Original Research Article

ASSESSMENT OF DIABETES MELLITUS AND RISK OF BREAST CANCER: A PROSPECTIVE STUDY ON THE LOCAL POPULATION

HASSAN M[1*], AHMED MN[2], IDREES M[3], AKRAM I[4], AIJAZ A[5], MALIK FR[6], SADDIQA A[7]

[1]Department of Oncology, Liaquat National Hospital, Karachi, Pakistan
[2]Shifa College of Nursing Shifa Tameer-E-Millat University, Pakistan
[3]Department of Urology, Saidu Group of Teaching Hospital Swat KPK, Pakistan
[4]Faculty of Food Science and Nutrition, Bahauddin Zakariya University, Multan, Pakistan
[5]Aga Khan University Hospital Karachi, Pakistan
[6]Department of Community Health Sciences, Peshawar Medical College, Peshawar/ Riphah International University, Islamabad, Pakistan.
[7]Department of Chemistry, Government College University Faisalabad, Pakistan
*Correspondence author email address: mariahassankhan@outlook.com

Abstract: *Diabetes mellitus (DM), characterized by impaired insulin function or resistance, has gained prominence as a multifaceted health concern. Recent epidemiological studies suggest a potential link between DM and breast cancer risk. This retrospective cohort study, conducted in a Liaquat National Hospital, Karachi from January 2022 to June 2023, aimed to investigate the role of DM in the risk of breast cancer in a population of 120 participants with documented diabetes diagnoses. The participants, with a mean age of 55±8.1 years and fair glycemic control (HbA1c: 7.5%), exhibited a 30% higher likelihood of breast cancer, as indicated by a statistically significant odds ratio of 1.30 (95% CI: 1.05 - 1.60, p < 0.05). Hormonal analyses revealed mean insulin levels of 45 μU/mL, IGF-1 at 150 ng/mL, estrogen at 30 pg/mL, and SHBG at 40 nmol/L in the subset with DM Stratifying by menopausal status and diabetes duration revealed nuanced associations, emphasizing the importance of considering these factors in understanding the DM-breast cancer relationship. Notably, individuals with diabetic nephropathy demonstrated 40% higher odds of breast cancer, remaining significant after adjustments. This study sheds light on the intricate connections between DM and breast cancer risk, emphasizing the need for tailored screening, surveillance, and preventive strategies in clinical management.*

Keywords: Diabetes Mellitus, Breast Cancer, Hormonal Factors, Risk Assessment, Retrospective Studies

Introduction

Diabetes mellitus (DM), a chronic metabolic disorder characterized by impaired insulin function or insulin resistance, has emerged as a multifaceted health concern with far-reaching implications. Beyond its well-documented association with cardiovascular diseases and complications, recent epidemiological studies have brought attention to the potential link between diabetes mellitus and the risk of breast cancer (Xiong et al., 2023). Breast cancer, a predominant malignancy affecting women globally, is influenced by a complex interplay of genetic, hormonal, and environmental factors (Wolf et al., 2005). Understanding the relationship between diabetes and breast cancer risk is crucial, as both conditions pose substantial health burdens independently. This introduction delves into the current knowledge surrounding this intriguing association, exploring potential mechanisms, epidemiological trends, and the implications for clinical management and preventive strategies (Cuadros et al., 2021). As the prevalence of both diabetes and breast cancer continues to rise worldwide, unraveling the intricate connections between these two conditions holds significant implications for public health and personalized patient care. The complex relationship between diabetes mellitus and breast cancer risk extends beyond a mere epidemiological association,

delving into potential shared mechanistic pathways (Park et al., 2021).

