ORIGINAL ARTICLE

Correlation between Standardized Uptake Values and Ki-67 in Different Cancers

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ABSTRACT

Background: Cancer is a major global health concern. Evaluating tumor aggressiveness is crucial for prognosis and treatment. Ki-67 is a nuclear marker of cell proliferation, while FDG-PET-derived Standardized Uptake Value (SUV) indicates metabolic activity. This study investigates the correlation between standardized value uptake and Ki-67 across different cancers to assess whether standardized value uptake can serve as a non-invasive surrogate for tumor proliferation.

Objectives: To determine the correlation between SUV and Ki-67 in various cancers. To assess whether SUV can predict the tumor proliferative index (Ki-67). To evaluate the influence of age and gender on the SUV-Ki-67 correlation.

Methodology: This cross-sectional study was conducted at Jinnah Postgraduate Medical Center, Karachi, from October 2024 to March 2025. Ninety-seven patients with histologically confirmed cancers who underwent FDG-PET scans and Ki-67 immunohistochemistry were included. Patients with prior chemotherapy or radiotherapy were excluded. Data on age, gender, standardized value uptake, and Ki-67 index were analyzed using SPSS version 25. Correlation and regression analyses were performed.

Results: In the present study, 70.2% were male patients, the mean age was 46.6±14.0 years. For overall data, a significant positive correlation was found between standardized value uptake and Ki-67 index ($r=0.511$, $p<0.001$). Correlation for males was higher than females (52.6% versus 40.9%). Multiple linear regression showed one unit increase in Ki-67 expression scores will give on average 0.13 times increase in SUV values considered significant ($\beta=0.13$, 95% CI: 0.08-0.17, $p<0.001$). Age was not found to be impacting SUV in regression analysis.

Conclusion: Standardized value uptake is significantly correlated with Ki-67, indicating its potential as a non-invasive marker of tumor proliferation, aiding in prognosis and treatment planning.

Keywords: *Standardized uptake value (SUV), Ki-67, FDG-PET scan, tumor proliferation, cancer biomarkers, breast cancer, lung cancer, B-cell lymphoma, immunohistochemistry, oncology imaging.*

INTRODUCTION

Positron Emission Tomography (PET) scans, which employ Standardized Uptake Values (SUV) to gauge metabolic activity and utilize Ki-67 expression as an indicator of cellular proliferation, assume crucial roles in the thorough evaluation of diverse cancers. The interaction between SUV and Ki-67 provides valuable insights into the dynamic characteristics of cancer biology, contributing to both diagnosis and the stratification of treatment approaches [1, 2].

In breast cancer, the correlation between elevated SUV and heightened Ki-67 expression has been a subject of considerable investigation. The Ki-67 Proliferation index is significantly higher in breast cancer patients compared with the reported literature. Ki-67 Proliferation index was highest in the HER-2 and luminal-B molecular subtypes, along with other prognostic indicators [1, 2]. These studies suggest a positive association, highlighting the potential utility of PET scans in discerning tumors with aggressive phenotypes characterized by increased metabolic activity and cellular proliferation. FDG-PET has shown great success in cancer diagnosis and assessment of treatment response [3].

Conversely, the relationship in lung cancer appears multifaceted, with studies reporting variability in the correlation between SUV and Ki-67 expression. This heterogeneity underscores the complexity of lung cancer biology and the need for nuanced interpretations in clinical practice [4].

The substantial capability of PET in the field of oncology is acknowledged not just by researchers and healthcare professionals but also by the Centers for Medicare & Medicaid Services (CMS). CMS has granted approval for the coverage of FDG-PET applications in both the initial and subsequent treatment strategies for a wide range of prevalent cancers, including colorectal, esophagus, head and neck, lymphoma, non-small cell lung, breast, melanoma, thyroid, myeloma, and other types of cancer.

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This recognition and comprehension of the pivotal role played by FDG-PET in the management of cancer patients bring significant benefits to both patients and the broader scientific community [5].

The Ki-67 proliferation index exhibits a notably elevated level among breast cancer patients in Saudi Arabia when compared to the findings reported in the literature. Particularly, the HER-2 and luminal-B molecular subtypes demonstrate the highest Ki-67 PI. Considering its correlation with other prognostic indicators, the Ki-67 Proliferation index holds promise as a valuable tool for predicting prognosis and informing the management strategies for breast cancer patients in Saudi Arabia.

