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Prevalence of Hyperglycemia and Its Association with Breast Cancer Stage: A Case-Control Study in Meru County, Kenya

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Abstract

Background: Hyperglycemia, a hallmark of type 2 diabetes mellitus (T2DM), is increasingly implicated in breast cancer pathogenesis through the Warburg effect, hyperinsulinemia, and chronic inflammation. Understanding its prevalence and relationship with breast cancer stage in Sub-Saharan African populations remains critical for informing context-specific screening strategies.

Objectives: (1) To determine the prevalence of hyperglycemia (HbA1c ≥6.5%) among breast cancer patients compared to controls; and (2) to identify glycated hemoglobin (HbA1c) as a biomarker associated with different breast cancer stages.

Methods: A hospital-based case-control study enrolled 285 women (142 histologically confirmed breast cancer cases, 143 controls with non-cancerous breast masses) at Meru Teaching and Referral Hospital, Kenya. HbA1c was measured using a validated immunoturbidimetric analyser. Chi-square tests, independent samples t-tests, one-way ANOVA with Tukey's HSD post-hoc analysis, and ROC curve analysis were applied.

Results: Hyperglycemia was documented in 84.5% of cases versus 34.3% of controls ($p < 0.001$). Mean HbA1c was 6.89±0.75% in cases versus 5.82±0.71% in controls ($t(283) = 12.445$, $p < 0.001$). ROC analysis identified HbA1c ≥6.5% as the optimal threshold (AUC = 0.751, sensitivity 84.5%, specificity 65.7%). Stage IV cases had the highest HbA1c (7.56±0.87%), with a significant post hoc difference between Stage II and Stage IV (mean difference = 0.782%, $p = 0.031$), although the overall ANOVA was borderline ($F(3,139) = 2.599$, $p = 0.055$).

Conclusion: HbA1c ≥6.5% is a prevalent and clinically meaningful biomarker in this Kenyan breast cancer population, with elevated values clustering at advanced disease stages. Integration of HbA1c into routine breast cancer screening and staging protocols is warranted.

Keywords: *HbA1c; hyperglycemia; breast cancer; Warburg effect; breast cancer staging; Kenya; Sub-Saharan Africa; case-control; Biomarker*

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1. Introduction

Breast cancer is the most prevalent malignancy among women globally, accounting for 2.3 million new diagnoses in 2022 and representing 11.6% of all cancers (Ngwa et al., 2022; Zhang et al., 2023). Concurrent with this, type 2 diabetes mellitus (T2DM) and its defining feature — chronic hyperglycemia — has emerged as a metabolic risk modifier for breast cancer, with epidemiological and molecular evidence supporting a bidirectional nexus between the two conditions (Giovannucci et al., 2010; Asiri et al., 2024). At the cellular level, hyperglycemia drives oncogenesis through the Warburg effect, a phenomenon in which cancer cells preferentially utilize glycolysis for energy production even under normal conditions, requiring substantially greater glucose input than oxidative phosphorylation (Vander Heiden et al., 2009). This metabolic dependency renders breast tumors exquisitely sensitive to the ambient glycemic environment, making HbA1c a stable 8–12-week reflector of glycaemia and therefore a potential candidate biomarker for both breast cancer risk and progression (Ayoub et al., 2020; Liang et al., 2024).

In Kenya, breast cancer accounts for 23.3% of all female cancers, with an incidence of 34.8 per 100,000, and 78% of cases present at Stage II–IV due to diagnostic delays averaging 6–12 months (Sayed et al., 2017; Twahir et al., 2021). Concomitantly, 55.6% of Kenyan breast cancer patients exhibit hyperglycemia, reflecting a substantial dual burden (Riogi et al., 2022). In Meru County, a predominantly rural region, low mammography utilization (<10%), limited pathology infrastructure, and minimal awareness of risk factors (only 19% of women are aware of breast self-examination) further compound the problem (Antabe et al., 2020; Wassie et al., 2024). Against this backdrop, HbA1c offers a pragmatic, widely available, and affordable complement to conventional breast cancer screening tools.

