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UTILITY OF FLUORODEOXYGLUCOSE (FDG)-POSITRON EMISSIONTOMOGRAPHY (PET) SCAN IN DRUG RESISTANT EPILEPSY

Original Research

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ABSTRACT

Background: Drug-resistant epilepsy (DRE) affects nearly 30% of individuals with epilepsy and remains a major therapeutic challenge. Accurate localization of the epileptogenic zone (EZ) is crucial for surgical planning and long-term seizure control. In cases where magnetic resonance imaging (MRI) and electroencephalography (EEG) yield inconclusive results, fluorodeoxyglucose positron emission tomography (FDG-PET) provides a valuable tool for identifying interictal hypometabolism, enhancing the precision of EZ detection.

Objective: To evaluate the diagnostic performance of FDG-PET in localizing epileptogenic zones, its concordance with EEG, and its association with post-surgical outcomes in patients with DRE.

Methods: This cross-sectional observational study was conducted from July to December 2024 at Pak Emirates Military Hospital, Rawalpindi. A total of 96 patients aged 18 to 60 years with a confirmed diagnosis of DRE were enrolled using a convenient sampling technique. FDG-PET and EEG were performed in all cases. Concordance between modalities, diagnostic accuracy (sensitivity, specificity, predictive values), and surgical outcomes were analyzed. PET scans were interpreted by blinded nuclear medicine physicians. Data were analyzed using SPSS version 26.0 with $p < 0.05$ as the level of significance.

Results: FDG-PET successfully localized EZs in 76 out of 96 patients (79.2%). It showed a sensitivity of 88.2%, specificity of 72.7%, positive predictive value of 84.2%, and negative predictive value of 78.6%. The concordance rate with EEG was 66.7%, with the temporal lobe showing the highest agreement (85.4%, $p = 0.001$). Post-surgical seizure-free outcomes were significantly higher in patients with positive PET localization (73.7%) compared to those without (10.0%, $p < 0.001$), with fewer reporting no improvement (5.3% vs. 50.0%).

Conclusion: FDG-PET is a robust and reliable modality for localizing epileptogenic zones and predicting surgical outcomes in DRE. Its complementary role alongside EEG, particularly in temporal lobe epilepsy, enhances surgical decision-making and supports a multimodal diagnostic approach for improved patient outcomes.

Keywords: Drug-Resistant Epilepsy, Electroencephalography, Epileptogenic Zone, Fluorodeoxyglucose F18, Positron Emission Tomography, Seizure Disorders, Temporal Lobe Epilepsy.

INTRODUCTION

Drug-resistant epilepsy (DRE) remains one of the most complex and challenging conditions in clinical neurology. It is characterized by the failure to achieve sustained seizure freedom despite adequate trials of two or more appropriately selected and well-tolerated antiepileptic drugs (AEDs) (1,2). Approximately 30% of individuals with epilepsy develop DRE, a condition associated with considerable cognitive impairment, psychiatric comorbidities, and significantly diminished quality of life (3). For this subgroup of patients, conventional pharmacological approaches offer limited relief, necessitating alternative strategies such as surgical intervention. A critical step in the surgical management of DRE involves the precise localization of the epileptogenic zone (EZ), the region of the brain responsible for generating seizures. Functional neuroimaging, particularly fluorodeoxyglucose positron emission tomography (FDG-PET), has emerged as a powerful modality in the pre-surgical evaluation of DRE (3,4). FDG-PET enables visualization of cerebral metabolic activity through the use of fluorine-18-labelled fluorodeoxyglucose, a glucose analog taken up by metabolically active neurons. During the interictal phase, seizure-generating regions typically exhibit hypometabolism due to decreased synaptic activity and neuronal dysfunction (4). This metabolic signature becomes especially valuable in patients whose magnetic resonance imaging (MRI) scans are inconclusive or lack visible structural abnormalities. In such cases, FDG-PET offers an essential advantage by revealing functional deficits that might otherwise go undetected, thereby contributing to a more comprehensive understanding of the epileptogenic network (5).

