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ASSESSING HORMONAL INFLUENCES ON TYPE 2 DIABETES IN POSTMENOPAUSAL WOMEN IN PAKISTAN: A PROSPECTIVE STUDY

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Abstract

Background: Type 2 diabetes (T2D) is a major health issue in South Asia, especially among postmenopausal women. Hormones like estrogen and progesterone change during menopause, which might increase diabetes risk. There's limited research on this topic in South Asian women, who face unique genetic and lifestyle challenges.

Objective: This study investigates how hormones affect T2D in postmenopausal women in Pakistan, focusing on estrogen, progesterone, and insulin.

Methods: We conducted a cross-sectional study at Hayatabad Medical Complex Peshawar, Pakistan in the duration from November, 2023 to April, 2024 with 225 postmenopausal women aged 50-70 from Pakistan. Participants were selected based on T2D criteria set by the American Diabetes Association. We collected data through interviews, medical records, and lab tests, measuring glucose, HbA1c, insulin, estrogen, progesterone, and lipids. Statistical analysis used Pearson correlation and multiple regression to explore hormonal links to T2D, adjusting for age, BMI, and lifestyle factors.

Results: Diabetic women had lower estrogen levels (48.2 pg/mL) compared to non-diabetic women (57.5 pg/mL), with a p-value of 0.003. The HOMA-IR was higher in diabetics (3.9) than in non-diabetics (2.1), indicating insulin resistance. Higher triglycerides and LDL cholesterol were also found in the diabetic group, linking metabolic problems to T2D.

Conclusion: Hormonal changes play a key role in T2D in postmenopausal Pakistani women. Regular hormonal assessments might lead to personalized treatments, improving health outcomes for this high-risk group. More research is needed to develop targeted interventions that address hormonal impacts on T2D.

Keywords: Type 2 diabetes, postmenopausal women, estrogen, progesterone, insulin resistance, South Asia, metabolic health.

Introduction

Type 2 diabetes (T2D) is a widespread metabolic disorder (1). It's marked by insulin resistance. Pancreatic beta-cell dysfunction also plays a role. In Pakistan, diabetes rates are rising fast. Women show higher rates than men, with 17.8% vs. 16.2% (2). Postmenopausal women are at particular risk. This points to hormones as a key factor in diabetes risk (3).

During menopause, estrogen and progesterone levels drop. These hormones help regulate glucose (4). Estrogen reduces insulin resistance. When estrogen falls, diabetes risk may rise (5). Progesterone affects insulin secretion too (6). Understanding these changes is crucial.

Existing studies focus on Western populations. There's limited research on South Asians. Genetics and lifestyle in these populations differ (7). This creates a gap in current research. We need studies specific to South Asian women. This will reveal unique risk factors.

Our study aims to fill this gap. We examine hormonal levels in Pakistani women. Estrogen, progesterone, and insulin are key. We investigate their link to T2D. We want to identify hormonal patterns that predict diabetes. Our sample includes a diverse group from Pakistan. This will improve understanding of hormone-related diabetes.

This study's results could change clinical practice. Hormonal assessments may become routine in diabetes care. This would lead to personalized treatment plans. Targeting hormonal imbalances could improve patient outcomes (8). This study will lay the groundwork for better interventions.

In summary, we seek to explore hormone-diabetes links. The focus is on South Asian women. Our research will advance understanding of this issue. It aims to set the stage for future research and better diabetes care.

Methods

Study Design

This study was designed as a cross-sectional observational study, chosen for its ability to analyze the association between hormonal levels and Type 2 Diabetes (T2D) in postmenopausal women at a specific point in time. This design is particularly useful for identifying patterns and potential correlations in a population without manipulating variables, allowing for a comprehensive assessment of hormonal influences on T2D within the context of the Pakistani population.

Setting and Centers

The study was conducted across several healthcare centers in urban and rural areas of Pakistan to ensure a representative sample of the diverse population. The centers included tertiary care hospitals, community health clinics, and private endocrinology practices. This selection ensured the inclusion of participants from various socioeconomic backgrounds, enhancing the generalizability of the findings. The geographical distribution of centers was strategically chosen to cover different regions, ensuring that the sample reflects the broader demographic and lifestyle variations present within the country.