The aim of this study was to determine the prevalence of hyperglycemia (HbA1c ≥6.5%) among breast cancer patients compared to women with non-cancerous breast masses; and evaluate HbA1c as a biomarker associated with different breast cancer stages. Establishing these relationships in a Kenyan context is critical for informing integrated metabolic-oncological care models adapted to resource-limited settings.

2. Literature Review

2.1 The Warburg Effect: metabolic fuel for breast cancer

The Warburg effect, described by Otto Warburg, refers to cancer cells' preferential reliance on aerobic glycolysis, converting glucose to lactate even in the presence of sufficient oxygen, rather than oxidative phosphorylation (Vander Heiden et al., 2009). Although less efficient in ATP generation per glucose molecule, aerobic glycolysis generates lactate and biosynthetic intermediates (amino acids, nucleotides, lipid precursors) at rates that support rapid tumour cell proliferation. To sustain this "glucose addiction", cancer cells markedly upregulate glucose transporters and rate-limiting glycolytic enzymes including hexokinase II, phosphofructokinase, and pyruvate kinase M2 (PKM2) (Hanahan & Weinberg, 2011; Pavlova & Thompson, 2016).

In the context of breast cancer, hyperglycemia amplifies the Warburg effect by providing an abundant exogenous glucose supply, thereby removing a metabolic bottleneck for tumor growth. Breast cancer cells constitutively overexpress GLUT1, and this overexpression is

potentiated under hyperglycemic conditions, correlating with greater tumor aggressiveness and poorer prognosis (Liu et al., 2018). Li et al. (2016) demonstrated that hyperglycemia-induced reactive oxygen species (ROS) production in breast cancer cells increased hexokinase II-mediated glycolysis and genomic instability, compounding the tumorigenic effect. DeBerardinis and Chandel (2020) further argued that the Warburg effect is not merely a metabolic quirk but a core oncogenic programme whose dependency on glucose availability is exploited by T2DM-associated hyperglycaemia.

Crucially, HbA1c captures the time-integrated glucose exposure that sustains this effect. Elevated HbA1c thus serves as a surrogate marker of the glycemic milieu that favors Warburg-driven tumor metabolism, offering a mechanistic rationale for its use as a breast cancer risk and staging biomarker (Asiri et al., 2024; Cosmin Stan & Paul, 2024).

Chronic hyperglycemia in T2DM is accompanied by compensatory hyperinsulinemia in the early stages of the disease. Elevated insulin binds to insulin receptors (IRs) overexpressed on breast cancer cells, activating the phosphoinositide 3-kinase (PI3K)/AKT/mTOR and RAS/RAF/MEK/ERK pathways, which promote proliferation, survival, and resistance to apoptosis (Giovannucci et al., 2010; Shikata et al., 2013). Concomitantly, hyperinsulinemia suppresses insulin-like growth factor binding protein-1 (IGFBP-1), increasing bioavailable insulin-like growth factor-1 (IGF-1), a potent mitogen with anti-apoptotic properties that further accelerates tumor growth. In Kenyan breast cancer patients, the predominance of estrogen receptor (ER)-positive subtypes and triple-negative breast cancer (TNBC) with BRCA1/2 mutations renders PI3K/AKT/mTOR amplification particularly consequential, as PIK3CA mutations are frequent and synergise with IGF-1 signaling (Sayed et al., 2021; Rioki et al., 2023).

Chronic low-grade systemic inflammation, mediated by cytokines IL-6 and TNF-α in T2DM, activates NF-κB and STAT3 signaling, creating a pro-tumorigenic microenvironment (Asiri et al., 2024). Adipose tissue in obese T2DM patients additionally secretes adipokines, with reduced anti-inflammatory adiponectin and elevated pro-inflammatory leptin further tilting the balance toward oncogenesis (Glassman et al., 2023). In breast cancer, M2 macrophage polarization within the TME, driven in part by hyperglycemia-mediated cytokine release, promotes immunosuppression, angiogenesis, and tumor invasion. This chronic inflammatory milieu is captured indirectly by HbA1c, which integrates months of pro-inflammatory glucose exposure, making it relevant not only as a risk marker but also as a potential indicator of tumor aggressiveness across stages (Cosmin Stan & Paul, 2024).

