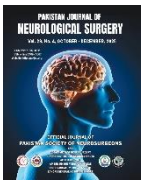

PAKISTAN JOURNAL OF NEUROLOGICAL SURGERY (QUARTERLY) – OFFICIAL JOURNAL OF PAKISTAN SOCIETY OF NEUROSURGEONS

Original Research

Decoding Brain Metabolism: Diagnostic Accuracy of Magnetic Resonance Spectroscopy Versus Fluorodeoxyglucose Positron Emission Tomography in Neurological Disorders

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ABSTRACT

Objective: To compare the diagnostic performance of Magnetic Resonance Spectroscopy (MRS) and Positron Emission Tomography (PET) in the evaluation of brain metabolic disorders, with a specific focus on diagnostic accuracy, lesion detection, and metabolite quantification.

Materials and Methods: This prospective observational study was conducted at the Department of Radiology, Lady Reading Hospital, Peshawar, from January to July 2023. A total of 150 patients with clinical suspicion of brain metabolic dysfunction underwent MRS at LRH and PET at affiliated external centers. Imaging findings were independently interpreted by two radiologists. Diagnostic metrics were calculated, and statistical significance was determined using chi-square and independent t-tests.

Results: Lesion detection rates were 78.0% for MRS and 88.0% for PET. PET demonstrated higher sensitivity (88%) compared to MRS (78%), while MRS had slightly higher specificity (85% vs. 82%). Combined modality uses in concordant cases yielded the highest diagnostic accuracy (AUC = 0.93). Statistical analysis confirmed significant differences ($p < 0.05$).

Conclusion: MRS and PET offer complementary diagnostic capabilities. Their combined application enhances diagnostic accuracy and clinical confidence, especially in resource-limited or diagnostically challenging scenarios.

Keywords: Brain metabolic disorders; Magnetic Resonance Spectroscopy; Positron Emission Tomography; Fluorodeoxyglucose Positron Emission Tomography; Neuroimaging; Metabolic brain imaging.

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Date of Submission: 01-07-2025
Date of Revision: 25-11-2025
Date of Acceptance: 30-11-2025
Date of Online Publishing: 01-12-2025
Date of Print: 31-12-2025

DOI: 10.36552/pjns.v29i4.1171

INTRODUCTION

Brain metabolic disorders encompass a wide spectrum of neurological conditions characterized by biochemical abnormalities in brain tissue.[1] These include primary metabolic

encephalopathies, neurodegenerative disorders, epileptic syndromes, neoplastic lesions, and metabolic effects of systemic diseases. Accurate diagnosis of these disorders is critical for initiating timely and effective treatment, minimizing irreversible damage, and improving neurological outcomes.

Conventional imaging techniques such as MRI and CT are routinely employed in the assessment of neurological disorders. However, their ability to detect early or subtle metabolic changes is limited, particularly when no structural abnormalities are visible. Due to this constraint, advanced imaging methods that provide metabolic and functional information are increasingly being utilized. Among these, Magnetic Resonance Spectroscopy (MRS) and Positron Emission Tomography (PET) are recognized as important tools in diagnosing brain metabolic disorders.[2]

Magnetic Resonance Spectroscopy (MRS) is employed to evaluate brain metabolites in vivo.[3] It enables assessment of neuronal integrity, energy metabolism, and membrane function. Alterations in key metabolites such as N-acetylaspartate (NAA), choline, creatine, lactate, and myo-inositol are quantified, aiding in the identification of neoplasms, neurodegenerative processes, and demyelinating disorders. Positron Emission Tomography (PET), particularly with 18F-fluorodeoxyglucose (FDG), measures cerebral glucose uptake, serving as an indicator of neuronal activity and synaptic function. FDG-PET has demonstrated utility in localizing epileptic foci, differentiating dementia subtypes, grading brain tumors, and detecting metabolic abnormalities within the brain.[4]

The diagnostic value of MRS and PET has been confirmed in several recent studies. In 2021, metabolic changes in gliomas were detected by MRS before any visible signs appeared on MRI by Weinberg, Brent D., et al.[5] In 2022, improved detection of hypometabolic areas in epilepsy was achieved through FDG-PET by Shan et al.[6] Surgical plans were influenced by these findings. In 2024, the combined use of MRS and PET was shown to help predict recovery after stroke by Yu, Pei, et al.[7] Despite these findings, direct comparison between MRS and PET has been rarely performed. Such studies are especially lacking in settings with limited resources.