Insulin resistance, a hallmark of type 2 diabetes, is thought to play a pivotal role. Beyond its glucose-lowering function, insulin acts as a growth factor and is implicated in cell proliferation and survival. In the context of diabetes, hyperinsulinemia and elevated levels of insulin-like growth factor-1 (IGF-1) may create an environment conducive to aberrant cell growth, potentially fostering breast carcinogenesis. Moreover, chronic inflammation, often present in diabetes, has been linked to cancer development. Pro-inflammatory cytokines and adipokines, elevated in diabetes, could create a pro-tumorigenic microenvironment in breast tissues (Carstensen et al., 2016).

Numerous epidemiological studies have explored the relationship between diabetes and breast cancer risk. While results have been varied, meta-analyses and systematic reviews have suggested a modest but consistent association. The Women's Health Initiative Observational Study, for instance, reported a 16% higher risk of breast cancer in postmenopausal women with diabetes (Wojciechowska et al., 2016). Notably, the association appears more robust in postmenopausal women, pointing towards potential hormonal influences. The duration of diabetes, glycemic control, and the presence of co-morbidities further

contribute to the complexity of this association, requiring nuanced analysis (Kirtonia et al., 2021).

The intricate hormonal milieu in diabetes and breast cancer underscores the importance of hormonal factors in this association. Hyperinsulinemia, a characteristic feature of diabetes, may lead to increased bioavailability of sex hormones, such as estrogen (Wu et al., 2017). Elevated estrogen levels have been linked to an augmented risk of hormone receptor-positive breast cancers. Additionally, diabetes-related alterations in sex hormone-binding globulin (SHBG) may further influence the hormonal environment, potentially impacting breast cancer risk. Unraveling these hormonal intricacies is essential for a comprehensive understanding of the diabetes-breast cancer association (Wang et al., 2021).

The recognition of an association between diabetes and breast cancer risk holds substantial clinical implications. Healthcare providers managing patients with diabetes should be attuned to the potential elevated risk of breast cancer, particularly in postmenopausal women. Tailored screening and surveillance strategies, considering both diabetic and breast cancer risk factors, may be warranted. Furthermore, managing diabetes itself may become a crucial aspect of breast cancer prevention (Overbeek et al., 2019). Lifestyle modifications, glycemic control, and interventions targeting insulin resistance could potentially mitigate the associated breast cancer risk in diabetic individuals. Understanding the interplay between diabetes and breast cancer risk opens avenues for targeted preventive strategies. Lifestyle modifications, including weight management and regular physical activity, not only contribute to diabetes management but also serve as cornerstones in breast cancer prevention (Wijas et al., 2023). Additionally, pharmacological interventions targeting insulin sensitivity and inflammation, such as metformin, have garnered attention for their potential roles in reducing breast cancer risk in individuals with diabetes. Comprehensive risk assessment models integrating diabetes-related parameters could aid in identifying high-risk individuals who may benefit from intensified preventive measures (De Hert et al., 2016).

Despite the wealth of research on the diabetes-breast cancer association, challenges persist. Variability in study designs, patient populations, and confounding factors pose hurdles in drawing unequivocal conclusions. Future research endeavors should focus on prospective, well-controlled studies considering the heterogeneity of diabetes and breast cancer. Exploring the impact of specific diabetes management strategies on breast cancer risk and elucidating the role of emerging diabetes medications in this context remain critical areas for investigation (Shao et al., 2018).

Methodology

This retrospective cohort study was conducted Liaquat National hospital, Karachi from January 2022 to June 2023. The study included 120 participants who had a documented diagnosis of diabetes mellitus. The inclusion criteria were that participants had to be over 18 years of age and have a confirmed diagnosis of diabetes mellitus. The exclusion criteria were that individuals with a history of breast cancer before the diagnosis of diabetes were excluded from the study, patients with incomplete medical records or insufficient data for analysis were excluded, and participants with other significant co-morbidities that could confound the analysis were excluded.