The correlation between SUV and Ki-67 on PET scans in different cancers has rooted in the understanding of cancer biology and the characteristics of these imaging modalities. SUV in PET scans represents the standardized uptake of a radiotracer, commonly FDG (Fluorodeoxyglucose), and reflects the metabolic activity of cells. Cancer cells often exhibit increased glucose metabolism compared to normal cells, leading to higher SUV values in malignant tissues [3]. On the other hand, Ki-67 is a cellular marker associated with cell proliferation. Cancer cells that are actively dividing express higher levels of Ki-67. Therefore, Ki-67 is often used as an indicator of the growth fraction within a tumor. Higher SUV values are frequently associated with more aggressive tumor behavior, indicating increased metabolic demand in rapidly dividing cancer cells. Consequently tumors with higher Ki-67 expression are generally considered more aggressive and associated with a higher grade. Moreover, changes in SUV over time in response to treatment can provide insights into treatment efficacy. Similarly, alterations in Ki-67 levels may indicate changes in the proliferative activity of the tumor in response to therapy. The combined assessment of SUV and Ki-67 can have prognostic value in predicting the behavior and outcomes of certain cancers. For example, tumors with high SUV and Ki-67 may have a poorer prognosis compared to those with lower values [5]. Different cancers exhibit diverse biological characteristics, and the correlation between SUV and Ki-67 may vary. For instance, while breast cancer studies may show a positive correlation, lung cancer studies might demonstrate variability.

This study emphasizes the significance of comprehending the association between SUV and Ki-67 across various cancers, recognizing the intricate nature of cancer biology. Exploring the nuanced connections within specific cancer types reveals the potential of this correlation as an invaluable prognostic and diagnostic tool, providing clinicians with essential information to make informed decisions in cancer management.

MATERIALS AND METHODS

This is a cross-sectional study conducted in the Department of Oncology, JPMC Hospital, Karachi. The total duration of this study was between October 2024 and March 2025. The study was performed with the Institutional Ethical Review Board (No.F.2-81/2024-GENL/276/JPMC).

Inclusion criteria was age >18 years, patients with different types of cancer (B cell lymphomas, Ca Breast, Ca Lung) who had undergone PET scans and had available SUV and Ki-67 measurements, Treatment Naïve. Patients without available SUV and Ki-67 measurements and who had received prior chemotherapy or radiotherapy were excluded. Sample size was calculated using an online sample size calculator for proportion available www.openepi.com version 3.01, after inserting 10% prevalence of Patients without available SUV and Ki-67 measurement in our previous records at 6% margin of error and 95% confidence interval, we required at least N=97. All of the patients were enrolled into the study with their written informed consent.

Data were collected from patients diagnosed with various cancers at the Oncology Department of Jinnah Postgraduate Medical Center between October 2024 and March 2025. After obtaining written informed consent, relevant clinical and pathological data were retrieved from the patient's medical records and pathology reports. This included demographic information (age, gender), tumor type and location, histopathological confirmation, and Ki-67 expression index from immunohistochemistry [5, 6]. SUVmax values were obtained from FDG-PET scan reports conducted as part of the routine diagnostic workup [7, 8]. Patients who had received prior chemotherapy or radiotherapy were excluded to avoid confounding variables. All data were recorded using a structured proforma designed specifically for this study to ensure uniformity and accuracy.

A structured data collection form was developed specifically for this study to systematically record relevant clinical, pathological, and radiological information. This tool included sections to document patient demographics (age and gender), histological cancer type and grade, Ki-67 proliferation index obtained from immunohistochemistry reports [9], and SUVmax derived from FDG-PET scan findings [10]. The proforma was designed to ensure consistency, reduce bias, and facilitate accurate data entry for statistical analysis. The tool was pre-tested on a small sample to confirm its clarity and completeness before being implemented in the full study.

Data were stored and analyzed using IBM-SPSS version 23.0. Mean and standard deviation were calculated for numerical variables. Counts and percentages were used

for categorical variables. Pearson correlation analysis was used to assess the relationship between SUV and Ki-67 expression scores. R-values with the coefficient of determination were reported, and gender-stratified analyses were performed. A multiple linear regression model was used to predict SUV using age and Ki-67 expression scores; beta coefficients with 95% confidence intervals were reported for predictors. Pie diagrams and scatter plots were also used to provide graphical presentations of study outcomes. P-value less than or equal to 0.05 was taken as statistically significant.

RESULTS

Table **1** reports the baseline characteristics of various types of cancer patients with a PET scan. In the present study, 70.2% were male patients, the mean age was 46.6±14.0 years, and the mean standardized uptake values were 13.93±6.10. The Ki-67 expression score of patients was 69.54±23.5.