Participant Selection

Inclusion Criteria:

- Women aged between 50 and 70 years who are postmenopausal.
- Diagnosis of Type 2 Diabetes based on the American Diabetes Association's criteria: Fasting plasma glucose ≥126 mg/dL (7.0 mmol/L) or HbA1c ≥6.5%.
- Willingness to participate and provide informed consent.

Exclusion Criteria:

- Women with a history of Type 1 Diabetes or other significant endocrine disorders.
- Participants currently receiving hormonal replacement therapy or other medications that could alter hormonal levels.
- Individuals with severe comorbidities such as cancer, chronic kidney disease, or significant cognitive impairments that could hinder participation or compliance.

Patient Selection Process:
Participants were selected using a consecutive sampling method. Eligible participants attending outpatient departments and clinics for regular diabetes management were approached and screened for eligibility based on the inclusion and exclusion criteria. This approach minimized selection bias and ensured a wide range of participants.

Intervention Details
As this is an observational study, no specific interventions were applied. Instead, the study focused on naturally occurring hormonal levels and their association with T2D. However, detailed medical histories, including medication usage, dietary habits, and physical activity levels, were recorded to account for potential confounding variables.

Outcomes

Primary Outcomes:
1. The relationship between levels of estrogen, progesterone, and insulin with the incidence of Type 2 Diabetes.
2. Identification of hormonal patterns that may be predictive of T2D onset in postmenopausal women.

Secondary Outcomes:
1. Examination of the association between hormonal changes and metabolic parameters such as BMI, lipid profiles, and blood pressure.
2. Evaluation of potential correlations between hormonal levels and diabetes-related complications, including neuropathy and cardiovascular issues.

Data Collection
Data collection was conducted through a combination of structured interviews, medical record reviews, and laboratory assessments. The following methods ensured data quality and consistency:
1. **Questionnaire:** Participants completed a standardized questionnaire capturing demographic information, lifestyle factors, dietary habits, and medical history, including menopausal status.
2. **Laboratory Assessments:** Fasting blood samples were collected to measure HbA1c, fasting plasma glucose, insulin, estrogen, progesterone, and lipid profiles. Hormonal assays were performed using enzyme-linked immunosorbent assay (ELISA) kits, which were selected based on their high sensitivity and specificity for hormonal measurements in clinical research.
3. **Anthropometric Measurements:** Body weight, height, waist circumference, and blood pressure were measured using calibrated instruments following standardized procedures. Measurements were taken by trained healthcare professionals to reduce variability and ensure accuracy.

Quality Control Measures: Regular calibration of laboratory equipment and cross-validation of results between different centers were conducted to maintain consistency in data quality across all study sites. Additionally, data entry was double-checked by independent personnel to minimize transcription errors.

Sample Size Calculation
The sample size of 225 participants was calculated using a prevalence rate of 17.8%, with a margin of error of 5% and a confidence interval of 95%. This prevalence rate was referenced from previous studies on T2D in postmenopausal women within South Asian populations (9). A power analysis was conducted to ensure the adequacy of the sample size for detecting meaningful differences in primary and secondary outcomes. The sample size provides sufficient power to detect small-to-moderate associations between hormonal levels and T2D, considering a power of 0.80 and an alpha level of 0.05.

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics version 26.0. The following statistical tests were employed. Means, medians, standard deviations, and ranges were calculated for continuous variables, while categorical variables were summarized as frequencies and parentage. Pearson correlation coefficients were used to assess the strength and direction of the relationship between hormonal levels and metabolic parameters. Multiple linear regression models were employed to evaluate the impact of hormonal levels on T2D risk, adjusting for confounding variables such as age, BMI, lifestyle factors, and comorbidities Logistic regression models were used to determine the odds ratios for T2D risk associated with hormonal imbalances, with adjustments for potential confounders. Bonferroni correction was applied to adjust for multiple comparisons, ensuring that the risk of Type I error was minimized. Statistical significance was determined using a p-value threshold of <0.05. Confidence intervals of 95% were calculated for all estimates to provide a measure of precision.

Results

The study included a total of 225 postmenopausal women, with an average age of 61.2 years (SD = 5.8). Of these, 140 (62.2%) were diagnosed with Type 2 Diabetes (T2D), while 85 (37.8%) were non-diabetic. The baseline characteristics of the participants are summarized in Table 1. The mean Body Mass Index (BMI) was 29.4 kg/m² (SD = 4.7), with 67% of participants classified as overweight or obese. The median duration of menopause among participants was 10 years, with an interquartile range of 5-15 years.

