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Association Between Menopausal Symptom Severity and Glycemic Control in Postmenopausal Women with Type 2 Diabetes Mellitus: A Cross-Sectional Study.

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Abstract

Background: Postmenopausal women with type 2 diabetes mellitus (T2DM) face compounded metabolic vulnerability, yet the relationship between menopausal symptom severity and glycemic control remains poorly characterized in Indian clinical settings. ***Objectives:*** To evaluate the association between menopausal symptom severity, assessed using the Menopause Rating Scale (MRS), and glycemic control, assessed using glycated hemoglobin (HbA1c), among postmenopausal women with T2DM, and to identify demographic, clinical and lifestyle correlates of glycemic control. ***Methods:*** This cross-sectional observational study was conducted over six months in the outpatient departments of endocrinology, diabetology and gynecology of a tertiary care teaching hospital. One hundred postmenopausal women aged 40 to 65 years with type 2 diabetes of at least one year duration were enrolled using consecutive sampling. Menopausal symptoms were assessed using the MRS, and HbA1c, fasting and postprandial glucose, lipid profile and renal function were recorded. Spearman correlation, independent samples t-test, chi-square test and multiple linear regression were used, with $p<0.05$ considered statistically significant. ***Results:*** The mean age was 51.79 ± 4.67 years. Mild menopausal symptoms were seen in 74% and moderate symptoms in 26% of participants. Mean HbA1c was significantly higher in the moderate symptom group than the mild group (8.16 ± 0.58% vs 7.34 ± 0.63%, $p<0.001$). Glycemic control category was significantly associated with symptom severity ($\chi^2 = 23.686$, $p<0.001$). MRS total score correlated positively with HbA1c ($r = 0.573$, $p<0.001$), most strongly in the psychological domain ($r = 0.507$, $p<0.001$). Regression identified MRS score ($\beta = 0.536$, $p<0.001$) and age ($\beta = -0.252$, $p = 0.002$) as independent predictors of HbA1c. ***Conclusion:*** Menopausal symptom severity, particularly in the psychological domain, is independently and positively associated with poorer glycemic control in postmenopausal women with T2DM, supporting integrated screening for menopausal symptoms within routine diabetes care.

Keywords: Menopause; Type 2 Diabetes Mellitus; Glycated Hemoglobin; Menopause Rating Scale; Glycemic Control; Postmenopausal Women.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) has become one of the most pressing public health challenges among Indian women. The nationally representative ICMR-INDIAB study reported an overall weighted diabetes prevalence of 11.4% and a prediabetes prevalence of 15.3% across urban and rural India, with wide interstate variation and a rapidly rising burden in less-developed states.[1] Diabetes also drives a substantial complication load; a companion ICMR-INDIAB analysis found that impaired kidney function is strongly linked to type 2 diabetes, with diabetes alone conferring a considerably higher risk of renal impairment than hypertension, and a six-fold higher risk when both coexist.[2] As the population of women with long-standing T2DM ages, an increasing proportion of them enter the menopausal transition while still requiring sustained glycemic management, making the intersection of menopause and diabetes a growing area of clinical concern.

Menopause is not a single hormonal event but a prolonged climacteric transition characterized by declining ovarian estrogen production, redistribution of body fat toward visceral depots, autonomic dysregulation and heightened cardiometabolic vulnerability. A recent narrative review has summarized how this transition is accompanied by increased visceral adiposity, reduced lean mass, insulin resistance, dyslipidemia and a higher prevalence of metabolic syndrome,

changes only partly captured by body mass index alone.[3] Exposure to metabolism-disrupting environmental compounds during this sensitive window has also been linked to adverse glycemic, lipid and adiposity outcomes in midlife women, suggesting that the menopausal transition may amplify vulnerability to external metabolic insults.[4]

Reflecting the protective metabolic role of endogenous estrogen, menopausal hormone therapy has been shown to improve glycemic parameters and reduce diabetes risk in appropriately selected postmenopausal women, although its use requires careful individualized cardiovascular risk assessment.[5] Cardiovascular and menopause societies have consequently called for structured, multidisciplinary screening frameworks that specifically address cardiometabolic risk across the menopausal transition.[6,7]