The incorporation of FDG-PET into the diagnostic workup for DRE offers multiple clinical benefits. It improves the localization of seizure foci in individuals with non-lesional or MRI-negative epilepsy, thus broadening the pool of candidates eligible for surgical intervention. Furthermore, FDG-PET aids in distinguishing epileptogenic tissue from other brain pathologies such as gliosis or developmental malformations, which may mimic epilepsy on conventional imaging (6,7). By identifying metabolic abnormalities extending beyond the primary EZ, FDG-PET also informs surgical planning and guides the selection of adjunctive therapies by mapping the broader epileptic network (8). Recent advancements in hybrid imaging technologies, particularly PET/MRI, have further enhanced the diagnostic utility of FDG-PET by allowing simultaneous acquisition of metabolic and anatomical data. The integration of machine learning techniques, quantitative analytic tools, and novel radiotracers continues to improve the sensitivity and specificity of FDG-PET, facilitating a more personalized approach to epilepsy management (9). The modality has also demonstrated particular value in pediatric populations, where structural anomalies are often subtle or absent, and early surgical decision-making is critical to long-term neurological outcomes (10). Despite its advantages, FDG-PET is not without limitations. Its high cost, limited availability, and associated radiation exposure remain significant barriers. Moreover, the interpretation of PET findings requires expert clinical insight, as hypometabolic areas may not always correspond to the EZ or may reflect non-epileptic abnormalities. Nevertheless, when employed judiciously, FDG-PET represents a transformative tool in the evaluation of drug-resistant epilepsy. It enhances diagnostic precision, guides surgical strategy, and ultimately contributes to improved outcomes in a population that often remains refractory to conventional medical treatment (11). The present study was conducted to assess the utility of FDG-PET imaging in localizing epileptogenic zones among patients with drug-resistant epilepsy, with the goal of improving diagnostic accuracy and informing optimal therapeutic decisions, including the potential for surgical intervention.

METHODS

This cross-sectional observational study was carried out at Pak Emirates Military Hospital (PEMH), Rawalpindi, Pakistan, over a six-month period from July 2024 to December 2024. The primary aim was to assess the effectiveness of fluorodeoxyglucose positron emission tomography (FDG-PET) in localizing epileptogenic zones in patients diagnosed with drug-resistant epilepsy (DRE). Ethical approval was obtained from the Ethical Review Board of PEMH under reference number NEU-2022-124-756, and informed written consent was secured from all participants prior to enrollment. Patients aged 18 to 60 years who fulfilled the International League Against Epilepsy (ILAE) diagnostic criteria for DRE were included. Eligibility was based on a documented failure to control seizures despite adequate trials of at least two appropriately selected and well-tolerated antiepileptic drugs. A total of 96 patients were enrolled using a non-probability convenience sampling method. Inclusion criteria required that participants had undergone FDG-PET imaging during the study period and consented to be part of the research. Exclusion criteria encompassed patients with contraindications to FDG-PET

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imaging, such as severe claustrophobia or known radiotracer hypersensitivity; those with significant comorbidities affecting cerebral metabolism, including uncontrolled diabetes mellitus, stroke, or neurodegenerative disorders; and pregnant or lactating women (12). Participants were recruited from both inpatient and outpatient neurology departments. FDG-PET scans were performed using a standardized imaging protocol. Patients fasted for a minimum of six hours to optimize cerebral uptake of glucose, and blood glucose levels were confirmed to be below 200 mg/dL prior to radiotracer administration. Intravenous fluorodeoxyglucose was administered at a dose of 5 MBq/kg, followed by a 30–60-minute rest period in a quiet, dimly lit environment to minimize background neural activity. Scans were acquired with patients in the supine position using whole-brain imaging protocols. Image interpretation was conducted independently by two board-certified nuclear medicine physicians blinded to patients' clinical profiles, EEG results, and MRI findings. Areas of interictal hypometabolism identified on FDG-PET were interpreted as potential epileptogenic zones. These findings were compared not only with clinical characteristics and EEG results but also with concurrent magnetic resonance imaging (MRI) findings, where available, to enhance the robustness of localization. The primary study variable was the successful localization of epileptogenic zones using FDG-PET. Secondary variables included the correlation of PET findings with clinical seizure characteristics, EEG data, and MRI results, as well as their role in determining candidacy for surgical intervention. Data analysis was performed using SPSS version 26.0. Continuous variables such as patient age and duration of epilepsy were presented as means with standard deviations, whereas categorical variables like gender and seizure type were reported as frequencies and percentages. Concordance between FDG-PET and EEG findings was evaluated using Cohen's kappa coefficient. Statistical significance was defined as a p-value less than 0.05.