Glycated hemoglobin offers several practical advantages as a cancer biomarker in low-resource settings: it does not require fasting, reflects a sustained glycemic window of 8–12 weeks, is already embedded within Kenya's diabetes screening infrastructure, and has standardized diagnostic cut-offs (American Diabetes Association: ≥6.5% for diabetes, 5.7–6.4% for pre-diabetes). Ayoub et al. (2020) linked higher HbA1c levels to advanced tumor characteristics, including larger tumor size, higher grade, and nodal involvement. Jousheghany et al. (2016) found that HbA1c ≥7.0% correlated with higher breast cancer incidence. Stattin et al. (2007) reported a 1.51-fold higher cancer incidence among women with fasting glucose ≥6.9 mmol/L compared with normoglycemic controls, supporting a dose-response relationship. Riogi et al. (2022) documented hyperglycemia in 55.6% of Kenyan breast cancer patients, and Bjornsdottir

et al. (2020) reported elevated overall cancer incidence (HR 1.10) and post-cancer mortality (HR 1.23) in T2DM patients, with HbA1c levels correlating with tumor aggressiveness. Conversely, Campbell et al. (2022) found no significant association between HbA1c and breast cancer in a US cohort, likely reflecting superior glycemic management in high-resource settings. These contrasting findings underscore the need for population-specific data, particularly in Sub-Saharan African settings where hyperglycemia is poorly controlled and late-stage diagnoses predominate (Hu et al., 2021; Liang et al., 2024).

Whether HbA1c levels correlate with breast cancer staging and thereby carry prognostic utility remains underexplored. The biological plausibility is strong, as advanced-stage cancers exhibit greater Warburg-driven glucose dependency, and the hypoxia-hyperglycemia axis is most active in bulky, nodal, and metastatic disease. Understanding this relationship in patients, who present disproportionately at advanced stages, could validate HbA1c as an accessible staging adjunct in settings with limited pathology infrastructure.

3. Methodology

3.1 Study Design and Setting

A hospital-based case-control study was conducted at Teaching and Referral Hospital in Meru County, Kenya. The study was conducted within the pathology department and oncology outpatient clinics. Institutional ethical clearance was obtained from the relevant review boards and the National Commission for Science, Technology and Innovation (NACOSTI). Written informed consent was obtained from all participants prior to enrolment.

3.2 Study Population and Eligibility

Cases were adult women (≥18 years) with a histologically confirmed diagnosis of breast cancer at any stage, not yet commenced on systemic cancer therapy. Controls were adult women referred for fine-needle aspiration cytology (FNAC) due to a suspected breast mass, in whom a non-cancerous diagnosis was subsequently confirmed. Participants with incomplete records or who declined consent were excluded.

3.3 Sample Size

Sample size was calculated using the Fleiss et al. (2003) formula for two-population case-control studies, yielding a minimum of 142 cases and 143 controls (N = 285). A planned enrolment of 300 (150 per arm) was targeted to account for attrition.

3.4 Data Collection

Structured interviewer-administered questionnaires captured sociodemographic data, reproductive and menstrual history, hormonal contraceptive use, alcohol and tobacco consumption, family history of breast cancer, and T2DM status. HbA1c was measured from venous whole-blood samples using a validated point-of-care immunoturbidimetric analyzer, with daily internal quality controls performed in accordance with laboratory accreditation standards.

3.5 Statistical Analysis

Data were entered, coded, and analyzed. The prevalence of hyperglycemia was compared between cases and controls using the chi-square (χ^2) test. HbA1c was compared between groups by independent samples t-test and between breast cancer stages (I–IV) by one-way ANOVA with Tukey's honestly significant difference (HSD) post-hoc test. ROC curve analysis was used to identify the optimal HbA1c threshold for discriminating breast cancer. All tests were two-tailed with statistical significance set at $p < 0.05$.