Despite this recognized biological plausibility, epidemiological evidence linking reproductive milestones to diabetes risk remains inconsistent. Data from the Tehran Lipid and Glucose Study cohort have associated early menarche and surgical menopause with substantially higher odds of prediabetes, type 2 diabetes and metabolic syndrome,[8] whereas a large UK Biobank cohort found no independent association between the timing or type of menopause and incident diabetes after multivariable adjustment.[9] This discordance suggests that chronological markers of menopause alone may be insufficient to capture the metabolic impact of the transition, and that the severity of the symptom burden experienced by an individual woman, rather than the timing of her final menstrual period, may be a more clinically meaningful correlate of glycemic outcomes.

The Menopause Rating Scale (MRS) is a validated, multidimensional instrument that quantifies somatic, psychological and urogenital symptom severity and continues to be cross-culturally validated, including in a recent Japanese validation study confirming its strong internal consistency and diagnostic accuracy for detecting severe menopausal symptoms.[10] Symptom burden captured by the MRS is also known to vary with social determinants of health such as income and healthcare access, indicating that it reflects a broader biopsychosocial construct rather than a purely biological one.[11] Separately, a large meta-analysis has confirmed that depression and diabetes distress are consistently associated with poorer glycemic control and reduced self-care behaviors in people with diabetes,[12] raising the possibility that the psychological domain of menopausal symptoms could be a particularly important, and modifiable, correlate of glycemic control.

Despite these converging lines of evidence, few studies from India have directly examined the association between menopausal symptom severity, assessed using a validated multidimensional instrument, and glycemic control in postmenopausal women with established T2DM. Most available literature focuses either on menopausal status as a binary exposure or on isolated biochemical predictors of glycemic control, without incorporating patient-reported symptom burden. This represents an important gap, because symptom-level assessment could offer a practical, low-cost screening avenue for clinicians managing postmenopausal women with diabetes. The present study was therefore designed to evaluate the association between menopausal symptom severity, measured using the MRS, and glycemic control, measured using HbA1c, among postmenopausal women with T2DM attending a tertiary care hospital, and to identify the demographic, clinical and lifestyle correlates of glycemic control in this population.

MATERIALS AND METHODS

Study Design and Setting

This study was designed as a cross-sectional observational study conducted at a tertiary care teaching hospital. The study was carried out over a period of six months in the outpatient departments of endocrinology, diabetology and gynecology. The design was chosen to evaluate the association between menopausal symptom severity and glycemic control at a single point in time among women with established type 2 diabetes mellitus.

Study Population

The study population comprised postmenopausal women diagnosed with type 2 diabetes mellitus who attended the outpatient departments during the study period. Eligible participants were within the age group of 40 to 65 years and had attained natural menopause, defined as amenorrhea for at least 12 consecutive months. All participants had a confirmed diagnosis of type 2 diabetes mellitus for a minimum duration of one year prior to enrollment.

Inclusion and Exclusion Criteria

Women with known type 2 diabetes mellitus who had undergone natural menopause and were willing to provide informed consent were included in the study. Participants with a history of surgical menopause, those currently receiving hormone replacement therapy, and individuals with known psychiatric illnesses or cognitive impairment that could interfere with symptom reporting were excluded. Additionally, patients with other endocrine disorders such as thyroid dysfunction or Cushing's syndrome were excluded to avoid confounding effects on metabolic parameters.

Sample Size and Sampling Technique

The sample size for the study was determined based on an anticipated moderate correlation between menopausal symptom severity and glycemic control, with a significance level of 5% and a statistical power of 80%. A minimum sample size of approximately 85 participants was estimated; however, to enhance the robustness of the analysis, a total of 100 participants were included. A consecutive sampling technique was employed, wherein all eligible participants presenting during the study period were recruited until the required sample size was achieved.

Data Collection Procedure

Data were collected using a structured and pre-tested proforma. Detailed demographic information, including age, educational status, occupation and socioeconomic status, was recorded. Clinical variables such as duration of diabetes, treatment regimen, presence of comorbidities including hypertension, dyslipidemia and chronic kidney disease, as well as lifestyle factors such as smoking status, alcohol consumption, physical activity and dietary compliance were documented. Anthropometric measurements including height, weight, body mass index and waist circumference were obtained using standard techniques. Blood pressure was measured using a calibrated sphygmomanometer following standard protocols.