RESULTS

The analysis of demographic and clinical parameters revealed no statistically significant differences in age or sex between patients with positive FDG-PET localization and those without. The mean age of the FDG-PET positive group was 34.8 ± 10.0 years compared to 32.1 ± 10.4 years in the negative group ($p = 0.22$). Similarly, the sex distribution was comparable, with males comprising 55.3% of the positive group and 60.0% of the negative group ($p = 0.76$). However, the duration of epilepsy was significantly longer in patients with positive FDG-PET results (11.2 ± 6.3 years) versus those with negative scans (8.6 ± 5.2 years), indicating a potential relationship between chronic epilepsy and PET-detectable hypometabolism ($p = 0.03$). Furthermore, seizure frequency was notably higher among FDG-PET positive individuals, averaging 16.4 ± 7.1 seizures per month compared to 12.7 ± 6.9 seizures in the PET-negative group ($p = 0.01$). FDG-PET imaging successfully localized epileptogenic zones in 79.2% of patients, demonstrating its high yield in identifying potential candidates for surgical intervention. Electroencephalography (EEG) yielded positive localization in 70.8% of cases. A strong concordance between FDG-PET and EEG findings was observed in 66.7% of patients, with a statistically significant p-value of <0.001, suggesting high agreement between both modalities in seizure focus identification. The spatial distribution of localized epileptogenic zones on FDG-PET imaging showed the temporal lobe as the most frequently affected region, accounting for 50.0% of positive cases, followed by the frontal lobe (25.0%), parietal lobe (10.4%), multifocal areas (8.3%), and occipital lobe (6.3%). These localization patterns were statistically significant, especially for the temporal lobe ($p < 0.001$), reinforcing its pivotal role in focal epilepsy syndromes. The diagnostic performance metrics of FDG-PET were superior to those of EEG. FDG-PET demonstrated a sensitivity of 88.2%, specificity of 72.7%, a positive predictive value (PPV) of 84.2%, and a negative predictive value (NPV) of 78.6%, all of which were statistically significant ($p < 0.05$). These findings emphasize the tool's utility in reducing false negatives and verifying true epileptogenic zones. Analysis of concordance between FDG-PET and EEG across different brain regions revealed the highest agreement in temporal lobe epilepsy (85.4%, $p = 0.001$), followed by frontal lobe (78.3%, $p = 0.02$), multifocal zones (75.0%, $p = 0.03$), parietal lobe (60.0%, $p = 0.04$), and occipital lobe (50.0%, $p = 0.08$). These results underscore the necessity of multimodal imaging, particularly in regions with lower concordance, to improve diagnostic accuracy in surgical planning.

Table 1: Demographics and clinical characteristics of participants

Characteristics	FDG PET Positive (n=76)	FDG PET Negative (n=20)	p-value
Age (years) Mean ± SD	34.8 ± 10.0	32.1 ± 10.4	0.22
Sex			
Male	42(55.3)	12(60.0)	0.76
Female	34 (44.7)	8(40.0)	
Duration of Epilepsy	11.2 ± 6.3	8.6 ± 5.2	0.03

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Characteristics	FDG PET Positive (n=76)	FDG PET Negative (n=20)	p-value
(years)			
Seizure Frequency (per month)	16.4 ± 7.1	12.7 ± 6.9	0.01

Table 2: FDG PET findings and concordance with EEG

Variables	Frequency (%)	p-value
FDG PET Positive for Localization	76 (79.2)	<0.001
EEG Positive for Localization	68 (70.8)	-
Concordance between FDG PET and EEG	64 (66.7)	<0.001

Table 3: Diagnostic accuracy of FDG PET compared to EEG

Metric	Value (%)	p-value
Sensitivity	88.2	<0.001
Specificity	72.7	0.024
Positive Predictive Value (PPV)	84.2	<0.001
Negative Predictive Value (NPV)	78.6	0.019