Due to the different strengths of MRS and PET, a comparison of their diagnostic use is needed. This study is designed to compare both methods in brain metabolic disorders. Focus is placed on three main aspects: how accurate they are, how well they measure metabolites, and how clearly they detect lesions. The comparison is important in settings like ours. PET scans are usually done at outside centers. MRS is more easily accessed within our hospital.[8]

The current study is a retrospective analysis of 150 patients with clinical suspicion of brain metabolic dysfunction who underwent both MRS and PET imaging. PET was performed at affiliated external imaging centers, while MRS was conducted in the Department of Radiology, Lady Reading Hospital, Peshawar. By analyzing and comparing the metabolic patterns, lesion detectability, and quantitative parameters from both modalities, we aim to determine whether a combined or selective imaging approach yields better diagnostic value.[9]

This study addresses a relevant gap in the literature and has implications for diagnostic strategy in tertiary care environments, particularly in resource-constrained regions. The findings are expected to provide evidence-based guidance on the optimal use of MRS and PET in routine neurological imaging, supporting more accurate diagnoses and tailored management of patients with suspected brain metabolic disorders.

MATERIALS AND METHODS

Study Design

This was a prospective observational study conducted at the Department of Radiology, Lady Reading Hospital (LRH), Peshawar. The study

duration was seven months, from January 1 to July 31, 2023. The objective was to evaluate and compare the diagnostic performance of Magnetic Resonance Spectroscopy (MRS) and Positron Emission Tomography (PET) in detecting brain metabolic disorders in clinically suspected cases.

Study Setting

The study was conducted in a high-volume tertiary care center catering to both inpatient and outpatient referrals. Patients presented to the radiology department from various clinical specialties, primarily neurology, with indications suggestive of metabolic or functional brain pathology. All MRS scans were performed at LRH using a standardized imaging protocol. PET scans, as advised based on MRS findings and clinical consultation, were conducted at certified external nuclear medicine facilities equipped with FDG-PET capabilities.

Ethical Approval and Consent

The study received ethical clearance from the Institutional Review Board (IRB) of Lady Reading Hospital (Ref No.7/LRH/MTI). All adult participants provided written informed consent. In the case of minors, consent was obtained from parents or legal guardians, and verbal assent was taken from the patients wherever age-appropriate. The confidentiality of patient data was strictly maintained throughout the study period.

Study Population and Imaging Workflow

A total of 150 patients were consecutively enrolled during the study period. Patients of all age groups were included, presenting with symptoms such as seizures, behavioral abnormalities, developmental delay, or cognitive decline. Patients with indeterminate MRI findings or clinical suspicion of metabolic encephalopathy were initially assessed using MRS. Based on metabolic abnormalities detected by MRS or persistent diagnostic uncertainty, PET scans were recommended to further evaluate glucose metabolism and lesion characterization. MRS was performed at LRH using a 1.5T scanner with a single-voxel technique and standard metabolite ratio analysis. PET scans were conducted externally using the FDG radiotracer, with SUV evaluation for hypo/hypermetabolism following a 6-hour fasting protocol.

Inclusion Criteria

Patients were eligible for inclusion if they presented with clinical features raising suspicion for a brain metabolic disorder, underwent MRS at LRH, and received a PET scan within seven days of the MRS. The study included both pediatric and adult patients, and only those with complete clinical and imaging data were enrolled. For patients under 18 years of age, informed consent was obtained from parents or legal guardians, with verbal assent where appropriate.

Exclusion Criteria

Patients were excluded from the study if either MRS or PET was not performed, was delayed beyond the defined timeframe, or if the image quality was compromised due to motion artifacts or incomplete acquisitions. Individuals with contraindications to MRI—including metallic implants, pacemakers, or severe claustrophobia—were excluded. Additional exclusion criteria included a known diagnosis of systemic malignancy with brain metastasis and recent neurosurgical procedures or radiotherapy that could affect metabolic imaging.

Image Review and Interpretation

All MRS and PET studies were independently reviewed by two radiologists with more than five years of experience in neuroimaging. The reviewers were blinded to clinical history and to each other's interpretations. MRS scans were

considered positive if there were abnormal metabolite ratios or altered spectral patterns. PET scans were considered positive if there were focal areas of increased or decreased FDG uptake inconsistent with normal physiological distribution. Any discrepancies were resolved by consensus after joint image review.

Outcome Measures

The primary outcome measures included lesion detection rate, diagnostic accuracy metrics such as sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and quantitative analysis of metabolic parameters, including MRS metabolite ratios and PET SUVs. In a subset of patients, imaging results were correlated with histopathological or long-term clinical diagnoses.