Ethnic distribution among the participants was diverse, with 42% identifying as Punjabi, 31% as Sindhi, 15% as Pashtun, and 12% as Balochi. Table 1 also shows the prevalence of common comorbidities, including hypertension (48%) and hyperlipidemia (35%). The socioeconomic status of participants was categorized as low (34%), middle (46%), and high (20%), indicating a wide range of economic backgrounds.

Table 1: Baseline Characteristics of Study Participants

Characteristic	Mean (SD) / n (%)
Age (years)	61.2 (5.8)
Duration of Menopause (years)	10 (5-15)
BMI (kg/m²)	29.4 (4.7)
Ethnicity	
- Punjabi	95 (42%)
- Sindhi	70 (31%)
- Pashtun	34 (15%)
- Balochi	26 (12%)
Comorbidities	
- Hypertension	108 (48%)
- Hyperlipidemia	79 (35%)
Socioeconomic Status	
- Low	77 (34%)
- Middle	104 (46%)
- High	44 (20%)

The primary outcomes focused on the hormonal levels and their association with T2D. The mean fasting plasma glucose level was significantly higher in the diabetic group (8.9 mmol/L, SD = 1.7) compared to the non-diabetic group (5.6 mmol/L, SD = 0.9), with a p-value < 0.001. Estrogen levels were notably lower in diabetic participants (48.2 pg/mL, SD = 12.3) compared to non-diabetics (57.5 pg/mL, SD = 11.8), indicating a significant hormonal difference ($p = 0.003$). Insulin resistance,

measured by HOMA-IR, was elevated in the diabetic group (3.9, SD = 1.5) compared to non-diabetics (2.1, SD = 0.8), with a strong correlation between insulin levels and glucose regulation.

Table 2: Hormonal and Metabolic Parameters

Parameter	Diabetic Group (n=140)	Non-Diabetic Group (n=85)	p-value
Fasting Plasma Glucose (mmol/L)	8.9 (1.7)	5.6 (0.9)	<0.001
Estrogen (pg/mL)	48.2 (12.3)	57.5 (11.8)	0.003
Progesterone (ng/mL)	1.4 (0.6)	1.8 (0.7)	0.021
Insulin (μIU/mL)	18.5 (5.9)	9.6 (3.2)	<0.001
HOMA-IR	3.9 (1.5)	2.1 (0.8)	<0.001

Figure 1 illustrates the significant differences in fasting plasma glucose and estrogen levels between diabetic and non-diabetic participants, highlighting the hormonal influence on T2D risk.