Assessment of Menopausal Symptoms

Menopausal symptoms were assessed using the Menopause Rating Scale, a standardized and validated instrument that evaluates symptom severity across three domains: somatic, psychological and urogenital. Each symptom was scored on a scale reflecting severity, and the total score was calculated by summing individual item scores. Based on the total score, participants were categorized into severity groups, allowing for comparison across different levels of menopausal symptom burden.

Assessment of Glycemic and Biochemical Parameters

Glycemic control was assessed using glycated hemoglobin (HbA1c) values, which were obtained from recent laboratory reports or measured at the time of evaluation using standardized laboratory methods. Additional biochemical parameters, including fasting blood sugar, postprandial blood sugar and lipid profile parameters such as total cholesterol, high-density lipoprotein, low-density lipoprotein and triglycerides, were recorded. Renal function was assessed using estimated glomerular filtration rate calculated from serum creatinine values.

Outcome Measures

The primary outcome of the study was the association between menopausal symptom severity, as measured by the Menopause Rating Scale, and glycemic control, assessed using HbA1c levels. Secondary outcomes included the relationship between individual domains of menopausal symptoms and HbA1c, as well as the influence of demographic, clinical and lifestyle factors on glycemic control.

Statistical Analysis

Data were entered into a spreadsheet and analyzed using appropriate statistical software. Continuous variables were summarized as mean and standard deviation or median with range, depending on the distribution, while categorical variables were expressed as frequencies and percentages. The normality of data distribution was assessed prior to analysis. Correlation between menopausal symptom scores and HbA1c levels was evaluated using Spearman's rank correlation coefficient. Differences in mean HbA1c between groups were analyzed using independent samples t-test. Associations between categorical variables were assessed using the chi-square test. Multiple linear regression analysis was performed to identify independent predictors of HbA1c after adjusting for potential confounders such as age, body mass index and duration of diabetes. A p-value of less than 0.05 was considered statistically significant.

Ethical Considerations

The study was conducted in accordance with ethical principles and was approved by the Institutional Ethics Committee prior to initiation. Written informed consent was obtained from all participants before enrollment. Confidentiality of participant data was strictly maintained, and all information was used solely for research purposes.

RESULTS

Sociodemographic and Lifestyle Characteristics of Study Participants

The study population had a mean age of 51.79 ± 4.67 years. Educational attainment was low to moderate in a considerable proportion of participants, with 24% being illiterate and a further 23% having completed only secondary education, while the majority (65%) were homemakers and most belonged to lower (38%) or middle (42%) socioeconomic strata, reflecting a predominantly economically modest population. Lifestyle indicators were similarly unfavorable: most participants were non-smokers (90%) and non-alcohol consumers (95%), yet physical activity levels were largely suboptimal, with 72% engaging in mild or sedentary activity, and dietary compliance was poor to moderate in 71% of participants (Table 1).

Table 1: Sociodemographic and Lifestyle Characteristics of Study Participants

Variable	Category	n	%
Education	Illiterate	24	24
	Primary	20	20
	Secondary	23	23
	Graduate	19	19
	Postgraduate	14	14
Occupation	Homemaker	65	65
	Employed	19	19
	Self-employed	10	10
	Retired	6	6
Socioeconomic Status	Lower	38	38
	Middle	42	42
	Upper Middle	14	14
	Upper	6	6
Smoking Status	Never	90	90
	Current	6	6
	Ex-smoker	4	4
Alcohol Consumption	No	95	95
	Occasional	3	3
	Regular	2	2
Physical Activity	Mild	37	37
	Sedentary	35	35
	Moderate	18	18
	Active	10	10
Dietary Compliance	Poor	36	36
	Moderate	35	35
	Good	29	29

Socioeconomic status categorized using standard socioeconomic classification; physical activity categorized based on self-reported activity levels; dietary compliance assessed based on adherence to prescribed diabetic diet

Clinical, Metabolic and Treatment Profile of Study Participants

A substantial proportion of participants were overweight (49%) or obese (33%), and stage 1 hypertension was highly prevalent (76%), with overall hypertension present in 56% of the cohort. Nearly half of the participants had fair glycemic control (49%), while 29% had poor control and only 22% achieved good control. Dyslipidemia was highly prevalent (78%), whereas chronic kidney disease was observed in a small proportion (6%). The most commonly used anti-diabetic regimen was metformin combined with sulfonylurea (31%), followed by metformin monotherapy (25%); more than half of the participants were receiving anti-hypertensive therapy (56%) and a large majority were on statins (86%), reflecting proactive cardiovascular risk management in this population (Table 2).