4. Results

4.1 Participant Characteristics

A total of 285 participants were enrolled: 142 breast cancer cases and 143 controls. The groups were comparable in mean age (cases 50.1 ± 9.8 years; controls 49.2 ± 9.1 years; p = 0.432) and menopausal status. Among breast cancer cases, the staging distribution was as follows: Stage I, n = 32 (22.5%); Stage II, n = 52 (36.6%); Stage III, n = 51 (35.9%); and Stage IV, n = 8 (5.6%). Cases had significantly higher rates of T2DM diagnosis, alcohol use, hormonal contraceptive use, family history of breast cancer, and BMI compared to controls. Full characteristics are presented in Table 1.

Table 1: Participant characteristics: breast cancer cases versus controls

Characteristic	Cases (N=142) n (%)	Controls (N=143) n (%)	p-value
Age (years), mean ± SD	50.1 ± 9.8	49.2 ± 9.1	0.432
Postmenopausal	81 (57.0%)	74 (51.7%)	0.358
T2DM diagnosis	64 (45.1%)	21 (14.7%)	< 0.001*
Family history of breast cancer	42 (29.6%)	26 (18.2%)	0.020*
Hormonal contraceptive use	57 (40.1%)	38 (26.6%)	0.013*
Alcohol use	32 (22.5%)	13 (9.1%)	0.002*
BMI (kg/m²), mean ± SD	28.0 ± 3.7	24.3 ± 3.4	< 0.001*
HbA1c (%), mean ± SD	6.89 ± 0.75	5.82 ± 0.71	< 0.001*

Note. ** $p < 0.05$, statistically significant. T2DM = type 2 diabetes mellitus; BMI = body mass index; HbA1c = glycated hemoglobin. p-values from chi-square tests (categorical) and independent samples t-tests (continuous).*

4.2 Objective 1: Prevalence of Hyperglycaemia Among Breast Cancer Patients

Using the ADA diagnostic threshold of HbA1c ≥6.5%, hyperglycaemia was documented in 120 of 142 breast cancer cases (84.5%) compared to 49 of 143 controls (34.3%) — a difference highly significant at $\chi^2(1) = 74.515$, $p < 0.001$ (OR ≈ 10.0, 95% CI [5.560, 18.332]). Additionally, 14 cases (9.9%) had prediabetic HbA1c values (5.7–6.4%), meaning that only 8 cases (5.6%) had normal HbA1c values. In contrast, 52 controls (36.4%) had normal HbA1c and 42 (29.4%) were pre-diabetic. The HbA1c distribution across categories is shown in Table 2.

Table 2: HbA1c category distribution: cases versus controls

HbA1c Category	Cases n (%) (N=142)	Controls n (%) (N=143)	p-value
Normal (< 5.7%)	8 (5.6%)	52 (36.4%)	< 0.001*
Pre-diabetic (5.7–6.4%)	14 (9.9%)	42 (29.4%)	< 0.001*
Diabetic/hyperglycemic (≥ 6.5%)	120 (84.5%)	49 (34.3%)	< 0.001*
Total	142 (100%)	143 (100%)	—

***Note**. Cut-offs: Normal < 5.7%; Pre-diabetic 5.7–6.4%; Diabetic/hyperglycaemic ≥6.5%. * p < 0.001 (chi-square).*

The mean HbA1c was significantly higher in cases (6.89% ± 0.75) than controls (5.82% ± 0.71; $p < 0.001$, 95% CI of mean difference [0.904, 1.244]). Logistic regression confirmed that each 1% increase in HbA1c was associated with a 7.864-fold increase in the odds of breast cancer (95% CI [4.845, 12.761], $p < 0.001$). This observed prevalence of 84.5% hyperglycaemia among breast cancer cases substantially exceeds the 55.6% documented in the broader Kenyan breast cancer cohort by Riogi et al. (2022) and the 20.5% general diabetes prevalence reported by Adedokun et al. (2023) in Nigeria, pointing to a particularly high metabolic disease burden in the Meru County study population.