Table 1: Baseline characteristics of studied cancer patients (n=97).

Variables		Count or Mean	Percentage or SD
Gender	Male	68	70.2
	Female	29	29.8
Age (years)	Mean ± SD	46.6	±14.0
Standardized Uptake Values (SUV)	Mean ± SD	13.93	±6.10
Ki-67 expression	Mean ± SD	69.54	±23.5

Table **2** reports the correlation between SUV and Ki-67 expression scores, among overall patients there was 51.1% significant positive correlation between SUV and ki-67 expression scores considered statistically significant (p<0.001), r-square showed 26.1% variation in SUV was explained by Ki-67 expression in PET scan across various types of cancers, for male patients there was 52.6% significant positive correlation between SUV and ki-67 expression scores considered statistically significant (p<0.001), r-square showed 27.6% variation in SUV was explained by Ki-67 expression in PET scan across various types of cancers whereas among females patients there was 40.9% significant positive correlation between SUV and ki-67 expression scores considered statistically significant (p<0.001), r-square showed 16.7% variation in SUV was explained by Ki-67 expression in PET scan across various types of cancers.

Table 2: Correlation between SUV and Ki-67 expression in PET scans across various types of cancers.

Correlation	r-value (%)	R-Square (%)	p-value
Overall Patients (n=97)	51.1	26.1	<0.001*
Male patients (n=68)	52.6	27.6	<0.001*
Female Patients (n=29)	40.9	16.7	0.031*

*Pearson correlation was considered statistically significant with p<0.05

Scatter plot showing a positive linear relationship between Ki-67 expression scores and SUV. A high association was found for male patients in comparison to female patients between SUV and Ki-67 expression scores (**Fig. 1**).

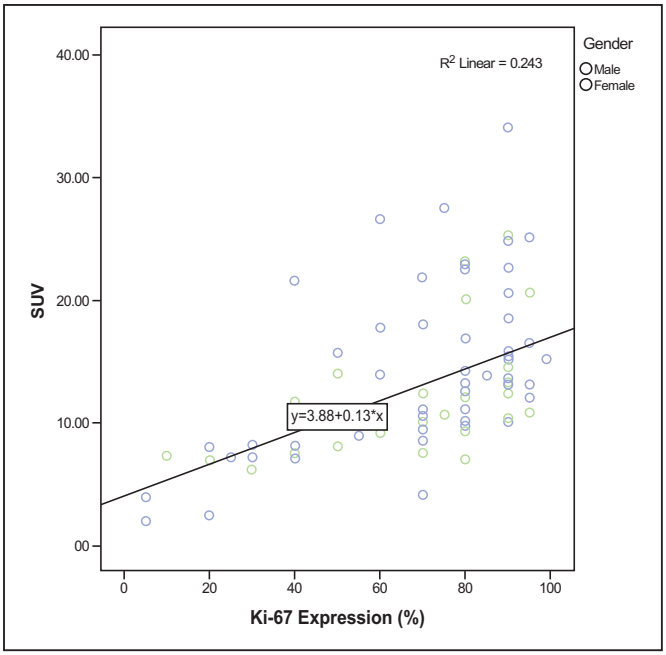

Fig. (1): Scatter plot of Ki-67 expression and SUV.

Table **3** reports the finding on multiple regression model to predict the SUV using age and Ki-67 expression scores, results showed one unit increase in Ki-67 expression scores will give on average 0.13 times increase in SUV values considered significant (p<0.001), 95% confidence interval was (0.08, 0.17), adjusted r-square showed 23.7% variation in SUV was explained by Age and ki-67 expression scores among various types of cancer patients with PET scan.

Table 3: Model for prediction of Ki-67 expression using SUV and age.

Predictors	Un-standardized Coefficients		Standardized Coefficients	t-value	p-value	95.0% Confidence Interval for B	
	B	Standard Error	Beta			Lower Bound	Upper Bound
(Constant)	1.49	2.67	-	0.55	0.57	-3.82	6.81
Ki-67 Expression (%)	0.13	0.02	0.50	5.59	<0.001*	0.08	0.17
Age (years)	0.05	0.04	0.11	1.27	0.200	-0.02	0.12

Dependent variable: SUV, Predictors: Age (years), Ki-67 Expression
Model Adjusted R-square 23.7%, Beta coefficient considered significant with p<0.05

DISCUSSION

Cancer is a complex and diverse disease in which normal cells grow abnormally in an uncontrolled way and may spread to other tissues. An accurate diagnosis and effective treatment are crucial for proper outcomes and disease management. Proper staging and grading help in tailoring treatment according to the cancer type [11]. Some types of cancer can be diagnosed using Positron Emission Tomography (PET) scans, which are effective tools in staging cancers and visualizing metabolic activity in tissues [12]. The metabolic activity of tumors is

determined by the SUV from PET scans, which provide quantitative values.