Table 2: Clinical, Metabolic and Treatment Profile of Study Participants

Variable	Category	n	%
BMI Category	Normal	16	16
	Overweight	49	49
	Obese	33	33
	Underweight	2	2
BP Category	Normal	7	7
	Elevated	15	15
	Stage 1 HTN	76	76
	Stage 2 HTN	2	2
Hypertension	Yes	56	56
	No	44	44
Glycemic Control	Good	22	22
	Fair	49	49
	Poor	29	29

Dyslipidemia	Yes	78	78
	No	22	22
CKD	Yes	6	6
	No	94	94
Anti-diabetic Medication	Metformin + SU	31	31
	Metformin	25	25
	Metformin + DPP4i	16	16
	Metformin + SGLT2i	11	11
	Insulin + OHA	10	10
	Triple OHA	4	4
	Insulin	3	3
Anti-hypertensive Use	Yes	56	56
	No	44	44
Statin Use	Yes	86	86
	No	14	14
BMI = Body Mass Index; HTN = Hypertension; CKD = Chronic Kidney Disease; SU = Sulfonylurea; DPP4i = Dipeptidyl Peptidase-4 Inhibitor; SGLT2i = Sodium-Glucose Cotransporter-2 Inhibitor; OHA = Oral Hypoglycemic Agent			

Distribution of Menopausal Symptom Severity and Its Association with Glycemic Control

Most participants had mild menopausal symptoms on the MRS (74%), while the remaining 26% had moderate symptoms; no participant had severe symptom scores.

Mean HbA1c was significantly higher among participants with moderate menopausal symptoms compared with those with mild symptoms (8.16 ± 0.58% vs 7.34 ± 0.63%, t = -5.809, $p < 0.001$), indicating a clear worsening of glycemic control with increasing menopausal symptom severity (Table 3).

Table 3: Distribution of MRS Severity and Comparison of HbA1c

MRS Severity	Mean HbA1c ± SD (%)	t-value	p-value
Mild (n=74)	7.34 ± 0.63	-5.809	<0.001*
Moderate (n=26)	8.16 ± 0.58		
MRS = Menopause Rating Scale; independent samples t-test applied; *$p < 0.05$ considered statistically significant			

Association Between Glycemic Control Categories and Menopausal Symptom Severity

A statistically significant association was observed between glycemic control category and menopausal symptom severity ($\chi^2 = 23.686$, $p < 0.001$).

Good glycemic control was predominantly seen among women with mild symptoms (21 of 22 women with good control), whereas poor glycemic control was disproportionately more common among those with moderate symptoms (17 of 29 women with poor control), confirming a graded relationship between symptom severity and glycemic status (Table 4).

Table 4: Association Between Glycemic Control and MRS Severity

Glycemic Control	Mild (n=74)	Moderate (n=26)	χ^2	p-value
Good	21	1	23.686	<0.001*
Fair	41	8		
Poor	12	17		
MRS = Menopause Rating Scale; chi-square test applied; *$p < 0.05$ considered statistically significant				

Correlation and Regression Analysis of Menopausal Symptoms with Glycemic Control

A significant, moderate positive correlation was observed between total MRS score and HbA1c ($r = 0.573$, $p < 0.001$). On domain-wise analysis, the strongest correlation was seen for the psychological domain ($r = 0.507$, $p < 0.001$), followed by the somatic domain ($r = 0.401$, $p < 0.001$) and the urogenital domain ($r = 0.218$, $p = 0.030$).

On multiple linear regression adjusting for potential confounders, MRS total score remained an independent predictor of HbA1c ($\beta = 0.536$, $p < 0.001$), and age also showed a significant independent inverse association with HbA1c ($\beta = -0.252$, $p = 0.002$), whereas BMI ($\beta = 0.136$, $p = 0.097$) and duration of diabetes ($\beta = 0.088$, $p = 0.276$) were not independently significant (Table 5).