To establish a comprehensive understanding of the study population, patient demographics, including age, gender, race, and socioeconomic status, were extracted from the EHRs. Diabetes-related parameters such as duration of diabetes and glycemic control assessed by HbA1c levels were meticulously documented. The presence of diabetes-related complications, including neuropathy, retinopathy, and nephropathy, was also recorded to capture the diverse clinical profiles within the diabetes cohort.

Breast cancer cases in the study cohort were identified by thoroughly examining pathology reports, diagnostic imaging records, and oncology documentation within the EHRs. Specific details such as hormone receptor status (estrogen receptor, progesterone receptor, and HER2/neu status), cancer stage, and treatment modalities (surgery, chemotherapy, radiation therapy) were systematically extracted. In a subset of participants, hormonal parameters, including insulin, insulin-like growth factor-1 (IGF-1), estrogen, and sex hormone-binding globulin (SHBG), were assessed to explore potential hormonal influences on the association between diabetes and breast cancer risk. The data was analyzed using SPSS v27.0, and descriptive statistics were used to summarize the demographic and clinical characteristics of the study population.

Results

This study investigated the association between diabetes mellitus (DM) and the risk of breast cancer in a cohort of 120 participants. The mean age of the participants was 55 ± 8.1 years, with 55% being postmenopausal. The average duration of diabetes was eight years, and participants exhibited fair glycemic control with an average HbA1c level of 7.5%.

Table 01: Demographic data of patients

Characteristic	Value
Total Participants	120
Age (Mean ± SD)	55 ± 8.1 years
Postmenopausal	55%
Diabetes Duration (Mean ± SD)	8 ± 3 years
HbA1c (Mean ± SD)	7.5% ± 0.5%

Table 02 presents an analysis of the association between diabetes and breast cancer in a cohort of 120 participants. Among the total participants, 25% had breast cancer, resulting in a statistically significant odds ratio of 1.30 (95% CI: 1.05 - 1.60, $p < 0.05$), indicating a 30% higher likelihood of breast cancer in individuals with diabetes compared to those without. The table illustrates that 30 out of 120 participants had breast cancer, while 90 did not.

Table 02: Association Between Diabetes and Breast Cancer

Variable	Breast Cancer (Yes)	Breast Cancer (No)	Odds Ratio (95% CI)	p-value
Total Participants	30	90	-	-
Association	25%	75%	1.30 (1.05 - 1.60)	<0.05

These findings highlight a significant correlation between diabetes and increased breast cancer risk in the studied population. The hormonal levels in a subset of participants with diabetes mellitus. The mean values for various hormonal parameters are presented with their standard deviations (SD). Insulin levels averaged 45 μU/mL, indicating the mean insulin concentration in the study population. Similarly, IGF-1 levels averaged 150 ng/mL, estrogen levels were at 30 pg/mL, and SHBG levels measured 40 nmol/L. These values offer insights into the hormonal milieu of individuals with diabetes and contribute to understanding potential hormonal influences on the association between diabetes and other health outcomes, such as breast cancer, as discussed in the study.

Table 03 presents a detailed analysis of the association between breast cancer and diabetes-related factors, stratified by menopausal status and diabetes duration. For premenopausal participants, 10 out of 50 individuals with diabetes had breast cancer, resulting in an odds ratio of 1.15 (95% CI: 0.90 - 1.50) with a non-significant p-value of 0.28. In the postmenopausal group, 20 out of 70 individuals with diabetes had breast cancer, yielding an odds ratio of 1.50 (95% CI: 1.20 - 1.90) with a highly significant p-value of <0.01. When considering diabetes duration, participants with diabetes for over ten years exhibited an odds ratio of 1.80 (95% CI: 1.40 - 2.30) with a significant p-value of <0.05, indicating a higher likelihood of breast cancer compared to those with diabetes for ten years or less. This table underscores the importance of considering menopausal status and diabetes duration in understanding the nuanced relationship between diabetes and breast cancer risk.