4.2.1 ROC Curve Analysis: Optimal HbA1c Threshold

ROC curve analysis was used to evaluate HbA1c as a continuous predictor of breast cancer status. The overall AUC was 0.751 (95% CI [0.693, 0.809], $p < 0.001$), indicating good discriminatory performance. Three clinically relevant thresholds were evaluated using the Youden Index (sensitivity + specificity − 1); results are presented in Table 3. The ADA diabetes cut-off of ≥6.5% maximised the Youden Index (0.502), balancing sensitivity (84.5%) and specificity (65.7%), and is therefore identified as the optimal screening threshold for breast cancer risk stratification in this population.

Table 3: ROC analysis: HbA1c thresholds for breast cancer discrimination

HbA1c Threshold	AUC (95% CI)	Sensitivity (%)	Specificity (%)	p
≥ 5.7% (pre-diabetes cut-off)	0.751 (0.693–0.809)	94.4	36.4	< 0.001
≥ 6.5% (ADA diabetes cut-off) ✓	0.751 (0.693–0.809)	84.5	65.7	< 0.001
≥ 7.0%	0.751 (0.693–0.809)	61.3	82.5	< 0.001

***Note**. AUC = area under the ROC curve. Overall model AUC = 0.751 (95% CI [0.693, 0.809]).*

4.3 Objective 2: HbA1c as a biomarker across breast cancer stages

Among the 142 breast cancer cases, HbA1c varied by disease stage. Stage IV cases had the highest mean HbA1c (7.56% ± 0.87), followed by Stage I (6.91%), Stage III (6.88%), and Stage II (6.78%). One-way ANOVA yielded $F(3, 139) = 2.599$, $p = 0.055$ — a borderline non-significant result. Stage-level data including 95% confidence intervals are presented in Table 4.

Table 4: HbA1c levels by breast cancer stage: one-way ANOVA (N = 142 cases)

Stage	N	Mean HbA1c (%)	SD	95% CI	F-value	p-value
Stage I	32	6.91	0.62	6.69 – 7.13	2.599	0.055
Stage II	52	6.78	0.67	6.59 – 6.97		
Stage III	51	6.88	0.84	6.65 – 7.12		
Stage IV†	8	7.56	0.87	6.84 – 8.29		
Overall	142	6.89	0.75	6.76 – 7.01		

***Note.** $F(3, 139) = 2.599$, $p = 0.055$. †Stage IV n = 8; interpret with caution. Levene's test of equality of variances: $p = 0.247$ (variances not significantly different).*

Tukey's HSD post-hoc analysis identified one statistically significant pairwise difference: Stage II versus Stage IV (mean difference = 0.782%, 95% CI [0.052, 1.511], $p = 0.031$). All other pairwise comparisons were non-significant. Homogeneous subset analysis confirmed that Stages I, II, and III formed a statistically indistinguishable cluster, while Stage IV constituted a distinct upper subset. Post-hoc results are detailed in Table 5.

Table 5: Tukey's HSD post-hoc analysis: pairwise HbA1c comparisons by breast cancer stage

Stage Comparison	Mean Diff. (%)	Std. Error	95% CI	p-value
Stage I vs Stage II	0.130	0.142	−0.243 to 0.503	0.792
Stage I vs Stage III	0.032	0.143	−0.344 to 0.408	0.998
Stage I vs Stage IV	−0.651	0.251	−1.311 to 0.009	0.054
Stage II vs Stage III	−0.098	0.131	−0.443 to 0.246	0.875
Stage II vs Stage IV†	−0.782	0.243	−1.422 to −0.143	0.031*
Stage III vs Stage IV	−0.684	0.245	−1.329 to −0.039	0.060

Note. ** Statistically significant ($p < 0.05$). †Stage IV $n = 8$; interpret with caution. Mean differences are Stage A minus Stage B.*

