular risk in postmenopausal diabetic women and underscores the need for regular monitoring.

The regression analysis investigates the impact of age, body mass index (BMI), group (premenopausal vs. postmenopausal), Blood pressure (systolic + diastolic) and blood glucose levels on mean carotid intima-media thickness (IMT) in diabetic females. Here's a breakdown of the findings:

- The regression model demonstrates a strong relationship (R = 0.766) between the predictors and IMT.
- The model explains 58.6% of the variance in IMT ($R^2 = 0.586$), indicating that the predictors contribute significantly to IMT differences.
- The adjusted $R^2 = 0.566$, which accounts for the number of predictors in the model and suggests a strong explanatory power.
- The standard error of the estimate is 0.15905, indicating the average deviation of observed IMT values from the predicted values.

- The F-statistic (28.574, $p < 0.001$) confirms that the regression model is statistically significant, meaning the predictors collectively influence the dependent variable (IMT).

4. Discussion

This study's findings demonstrate that postmenopausal diabetes women exhibit considerably greater carotid intima media thickness (CIMT) than their premenopausal counterparts. The mean CIMT in postmenopausal women was significantly elevated (1.0131 ± 0.16641 mm) compared to premenopausal women (0.6656 ± 0.16853 mm), indicating an elevated risk of cardiovascular illnesses within this demographic.

Menopause is associated with a decline in estrogen levels, which play a crucial role in maintaining arterial integrity by enhancing endothelial function and reducing inflammation. The loss of estrogen contributes to arterial stiffness and CIMT progression, as observed in studies by Willeit et al. (2020) and Lorenz et al. (2012).[15,16] The present study aligns with these findings, demonstrating that postmenopausal diabetic females exhibit significantly higher CIMT values. Additionally, our results are consistent with van den Munckhof et al. (2018), who reported age-related CIMT thickening.[17]

Diabetes mellitus is a well-established risk factor for vascular complications, including atherosclerosis. Hyperglycemia leads to endothelial dysfunction and arterial wall thickening, accelerating CIMT progression.[18-25] Our findings support this relationship, as postmenopausal diabetic females had significantly higher blood glucose levels (239.62 ± 81.08 mg/dL) compared to premenopausal diabetic females (156.25 ± 47.44 mg/dL). Prior research by Zhou et al. (2020) demonstrated that elevated fasting plasma glucose levels independently predict CIMT increases, even in non-diabetic individuals.[19] Regression analysis in our study confirmed that blood glucose levels ($B = 0.001$, $p < 0.001$) were a significant predictor of increased CIMT.

Unlike previous studies that focused on hypertension as a primary determinant of CIMT, our study included diabetic females with varying BMI and blood pressure levels without preselecting hypertensive patients. The mean BMI in the premenopausal and postmenopausal groups was 26.4 ± 3.2 kg/m² and 27.1 ± 3.5 kg/m², respectively, showing no significant correlation with CIMT ($p = 0.08$). Similarly, blood pressure, while recorded for all participants, was not identified as a primary determinant of CIMT progression. These findings contrast with research by Berraho et al. (2012), which reported a strong association between hypertension and CIMT.[20] The absence of such correlation in our study may be due to the random inclusion of participants rather than a specific focus on individuals with established hypertension or obesity.

Furthermore, some studies have reported no significant difference in CIMT between premenopausal and postmenopausal women. While these discrepancies may be attributed to variations in study populations, methodologies, or confounding factors, they highlight the complexity of CIMT progression and the need for further investigation. Factors such as genetic predisposition, medication use, and dietary variations may account for these differences.

Several potential confounders, such as genetic predisposition, lifestyle factors (physical activity, diet), and medication use, were not extensively analyzed in this study. Prior research suggests that these factors may significantly influence CIMT. For instance, physical activity and dietary habits are known to modulate cardiovascular risk, potentially affecting CIMT progression, as indicated by van den Munckhof et al. (2018) and Yusuf et al. (2020).[17,21] Additionally, genetic predisposition has been reported to influence CIMT independent of traditional risk factors, as observed in studies by Wang et al. (2019).[22-24] The influence of antihypertensive or lipid-lowering medications, which are known to alter vascular health, also warrants consideration in future research.

The findings underscore the necessity for targeted screening and early interventions to mitigate cardiovascular risks in postmenopausal diabetic women. Strategies such as intensive glycemic control, routine cardiovascular screening, and lifestyle modifications—including diet and exercise—should be prioritized. Continuous glucose monitoring and structured physical activity programs, as supported by Martens et al. (2021), have been shown to improve vascular outcomes.[23]

Conclusion:

This study revealed a significant increase in CIMT among postmenopausal diabetic females compared to their premenopausal counterparts, highlighting an elevated cardiovascular risk in the postmenopausal group. The findings underscore the role of menopause-associated hormonal changes, particularly the decline in estrogen, in accelerating vascular alterations. Furthermore, hyperglycemia was identified as a significant predictor of increased CIMT, reinforcing the critical need for effective glycemic control to mitigate cardiovascular complications in diabetic women. The results emphasize the importance of comprehensive cardiovascular risk assessment and early intervention strategies to prevent adverse vascular outcomes in this high-risk population.

Limitation:

This study has several limitations. Certain cardiovascular risk factors, such as lipid profiles and physical activity levels, were not included, which might have provided a more comprehensive understanding of their impact on CIMT. The use of a convenient sample of patients may limit the generalizability of the findings. Additionally, the study did not account for genetic predisposition, medication use, or dietary habits, all of which may have influenced CIMT progression. Furthermore, while the study focused on the sonographic evaluation of CIMT, incorporating electrocardiography (ECG) and other imaging modalities could have provided additional cardiovascular insights. Future studies should address these limitations by including a broader range of risk factors and utilizing a more diverse sample population.

Recommendations:

- Routine screening of carotid intima-media thickness (CIMT) should be incorporated into cardiovascular risk assessments for postmenopausal diabetic females to facilitate early detection of subclinical atherosclerosis.
- Targeted lifestyle interventions, including structured diet and exercise programs, are essential for reducing modifiable risk factors.
- Optimizing glycemic control and managing other metabolic parameters should be prioritized to mitigate cardiovascular risk.
- Longitudinal studies are needed to monitor CIMT progression over time in diabetic women, with a focus on identifying critical windows for effective intervention and prevention of adverse cardiovascular outcomes.
- Future research should incorporate a broader range of risk factors, including genetic predisposition, medication use, and dietary habits, to provide a more comprehensive understanding of CIMT progression in diabetic women.

Disclosure /Conflict of interest:

The authors have no conflict of interest. This research didn’t receive any specific grant from funding agencies in the public, commercial or not for profit sectors.

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