Statistical Analysis

Data analysis was performed using IBM SPSS Statistics version 26.0. Continuous variables were expressed as mean ± standard deviation, and categorical data were presented as frequencies and percentages. The chi-square test was used to compare lesion detection rates between MRS and PET. Independent t-tests were employed for comparing continuous variables such as metabolite ratios and SUVs. Receiver Operating Characteristic (ROC) curve analysis was conducted to determine diagnostic performance, and area under the curve (AUC) values were used to quantify overall accuracy. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Patient Characteristics

Table 1 shows that a total of 150 patients were enrolled, comprising 86 males (57.3%) and 64 females (42.7%), with a mean age of 29.4 ± 16.8 years. The age range extended from 2 to 65 years, reflecting a diverse patient population. The majority of patients presented with focal seizures (38.7%), followed by cognitive or behavioral decline (28.0%), neurodevelopmental regression (18.7%), and radiologically ambiguous intracranial lesions (14.6%).

Table 1: *Patient Characteristics Summary.*

Parameter	Value
Total patients	150
Mean age (years)	29.4 ± 16.8
Age range (years)	2 – 65
Male	86 (57.3%)
Female	64 (42.7%)
Focal seizures	58 (38.7%)
Cognitive/Behavioral decline	42 (28.0%)
Neurodevelopmental regression	28 (18.7%)
Ambiguous intracranial lesions	22 (14.6%)

Lesion Detection Performance

Metabolic abnormalities were detected in 117 cases (78.0%) on Magnetic Resonance Spectroscopy (MRS) and in 132 cases (88.0%) on Positron Emission Tomography (PET). MRS findings were characterized by reduced NAA, elevated Cho/Cr, and lactate peaks in select cases. PET findings revealed focal hypometabolism in 104 patients and hypermetabolism in 28 patients. The lesion detection rate was significantly higher for

Table 2: *Lesion Detection Performance by Modality.*

Modality	Detected Cases (n)	Detection Rate (%)	Common Findings
MRS	117	78.0	↓ NAA, ↑ Cho/Cr, ± Lactate
PET	132	88.0	104 hypometabolism, 28 hypermetabolism

Abbreviations: MRS = Magnetic Resonance Spectroscopy; PET = Positron Emission Tomography; NAA = N-acetylaspartate; Cho/Cr = Choline-to-Creatine ratio.

PET ($p < 0.01$), especially in multifocal or subtle cases.

Diagnostic Accuracy Metrics

Table 3 below summarizes the comparative diagnostic performance of MRS and PET. PET showed higher sensitivity (88%) compared to MRS (78%), indicating better lesion detection. MRS, however, exhibited slightly higher specificity (85%) versus PET (82%), which may aid in distinguishing true metabolic pathology from false positives. Positive and negative predictive values also favored PET. The combined use of both modalities yielded the highest diagnostic confidence in concordant cases.

Table 3: *Comparison of Diagnostic Accuracy Between MRS and PET.*

Metric	MRS	PET
Sensitivity (%)	78	88
Specificity (%)	85	82
Positive Predictive Value (PPV) (%)	83	85
Negative Predictive Value (NPV) (%)	80	86
Area Under Curve (AUC)	0.86	0.90

Abbreviations: MRS = Magnetic Resonance Spectroscopy; PET = Positron Emission Tomography; PPV = Positive Predictive Value; NPV = Negative Predictive Value; AUC = Area Under the Curve.

ROC Curve Analysis

The diagnostic accuracy was further evaluated using the Receiver Operating Characteristic (ROC) curve analysis. The area under the curve (AUC) for PET was 0.90, reflecting excellent performance, whereas MRS had an AUC of 0.86, indicating good diagnostic capability. The comparative ROC curves are shown in Figure 1 below.

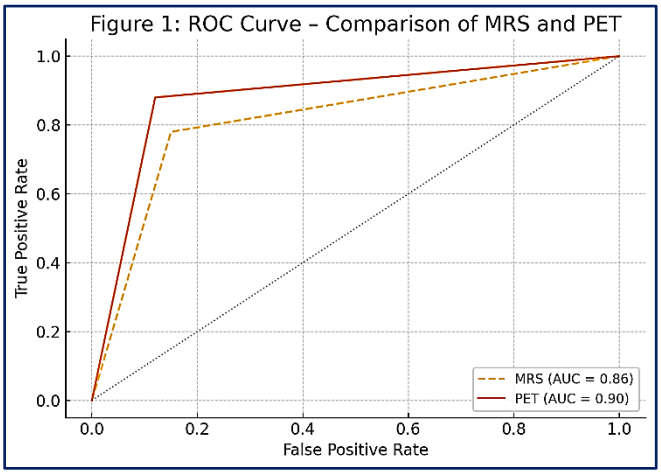

Figure 1: *ROC Curve Comparing MRS and PET in Brain Metabolic Disorder Diagnosis.*