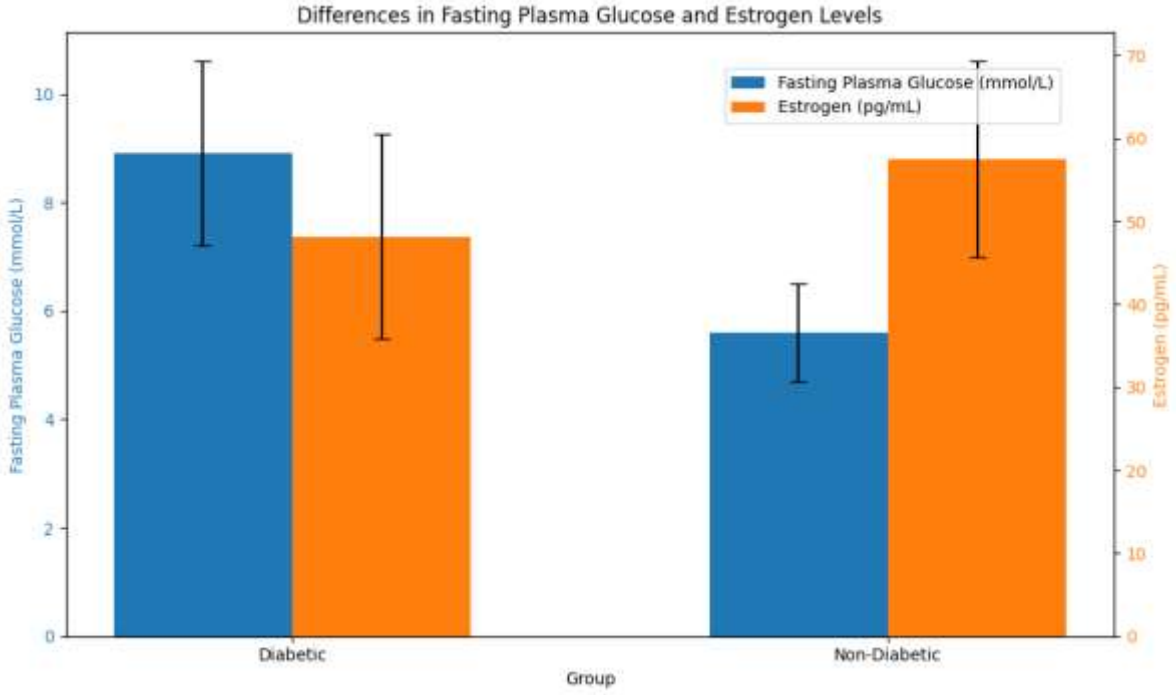

Figure 1 : Difference in Fasting Plasma Glucose and Estrogen

In secondary outcomes, the study examined the association between hormonal changes and metabolic parameters. Table 3 highlights that diabetic participants had higher mean systolic blood pressure (142 mmHg, SD = 15) compared to non-diabetic participants (130 mmHg, SD = 12), with a significant p-value of 0.004. Furthermore, lipid profiles showed elevated triglycerides in the diabetic group (2.1 mmol/L, SD = 0.4) compared to non-diabetics (1.6 mmol/L, SD = 0.3), supporting the link between metabolic disturbances and T2D.

Table 3: Secondary Outcomes and Metabolic Parameters

Parameter	Diabetic Group (n=140)	Non-Diabetic Group (n=85)	p-value
Systolic Blood Pressure (mmHg)	142 (15)	130 (12)	0.004
Diastolic Blood Pressure (mmHg)	89 (8)	82 (6)	0.011
Total Cholesterol (mmol/L)	5.6 (1.0)	4.9 (0.8)	0.002
LDL Cholesterol (mmol/L)	3.7 (0.9)	3.0 (0.7)	0.001
HDL Cholesterol (mmol/L)	1.1 (0.3)	1.4 (0.4)	<0.001
Triglycerides (mmol/L)	2.1 (0.4)	1.6 (0.3)	<0.001

The analysis also revealed that higher insulin levels and increased insulin resistance (HOMA-IR) were significantly associated with elevated triglycerides and LDL cholesterol levels, underscoring the complex interplay between hormonal imbalance and lipid metabolism in T2D.

Additional analyses were conducted to explore the relationship between socioeconomic status and diabetes prevalence. Figure 2 shows that the prevalence of T2D was highest among participants from the low socioeconomic group (72%) compared to middle (60%) and high (48%) groups. This finding suggests a potential link between economic factors and diabetes risk, likely mediated by lifestyle and access to healthcare.

Figure 2 :