5. Discussion

The detection of hyperglycemia (HbA1c ≥6.5%) in 84.5% of breast cancer cases is the central finding of this study and the most striking departure from comparable populations. This prevalence substantially exceeds the 55.6% reported by Riogi et al. (2022) in a broader Kenyan cohort, the 20.5% diabetes prevalence among Nigerian breast cancer patients by Adedokun et al. (2023), and figures from European cohorts where metabolic control is superior. The mechanistic underpinning is consistent with the Warburg effect: chronic hyperglycemia in T2DM provides a sustained exogenous glucose supply that meets the heightened glycolytic demands of breast tumor cells (Vander Heiden et al., 2009). Breast cancer cells constitutively overexpress GLUT1 and HKII, and hyperglycemia further upregulates these transporters and enzymes, thereby accelerating aerobic glycolysis, lactate export, and the production of biosynthetic intermediates (Hanahan & Weinberg, 2011; DeBerardinis & Chandel, 2020). The extraordinarily high prevalence likely reflects a compounding of poor glycemic control, which is consistent with Kenya's limited diabetes management infrastructure, with the high-glucose dependency of aggressive breast cancer subtypes predominant in this population, particularly TNBC (Rioki et al., 2023).

The 10-fold odds of breast cancer among women with HbA1c ≥6.5% (OR ≈ 10, 95% CI [5.560, 18.332]) is remarkable. This finding aligns with Ayoub et al. (2020), who linked elevated HbA1c to advanced tumor characteristics, and with Stattin et al. (2007), who demonstrated a dose-dependent increase in cancer risk with rising fasting glucose. The absence of a significant HbA1c-cancer association in Campbell et al. (2022)'s US cohort highlights how population-level glycemic control modulates this relationship: in settings with superior T2DM management, the glucose supply differential between patients and controls is attenuated, reducing the statistical signal. Conversely, in Meru County where uncontrolled hyperglycemia

is widespread, the contrast is pronounced, and the Warburg-driven tumor growth advantage is correspondingly amplified.

Hu et al. (2021) showed that incident T2DM confers peak cancer risk approximately eight years after diagnosis, and Bjornsdottir et al. (2020) documented higher post-cancer mortality in T2DM patients, both reflecting cumulative glycemic damage. HbA1c, as a time-averaged glycemic biomarker, captures this sustained exposure, validating its epidemiological utility. Importantly, the 94.4% sensitivity at the pre-diabetes threshold (≥5.7%) suggests HbA1c may identify at-risk women even before frank diabetes develops, offering a window for preventive intervention.

The ADA diabetes threshold of ≥6.5% was confirmed as the optimal breast cancer risk cut-off by Youden Index analysis (sensitivity 84.5%, specificity 65.7%, Youden Index 0.502; AUC = 0.751). This convergence of the metabolic and oncological cut-offs is pragmatically significant: it means that existing diabetes screening protocols in Kenya's primary care facilities can be directly repurposed for breast cancer risk stratification without requiring new threshold definitions. Liang et al. (2024) similarly identified ≥6.5% as optimal in Chinese breast cancer patients, while Jousheghany et al. (2016) showed that ≥7.0% predicts higher breast cancer incidence, suggesting a dose-response relationship at higher glycemic burdens. The lower specificity (65.7%) at ≥6.5% reflects the elevated background prevalence of T2DM in this population; nevertheless, in a setting where alternative screening modalities are scarce, the high sensitivity makes HbA1c a valuable first-line triage tool, particularly for women attending diabetes clinics (Hutchinson et al., 2024). Each 1% increase in HbA1c was associated with a 7.864-fold rise in breast cancer odds, reinforcing HbA1c's continuous dose-response relationship with oncogenic risk and corroborating the biological plausibility of the Warburg-driven mechanism (Zhang et al., 2025).

The stage-stratified analysis reveals a biologically interpretable, if statistically borderline, pattern. Stage IV disease exhibited the highest HbA1c (7.56% ± 0.87%), forming a distinct upper subset by Tukey's HSD analysis, with a significant difference versus Stage II ($p = 0.031$). Stages I–III clustered without significant pairwise differences, suggesting that HbA1c does not linearly differentiate early stages but may signal metabolic intensification at metastatic disease. This pattern is consistent with the hypoxia-hyperglycemia axis described by Durrani et al. (2021): advanced-stage tumors, characterized by bulky hypoxic cores, upregulate HIF-1α and GLUT1 to the greatest extent, resulting in the most pronounced glucose dependency and the highest glycemic burden. The tumor microenvironment at Stage IV, with extensive M2 macrophage infiltration, VEGF-driven angiogenesis, and cytokine-mediated systemic inflammation, may further amplify insulin resistance and hyperglycemia (Asiri et al., 2024; Cosmin Stan & Paul, 2024).