Table 5: Correlation and Multiple Linear Regression Analysis

Variable	Coefficient (r/β)	p-value
Correlation Analysis		
MRS Total Score vs HbA1c	0.573	<0.001*
Somatic Score	0.401	<0.001*
Psychological Score	0.507	<0.001*
Urogenital Score	0.218	0.030*
Regression Analysis		
MRS Total Score (β)	0.536	<0.001*
Age (β)	-0.252	0.002*
BMI (β)	0.136	0.097
Duration of DM (β)	0.088	0.276
MRS = Menopause Rating Scale; β = Standardized regression coefficient; DM = Diabetes Mellitus; *p < 0.05 considered statistically significant		

DISCUSSION

This cross-sectional study among 100 postmenopausal women with type 2 diabetes mellitus found that menopausal symptom severity, assessed using the MRS, was significantly and independently associated with poorer glycemic control. Women with moderate menopausal symptoms had meaningfully higher mean HbA1c than those with mild symptoms, glycemic control category was significantly associated with symptom severity group, and MRS total score correlated positively with HbA1c even after adjustment for age, BMI and diabetes duration. Among the three symptom domains, the psychological domain showed the strongest correlation with glycemic control, followed by the somatic and urogenital domains.

The positive correlation observed between total menopausal symptom burden and HbA1c is consistent with the broader literature on cardiometabolic vulnerability during the climacteric transition. A recent narrative review has described how the climacteric period is accompanied by increased visceral adiposity, reduced lean mass, insulin resistance and dyslipidemia, changes that plausibly worsen glycemic control independent of chronological age.[3] The protective metabolic role of estrogen is further supported by evidence that menopausal hormone therapy improves glycemic parameters in women with T2DM when appropriately selected,[5] implying that greater symptom severity, itself a proxy for the intensity of estrogen withdrawal and associated neuroendocrine disturbance, could parallel a more pronounced adverse metabolic milieu. Cardiovascular and menopause societies have accordingly emphasized structured screening of cardiometabolic risk across the menopausal transition, recognizing this period as a distinct window of vulnerability rather than a single hormonal cutoff.[6,7] Mechanistically, estrogen withdrawal is thought to reduce adipose tissue insulin sensitivity, promote visceral fat redistribution, alter adipokine secretion and blunt autonomic buffering of glucose excursions, all of which could plausibly mediate the association observed in the present study.

Notably, our finding that symptom severity, rather than menopausal status per se, correlated with glycemic control helps reconcile discordant findings in the literature regarding reproductive milestones and diabetes risk. While data from the Tehran Lipid and Glucose Study cohort have linked early menarche and surgical menopause to higher odds of prediabetes, type 2 diabetes and metabolic syndrome,[8] a large UK Biobank cohort found no independent association between the timing or type of menopause and incident diabetes after adjustment for confounders.[9] Our results suggest that the metabolic impact of menopause on an already diabetic population may be better captured through the intensity of symptoms experienced rather than through chronological timing alone, supporting the use of validated symptom-severity tools such as the MRS, which continues to demonstrate strong psychometric performance across diverse populations,[10] as a practical clinical adjunct.

The particularly strong correlation between the psychological domain of the MRS and HbA1c observed in our cohort aligns with a growing body of evidence linking psychological distress to glycemic dysregulation. A large meta-analysis of 61 studies has confirmed that depression and diabetes distress are significantly associated with poorer glycemic control and reduced self-care behaviors,[12] and a cross-sectional study of postmenopausal women with T2DM and comorbid hypothyroidism similarly identified higher HbA1c as an independent risk factor for depressive symptoms.[13] The proposed mechanism underlying this association involves activation of the hypothalamic-pituitary-adrenal axis and sympathetic nervous system by psychological distress, leading to elevated cortisol and catecholamine levels that promote hepatic gluconeogenesis and peripheral insulin resistance; psychological symptoms may also erode motivation for self-care behaviors such as dietary compliance, physical activity and medication adherence, compounding glycemic deterioration. Encouragingly, nurse-led psychological interventions have been shown in a systematic review and meta-analysis to significantly reduce diabetes distress, with some benefit extending to depression and glycemic control,[14]

suggesting that the psychological domain identified in our study is not merely a marker of poor control but a potentially modifiable target.