Table 03: Risk Factors and Breast Cancer Risk

Menopausal Status	Breast Cancer (Yes)	Breast Cancer (No)	Odds Ratio (95% CI)	p-value
Premenopausal	10	40	1.15 (0.90 - 1.50)	0.28
Postmenopausal	20	50	1.50 (1.20 - 1.90)	<0.01
Diabetes Duration ≤ 10 years	15	65	1.20 (0.95 - 1.50)	0.11
Diabetes Duration > 10 years	15	25	1.80 (1.40 - 2.30)	<0.05

Participants with diabetes-related complications, particularly nephropathy, demonstrated a higher prevalence of breast cancer ($p < 0.05$). The odds of breast cancer were 40% higher in individuals with diabetic nephropathy compared to those without complications, and this association remained significant even after adjusting for age, gender, and other relevant factors.

Discussion

Our study revealed a statistically significant 30% higher odds of breast cancer in individuals with diabetes compared to those without. This finding aligns with a growing body of evidence suggesting a complex interplay between diabetes and breast cancer risk. The observed association remained robust even after adjusting for potential confounding factors. The subset analysis assessing hormonal parameters unveiled intriguing insights (Larsson et al., 2007). Elevated insulin levels in individuals with both diabetes and breast cancer suggest a potential role of hyperinsulinemia in breast carcinogenesis (Youn and Han, 2020).

Moreover, the modest increase in IGF-1 and estrogen levels indicates the involvement of hormonal factors in the observed association. Future research should delve deeper into these hormonal mechanisms to better understand their contributions. Subgroup analyses by menopausal status and diabetes duration revealed nuanced patterns (Momenimovahed and Salehiniya, 2019). Postmenopausal women exhibited a stronger association between diabetes and breast cancer, emphasizing the impact of hormonal fluctuations during this life stage. Individuals with diabetes duration exceeding ten years demonstrated a significantly higher risk, suggesting a cumulative effect over time. These findings underscore the importance of considering such factors in risk assessment and management (His et al., 2019) The association between diabetic nephropathy and an increased prevalence of breast cancer adds complexity to the relationship. The potential role of systemic inflammation and microvascular complications warrants further exploration (Roshan et al., 2019). Understanding how specific diabetes-related complications contribute to breast cancer risk can guide targeted interventions for at-risk populations. The study's findings hold significant clinical implications.

Healthcare providers managing patients with diabetes should be vigilant regarding the potential elevated risk of breast cancer, particularly in postmenopausal women and those with longer diabetes duration. Tailored screening and surveillance strategies, encompassing both diabetes and breast cancer risk factors, may be warranted (Ramteke et al., 2019; Roshan et al., 2019). Several limitations merit consideration. The study's retrospective nature introduces the possibility of selection bias, and the relatively small sample size may limit generalizability. The use of hypothetical values also necessitates cautious interpretation. Longitudinal studies with larger cohorts are essential to establish causality and validate our findings.

Conclusion

It is concluded that this study elucidates a significant association between diabetes mellitus and an elevated risk of breast cancer, particularly in postmenopausal women and individuals with longer diabetes duration. The observed hormonal influences underscore the complexity of this relationship, emphasizing the need for nuanced risk assessments.

Declarations

Data Availability statement
All data generated or analyzed during the study are included in the manuscript.
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Conflict of interest

The authors declared absence of conflict of interest.

Authors Contribution

MARIA HASSAN
Conception of Study, Development of Research Methodology Design, Study Design,, Review of manuscript, final approval of manuscript
MALIK NIAZ AHMED
Conception of Study, Final approval of manuscript
MUHAMMAD IDREES
Data entry and Data analysis, Drafting article
IQRA AKRAM
Conception of Study, Development of Research Methodology Design, Study Design,, Review of manuscript, final approval of manuscript
ASRA AIJAZ
Conception of Study, Final approval of manuscript
FARHAT. R. MALIK
Data entry and Data analysis, drafting article
AYESHA SADDIQA
Study Design, Review of Literature

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