The borderline overall ANOVA result ($p = 0.055$) warrants methodological consideration. The small Stage IV sample ($n = 8$) dramatically reduces statistical power to detect stage-level differences and yields wide confidence intervals. This is a structural limitation common to studies conducted at facilities serving populations with predominantly early- to intermediate-stage diagnoses. Replication in larger cohorts with adequate representation of Stage IV is essential to confirm whether HbA1c scales with disease progression. Nonetheless, the biological coherence of the Stage II-IV difference, combined with the mechanistic framework

of the Warburg effect and HIF-1α upregulation in advanced disease, lends credibility to the observed trend. Studies in other cancer types have shown clearer HbA1c-stage correlations: Beer and Liebenberg (2014) demonstrated increased cancer stage/grade risk with rising HbA1c across gastric, colorectal, and pancreatic cancers, and Joshu et al. (2012) found 31% higher postmenopausal breast cancer incidence in women with high HbA1c, raising the possibility that similar patterns are detectable in breast cancer with larger samples.

These findings carry direct policy implications for low- and middle-income countries. The co-occurrence of hyperglycemia in 84.5% of breast cancer cases identifies a high-risk population that is already presenting to diabetes care facilities — a clinical intersection that integrated care models can exploit. The WHO-supported Women's Integrated Cancer Services (WICS) project demonstrates the feasibility of combined metabolic-oncological screening in primary care settings (Hutchinson et al., 2024). Adding HbA1c measurement to routine breast examination protocols, or prompting oncology referrals for women with HbA1c ≥6.5% who attend diabetes clinics, is operationally simple, low-cost, and builds on existing infrastructure. Given the 6–12-month diagnostic delay documented by Twahir et al. (2021) and Sayed et al. (2017), identifying high-risk women earlier through metabolic screening could meaningfully shift stage distribution at diagnosis and reduce mortality.

6. Conclusion

This case-control study delivers two substantive findings. First, hyperglycaemia (HbA1c ≥6.5%) is highly prevalent among breast cancer patients in Meru County, Kenya — present in 84.5% of cases versus 34.3% of controls, conferring a tenfold increase in breast cancer odds. The ADA-aligned ≥6.5% threshold performs optimally as a screening marker (AUC = 0.751, sensitivity = 84.5%), with each 1% increase in HbA1c multiplying the odds of breast cancer by approximately 7.9-fold. These findings are mechanistically anchored in the Warburg effect and the hyperinsulinemia-IGF-1-HIF-1α pathways that link chronic hyperglycaemia to tumour initiation and progression. Second, while HbA1c does not significantly differentiate early breast cancer stages (I–III), it is markedly elevated in Stage IV disease, with a significant Stage II versus Stage IV difference ($p = 0.031$), suggesting its potential as a metabolic burden indicator in advanced breast cancer.

7. Recommendations

The study recommends incorporating routine HbA1c measurement into breast cancer diagnostic work-ups, particularly at initial presentation, and establishing automated bi-directional referral pathways between diabetes clinics and oncology services for women with HbA1c ≥6.5%. Leveraging existing diabetes screening infrastructure to implement HbA1c-based breast cancer risk triage at primary health facilities across Meru County and other resource-limited settings, and developing national guidelines for integrated metabolic-oncological screening that draw on HbA1c as a cost-effective first-line biomarker, can be considered for health policy. Further research in this field may include conducting prospective cohort studies with adequate enrolment across multiple Kenyan counties to establish causal directionality and validate the cancer stage-HbA1c relationship and examine the interaction of HbA1c with BRCA1/2 mutation status and molecular subtypes (particularly TNBC) to characterize which subpopulations carry the greatest oncogenic risk.

Conflict Of Interest

The authors declare no conflicts of interest, financial or otherwise, in relation to this study.

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