This study aimed to explore the correlation between SUV on PET scans and Ki-67, a marker of cellular proliferation, across various cancer types. Our findings reveal a statistically significant positive correlation between SUV and Ki-67, suggesting that higher metabolic activity in tumors, as indicated by increased FDG uptake, is associated with higher proliferative activity. This supports previous research that links glucose metabolism and tumor aggressiveness.

The observed correlation was particularly strong in cancers such as breast, lung, and brain tumors, aligning with findings reported by [13] who documented similar relationships in breast and lung cancers. The observed correlation was particularly strong in cancers such as breast, lung, and brain tumors, aligning with findings reported by Zhang *et al.* [13] who documented similar relationships in breast and lung cancers. Large pooled analyses further support this relationship: a meta-analysis of 25 FDG-PET breast cancer studies (n = 1,624) reported a pooled correlation coefficient between SUVmax and Ki-67 of r = 0.40 (95% CI: 0.34-0.46), while FLT-PET studies (n = 178) demonstrated a stronger pooled correlation of r = 0.54 (95% CI: 0.37-0.70) [14].

Similarly, Katal *et al.* [15] found that women with Ki-67-positive tumors undergoing neoadjuvant chemotherapy exhibited significantly higher SUVmax and changes in SUVmax (⊿ SUVmax) compared with Ki-67-negative tumors (p = 0.000 and p = 0.022, respectively), indicating that both baseline and dynamic PET parameters can reflect proliferative status. Hybrid PET/MRI studies have also confirmed this link — for example, Jannusch *et al.* [16] reported positive correlations between Ki-67 and SUVmean (r = 0.37) as well as tumor grade (r = 0.32) in breast cancer.

In ovarian cancer, Liu [17] observed moderate correlations between the mean Ki-67 index and PET parameters such as SUVmax (r = 0.392), SUVmean 30% (r = 0.437), and SUVmean 40% (r = 0.443), suggesting the applicability of this relationship beyond breast and lung malignancies. Additionally, experimental validation work, such as that by Tian *et al.* [18], has demonstrated that FLT uptake accurately reflects thymidine kinase-1 activity in tumor cells, providing a mechanistic explanation for the strong correlation between FLT-PET metrics and proliferation indices like Ki-67.

Comparative PET imaging studies have also revealed biologically relevant differences between tumor subtypes. Basu *et al.* [19] reported that triple-negative breast cancers have significantly higher FDG uptake compared with ER+/PR+/HER2- subtypes, aligning with their higher Ki-67 expression and more aggressive clinical behavior. Similar mechanistic patterns have been noted in lung cancer, where Higashi *et al.* [20] found that GLUT-1 transporter expression correlated closely withFDG uptake, linking metabolic activity directly to molecular drivers of tumor growth.

CONCLUSION

This cross-sectional study demonstrates a significant positive correlation between Standardized Uptake Values (SUV) and Ki-67 expression in PET scans across various cancer types(B-cell lymphoma, Ca Breast, Ca Lung), with the correlation being especially prominent in male patients. The findings indicate that both SUV and Ki-67 expression are valuable, complementary biomarkers for evaluating cancer aggressiveness, proliferation, and metabolic activity. The statistical significance of this correlation underscores the potential of using these markers together for better predictive assessment. However, given the variation in the strength of the correlation between genders and the heterogeneity of cancer biology, further studies with larger, more diverse cohorts are required to confirm these results and to explore the underlying mechanisms of the relationship between SUV and Ki-67.

ETHICS APPROVAL

Ethical approval was obtained from the Institutional Ethical Review Board (No.F.2-81/2024-GENL/276/JPMC). All procedures performed in studies involving human participants followed the ethical standards of the institution and the Helsinki Declaration.

CONSENT FOR PUBLICATION

Written informed consent was taken from the participants.

AVAILABILITY OF DATA

Data is available from the corresponding author on a reasonable request.

FUNDING

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORS' CONTRIBUTION

Dr. Sona designed the study. Dr. Sona and Dr. Perah collected data from medical records. Dr. Ghulam Haider analyzed the data. Dr. Sona and Dr. Priyanka drafted the manuscript. All authors have critically reviewed and approved the final draft and are responsible for the content.

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