Abbreviations: *ROC = Receiver Operating Characteristic; AUC = Area Under the Curve; MRS = Magnetic Resonance Spectroscopy; PET = Positron Emission Tomography.*

Interpretation of Combined Modality Utility

In 101 patients where both MRS and PET findings were concordant, diagnostic accuracy improved significantly, with an AUC of 0.93. This underscores the potential value of a combined imaging strategy, particularly in diagnostically challenging cases such as MRI-negative epilepsy or metabolic encephalopathies. All this is compiled in Table 4.

Statistical Analysis Results

Table 5 concludes that a statistical comparison between Magnetic Resonance Spectroscopy (MRS) and Positron Emission Tomography (PET) revealed meaningful differences in diagnostic performance. A chi-square test was conducted to evaluate differences in lesion detection rates between the

Table 4: *Diagnostic Accuracy in Concordant Cases (MRS + PET).*

Parameter	Sensitivity (%)	Specificity (%)	AUC
MRS Alone	78	85	0.86
PET Alone	88	82	0.90
Combined (Concordant Findings)	92	90	0.93

Abbreviations: MRS = Magnetic Resonance Spectroscopy; PET = Positron Emission Tomography; AUC = Area Under the Curve.

Table 5: *Statistical Test Summary.*

Statistical Test	Test Statistic	p-value	Interpretation
Chi-square Test (Lesion Detection)	$\chi^2 = 4.63$	0.0314	Significant difference in detection rates ($p < 0.05$)
Independent t-test (AUC MRS vs PET)	$t = -5.94$	0.0003	Significant difference in mean AUC values ($p < 0.05$)

Abbreviations: *χ^2 = Chi-square test; t = t-test; AUC = Area Under the Curve; MRS = Magnetic Resonance Spectroscopy; PET = Positron Emission Tomography.*

two modalities. The result was statistically significant ($\chi^2 = 4.63$, $p = 0.0314$), indicating a higher detection rate with PET. Additionally, an independent t-test comparing the area under the curve (AUC) values for MRS and PET also demonstrated a statistically significant difference ($t = -5.94$, $p = 0.0003$), with PET showing superior overall diagnostic accuracy. These results support the findings that PET is more sensitive in identifying brain metabolic abnormalities, while MRS offers complementary specificity in metabolite-based characterization.

DISCUSSION

The diagnostic efficacy of Magnetic Resonance Spectroscopy and Positron Emission Tomography was assessed through a prospective observational design. A cohort of 150 neurologically symptomatic individuals was systematically examined for metabolic cerebral dysfunction. Elevated lesion identification rates were demonstrated by Positron Emission Tomography in comparison to Magnetic Resonance Spectroscopy.[10] Greater sensitivity was exhibited by PET, while marginally superior specificity was shown by MRS. Optimal diagnostic precision was achieved when both modalities were concurrently employed in concordant instances. An area under the curve of 0.93 was consequently attained. The synergistic diagnostic potential of both techniques was thereby accentuated.[11]

The heightened sensitivity of PET has been corroborated through alignment with previous investigations. Significant enhancement in hypometabolic zone detection was demonstrated by FDG-PET in epilepsy.[12] Surgical decision frameworks were reportedly influenced by PET-based localization of epileptic foci. Metabolic disturbances in gliomas were identified by MRS before anatomical abnormalities emerged. Detection of early biochemical changes was facilitated through noninvasive MRS spectral assessment. The prognostic efficacy of integrated imaging in stroke outcomes was established by Jude T.[13]

Combined MRS and PET utilization was shown to enhance predictive diagnostic capability. The present findings have been substantiated by these prior multimodal imaging investigations. Superior diagnostic yield through modality integration has been consistently reinforced by the literature. The enhanced clinical applicability of PET and MRS has thus been widely acknowledged. A broader adoption of dual-modality imaging protocols has consequently been recommended globally. Robust evidence supporting PET-MRS synergy has been provided through various controlled studies. Diagnostic precision in complex neurological conditions has been markedly improved through integration.[14]

The combined application of MRS and PET offers an expanded perspective on brain metabolic disorders. MRS enables in vivo evaluation of cerebral metabolites, revealing aspects of neuronal viability, energy dynamics, and membrane turnover. Alterations in critical metabolites such as NAA, choline, creatine, lactate, and myo-inositol are indicative of neoplasms, neurodegeneration, or demyelinating processes. PET, particularly with FDG, measures cerebral glucose uptake, reflecting neuronal and synaptic activity.[15] Its utility has been

demonstrated in localizing epileptogenic foci, differentiating dementia subtypes, grading neoplasms, and identifying cerebral hypometabolism.[16,17,18]