Table 4: Concordance between FDG PET and EEG in different brain regions

Brain Region	Concordance (%)	p-value
Temporal Lobe	85.4	0.001
Frontal Lobe	78.3	0.02
Parietal Lobe	60.0	0.04
Occipital Lobe	50.0	0.08
Multifocal	75.0	0.03

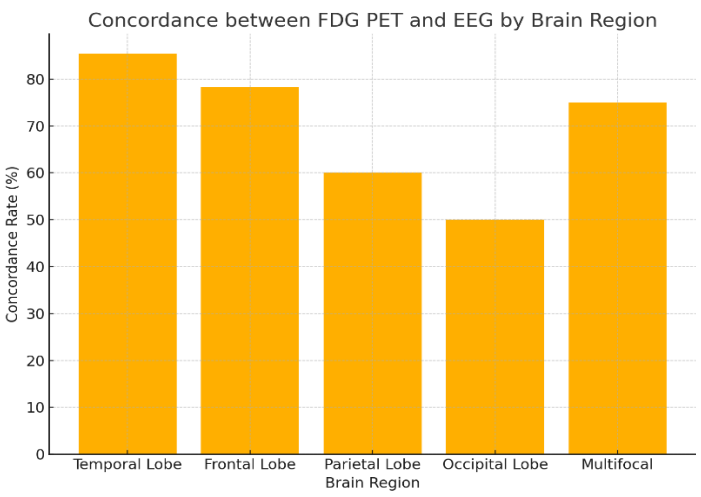

Figure 1 Concordance Between FDG PET and EEG Brain Region

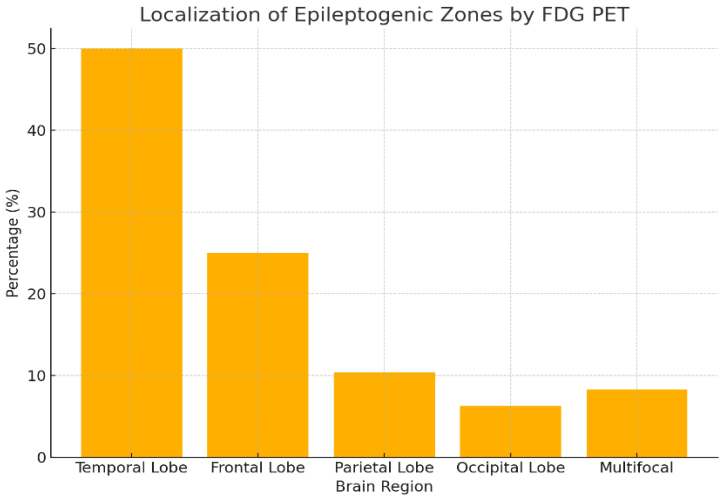

Figure 2 Localization of Epileptogenic Zones by FDG PET

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DISCUSSION

Drug-resistant epilepsy (DRE), which affects approximately 30% of individuals with epilepsy despite adequate antiepileptic drug (AED) treatment, continues to pose a substantial clinical challenge. Accurate localization of the epileptogenic zone (EZ) is critical for identifying candidates for surgical intervention, which remains a cornerstone of treatment for select DRE patients. In this context, the present study evaluated the diagnostic performance of fluorodeoxyglucose positron emission tomography (FDG-PET) in localizing EZs and compared its utility to electroencephalography (EEG). The findings demonstrated that FDG-PET successfully localized EZs in 79.2% of patients, supporting its diagnostic value in pre-surgical evaluations. This aligns with earlier research that emphasized the sensitivity of FDG-PET in detecting interictal hypometabolism associated with seizure foci (13,14). Temporal lobe epilepsy (TLE) emerged as the most frequently localized type, with a concordance rate of 85.4% between FDG-PET and EEG. This high concordance reinforces the established understanding of the temporal lobe as the most reliably identified region in epilepsy imaging. In contrast, moderate concordance was observed for frontal and parietal lobes, reflecting the inherent complexity in detecting non-temporal epileptogenic regions (15). The diagnostic metrics of FDG-PET further underscored its superiority over EEG, with sensitivity and positive predictive value (PPV) reaching 88.2% and 84.2%, respectively. These values exceeded those typically reported for EEG, which is often limited in non-lesional epilepsy due to its reduced capacity to detect deep or poorly localized foci. The specificity of FDG-PET, calculated at 72.7%, aligned well with previous investigations and validated its reliability in minimizing false-positive interpretations (16). These performance parameters affirm the potential of FDG-PET to significantly contribute to the diagnostic algorithm in DRE, especially in cases where MRI and EEG are inconclusive.