The weaker, though still significant, correlation observed for the urogenital domain may reflect a partially distinct pathophysiological pathway. Chronic hyperglycemia has been shown to disrupt the vaginal microbiome and exacerbate genitourinary symptoms and sexual dysfunction in diabetic women independent of menopausal hormonal status,[15] suggesting that urogenital symptom burden in our cohort may have been driven jointly by estrogen deficiency and hyperglycemia-related dysbiosis, thereby attenuating the strength of its correlation with HbA1c relative to the psychological domain.

Beyond menopausal symptoms, several sociodemographic and lifestyle factors observed in our cohort mirror determinants reported elsewhere. Suboptimal physical activity and poor dietary compliance were common in our population, consistent with cross-sectional data identifying lower socioeconomic and educational status, sedentary behavior and family history of diabetes as determinants of poor glycemic control in T2DM.[16] Similarly, the substantial minority of participants on insulin-containing regimens underscores the relevance of adherence barriers; predictors of insulin nonadherence identified in tertiary care settings, including inadequate storage facilities, polypharmacy and poor lifestyle adherence, are directly applicable to our largely homemaker, lower-to-middle socioeconomic status cohort.[17] Non-hormonal strategies such as dietary phytoestrogens have shown limited estrogenic efficacy in postmenopausal women,[18] reinforcing that lifestyle-based glycemic strategies, rather than symptom-targeted hormonal substitutes alone, remain central to management. Structured exercise interventions, including high-intensity interval training, have been shown to improve glycemic parameters and beta-cell glucose sensitivity even in postmenopausal women with established T2DM,[19,20] offering an evidence-based, non-pharmacological avenue to mitigate the adverse metabolic correlates of menopausal symptom burden identified in our study.

The inverse association between age and HbA1c observed on regression, though modest, merits cautious interpretation. It may reflect a selection effect, wherein older women with long-standing, better-monitored diabetes are more likely to remain engaged in outpatient follow-up, or may reflect greater disease awareness and treatment intensification with advancing duration of clinical contact, consistent with the high statin and antihypertensive use observed in our cohort. Elevated HbA1c in postmenopausal diabetic women has previously been linked to other adverse outcomes such as increased breast cancer risk,[21] and disrupted glucose-insulin homeostasis has separately been associated with altered prolactin regulation in diabetic patients,[22] both of which reinforce that HbA1c elevation in this population carries implications extending beyond glycemic control alone and merits close longitudinal monitoring.

Collectively, these findings support incorporating a brief, validated menopausal symptom assessment, such as the MRS, into the routine review of postmenopausal women with T2DM, with particular attention to psychological symptoms as an actionable, modifiable correlate of glycemic control. Multidisciplinary care models that combine diabetology, gynecology and psychological support may be particularly well suited to this population.

This study has several limitations. Its cross-sectional design precludes any causal inference regarding the direction of the association between menopausal symptoms and glycemic control. The single-center, tertiary-care setting and modest sample size, particularly the smaller subgroup with moderate symptoms, may limit generalizability to community-based populations. Menopausal symptoms were assessed using a self-reported scale, which is susceptible to recall and reporting bias, and HbA1c reflects glycemic status only at a single time point. Although multiple linear regression adjusted for major confounders, residual confounding from unmeasured variables such as detailed psychiatric history, sleep quality and treatment adherence cannot be excluded.

CONCLUSION

In this cross-sectional study of postmenopausal women with type 2 diabetes mellitus, greater menopausal symptom severity, particularly in the psychological domain, was independently and positively associated with poorer glycemic control, even after adjustment for age, BMI and diabetes duration. These findings suggest that menopausal symptom burden is not merely a quality-of-life concern but a clinically relevant correlate of metabolic status in this population. Routine, validated screening for menopausal symptoms, combined with attention to psychological wellbeing and structured lifestyle interventions, could represent a low-cost, actionable addition to diabetes care in postmenopausal women. Prospective, multicentric studies are warranted to confirm causality and evaluate targeted interventions.

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