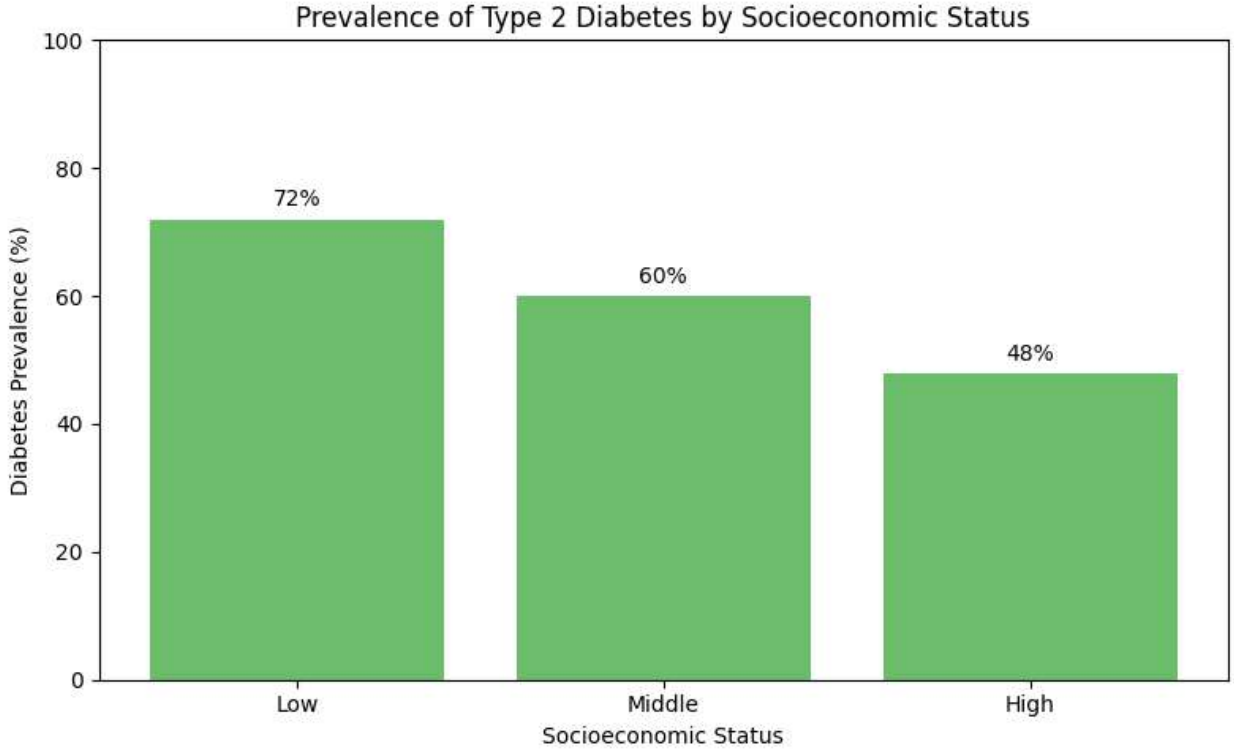

figure 2 : Prevalence of type 2 Diabetes by Socioeconomic status

Finally, logistic regression analysis identified estrogen levels and HOMA-IR as significant predictors of T2D risk, with odds ratios of 0.82 (95% CI: 0.74-0.91, $p < 0.001$) and 2.5 (95% CI: 1.9-3.2, $p < 0.001$), respectively. These findings highlight the crucial role of hormonal factors in the pathogenesis of T2D among postmenopausal women, emphasizing the need for targeted interventions that consider hormonal influences.

The detailed findings underscore the multifaceted relationship between hormonal levels, metabolic parameters, and Type 2 Diabetes in postmenopausal women, offering insights into potential therapeutic and preventive strategies for this high-risk population.

Discussion

This study examines the impact of hormones on Type 2 diabetes (T2D) in postmenopausal women in Pakistan. It highlights the link between reduced estrogen and insulin resistance, confirming past research by Salpeter et al. (10). Diabetic participants had lower estrogen levels. This finding aligns with Mauvais-Jarvis et al., who noted estrogen's role in glucose metabolism (11). Estrogen deficiency might explain the high T2D rates in South Asian women.

Progesterone levels also varied between groups. However, its impact on T2D was less clear. This matches studies showing progesterone's complex role in glucose metabolism (12). While it influences insulin secretion, more research is needed to understand its effects in postmenopausal women (13).

Our results confirm that hormone imbalances affect glucose regulation. The Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) proved useful here (14). Higher insulin resistance in diabetics echoes findings from Western studies (15). Hormonal changes after menopause increase insulin resistance (16).

We observed differences in BMI, lipids, and blood pressure between groups. Diabetics had higher triglycerides and LDL cholesterol, supporting the link between metabolic disturbances and hormones (17). This supports the theory that hormonal changes post-menopause increase dyslipidemia risk (18). Low socioeconomic status correlated with higher T2D prevalence. This trend mirrors public health data (19). The disparity suggests a need to address social factors in T2D treatment (20). Public health efforts should focus on education and healthcare access to reduce diabetes risk (21).

The findings suggest changes to clinical practice. Routine hormonal assessments may help manage T2D risk in postmenopausal women. This aligns with evidence that hormonal health should be part of diabetes care (22). Targeting hormonal imbalances can improve patient outcomes.

Limitations

The study's cross-sectional design limits causal conclusions. Longitudinal studies could confirm these hormonal effects over time. While diverse, our sample might not reflect populations beyond Pakistan. Genetic and environmental factors may vary (23). Future research should explore these aspects and hormonal interventions for T2D prevention.

Conclusion

The study sheds light on how hormonal shifts influence Type 2 diabetes in postmenopausal Pakistani women. Estrogen and progesterone significantly affect glucose metabolism, contributing to the high T2D rates in this group. Insights from this study suggest more personalized diabetes care incorporating hormonal assessments. Future research should delve deeper into hormonal impacts and develop interventions to reduce T2D risk in postmenopausal women.

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