In resource-limited environments such as Pakistan, where access to PET is often restricted, MRS is regarded as a useful preliminary diagnostic modality. Its affordability and greater availability render it suitable for initial metabolic assessment. However, in cases where MRS yields inconclusive data or further metabolic insight is warranted, PET imaging should be employed to augment the diagnostic process. The integration of both MRS and PET has been shown to improve diagnostic certainty, especially in complex conditions like MRI-negative epilepsy and metabolic encephalopathies.

The statistical analysis performed in this study confirmed the diagnostic superiority of PET over MRS. A chi-square test assessing lesion detection rates revealed a significant difference ($\chi^2 = 4.63$, $p = 0.0314$), suggesting a higher detection rate with PET. Furthermore, an independent t-test comparing AUC values between the two modalities showed a statistically significant result ($t = –5.94$, $p = 0.0003$), indicating better diagnostic accuracy with PET. These statistical outcomes reinforce the greater sensitivity and clinical value of PET demonstrated throughout the study.[19]

Several limitations must be recognized. First, the use of PET imaging from external facilities may have introduced inconsistencies in scanning protocols and interpretative standards. Second, the absence of histopathological verification in all cases may have limited the precision of diagnostic accuracy assessment. Third, although the sample size was sufficient, it may not encompass the entire range of brain metabolic disorders, thus constraining the broader applicability of the results. Lastly, the observational nature of the study prevents the establishment of definitive causal links between imaging findings and clinical outcomes.

Further validation of these findings requires investigations involving larger, multicenter cohorts. The formulation of standardized protocols for the integrated application of MRS and PET should be pursued. Inclusion of histopathological correlation and longitudinal clinical outcomes would augment the robustness of the evidence. Moreover, assessments of the cost-efficiency of employing both modalities in routine diagnostics, especially in under-resourced settings, are warranted. Ongoing advancements in imaging technologies and the emergence of hybrid PET/MRI systems may further refine diagnostic precision and optimize workflow efficiency.

In resource-constrained environments, simultaneous access to both MRS and PET can be difficult due to high costs. In our study setting, Magnetic Resonance Spectroscopy (MRS) was performed free of cost under the Sehat Card program at Lady Reading Hospital (LRH). Positron Emission Tomography (PET) was facilitated at Shaukat Khanum Memorial Cancer Hospital, Peshawar, where the Chairman of the Board of Governors is the same for both institutions. Through this administrative linkage, concessional arrangements were made, allowing PET studies to be conducted at grossly reduced rates whenever clinically required. This collaboration enabled us to implement a combined MRS–PET diagnostic strategy in selected patients without imposing an unsustainable financial burden. Such cooperative models, where institutional leadership facilitates cross-hospital collaboration, may provide a practical framework for integrating advanced neuroimaging in other limited-resource settings.

CONCLUSIONS

The synergistic diagnostic roles of Magnetic Resonance Spectroscopy and Positron Emission Tomography have been emphasized in the evaluation of cerebral metabolic dysfunctions. Greater sensitivity was demonstrated by Positron Emission Tomography, whereas higher specificity was associated with Magnetic Resonance

Spectroscopy. A notable enhancement in diagnostic accuracy was observed through their concurrent application. A multimodal imaging paradigm has been advocated to strengthen clinical certainty and refine therapeutic strategies in neurologically complex scenarios and resource-constrained environments. Validation of these observations has been suggested through larger multicenter studies to facilitate the formulation of unified diagnostic frameworks.

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Additional Information

Disclosures: The Authors report no conflict of interest.

Human Subjects: Consent was obtained from all patients/participants in this study.

Conflicts of Interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following:

Financial Relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work.

Other Relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

Data Availability Statement: For data sharing, interested researchers can contact the corresponding authors.

Funding: None.

AUTHORS CONTRIBUTIONS

Sr.#	Author's Full Name	Intellectual Contribution to Paper in Terms of:
1.	Iqra Ajmal	1. Study design and methodology.
2.	Maria Nisar	2. Paper writing.
3.	Remsha Hameed Khan	3. Data collection and calculations.
4.	Naseem ur Rahman	4. Analysis of data and interpretation of results.
5.	Azaz Ahsan	5. Literature review and referencing.
6.	Amina Hilal	6. Editing and quality insurer.