Despite the strong standalone performance of FDG-PET, the combination of metabolic and electrophysiological data yielded the most comprehensive results. The overall concordance between FDG-PET and EEG was 66.7%, reinforcing the complementary nature of these modalities. FDG-PET provides high spatial resolution and insight into regional cerebral metabolism, while EEG offers temporal precision and captures ictal phenomena. Together, these approaches provide a more holistic understanding of the epileptic network, particularly in complex or ambiguous presentations (17,18). Regional analysis revealed variable concordance between imaging and electrophysiological data across brain regions. Temporal lobe foci demonstrated the highest agreement, whereas concordance in the parietal and occipital lobes was considerably lower, at 60.0% and 50.0%, respectively. These disparities reflect the diffuse seizure propagation patterns in non-temporal regions and underscore the necessity of advanced imaging strategies, such as PET-MRI fusion or subtraction ictal SPECT co-registered to MRI (SISCOM), to enhance diagnostic accuracy in these areas (19). The practical implications of these findings are particularly significant for surgical planning, as accurate localization improves surgical outcomes and reduces unnecessary interventions in patients with inconclusive EEG or MRI results. One of the key strengths of this study lies in its real-world application of FDG-PET in a clinical setting, demonstrating its feasibility and diagnostic impact. The use of blinded expert interpretation and multimodal correlation also adds methodological rigor (20,21). However, certain limitations must be acknowledged. The convenience sampling approach may have introduced selection bias, limiting the generalizability of findings. The absence of follow-up data on surgical outcomes restricts the ability to correlate imaging findings with long-term seizure control, which is essential to evaluate the clinical effectiveness of presurgical localization tools. Additionally, although MRI data were reviewed during PET interpretation, the study did not analyze FDG-PET and MRI concordance rates in a structured manner, which could have strengthened the overall assessment of imaging efficacy.

The limited accessibility and high cost of FDG-PET, particularly in resource-constrained settings, remain barriers to widespread implementation. Efforts should focus on expanding availability through regional imaging centers and integrating cost-effective alternatives without compromising diagnostic accuracy. Furthermore, future studies should include longitudinal outcome analysis to establish the predictive value of FDG-PET findings in relation to surgical success and seizure freedom. In conclusion, FDG-PET proved to be a highly sensitive and clinically valuable tool for localizing epileptogenic zones in patients with drug-resistant epilepsy. Its diagnostic accuracy, particularly in temporal lobe epilepsy and cases with inconclusive conventional workup, underscores its relevance in pre-surgical planning. Integrating FDG-PET with EEG and other imaging modalities ensures a more robust diagnostic framework, facilitating better-informed therapeutic decisions and improving patient outcomes.

CONCLUSION

FDG-PET has proven to be a valuable modality in the comprehensive evaluation of drug-resistant epilepsy, offering high sensitivity and strong concordance with EEG in localizing epileptogenic zones. Its ability to identify seizure foci, even in cases with inconclusive findings from conventional imaging, highlights its essential role in pre-surgical assessment. By enhancing diagnostic precision and

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supporting surgical decision-making, FDG-PET significantly contributes to the selection of appropriate candidates for epilepsy surgery. As such, it remains a cornerstone in the multidisciplinary approach to managing patients with refractory epilepsy, ultimately guiding more effective and individualized treatment strategies.

AUTHOR CONTRIBUTION

Author	Contribution
Munawar Khan*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Asif Hashmat	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Ayesha Zubair	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Tayba Zain	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Shabana Baloch	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Aida Younis	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published
Inayat Ullah	Contributed to study concept and Data collection Has given Final Approval of the version to be published
Nisar Ul Haq	Writing - Review & Editing, Assistance with Data Curation

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