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MAGNETIC RESONANCE SPECTROSCOPY (MRS) IN CHARACTERIZATION OF FOCAL BRAIN LESION BY COMPARISON WITH HISTOPATHOLOGY

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ABSTRACT

Background

Focal brain lesions are a common neurological condition, which can be further divided into neoplastic or non-neoplastic types. Conventional MRI helps in the structural detail of the lesions, but it cannot clearly differentiate between neoplastic causes, infections, or non-neoplastic causes. Histopathology is considered the gold standard for the diagnosis of the condition, although it is an invasive procedure.

Objective

To determine the frequency of positive findings for focal brain lesions on MRS and confirmed through histopathology.

Study Design

Cross sectional study.

Place of Study

Radiology Department of Shifa International Hospital Islamabad.

Duration

This study was conducted from 20 June 2024 to 20 April 2025

Methodology

A total of 45 patients aged 18 to 60 years with focal brain lesions on conventional magnetic resonance imaging were included. All patients underwent magnetic resonance spectroscopy before surgery. Data were analyzed using Statistical Package for Social Sciences version 23. Fischer exact test were applied.

Results

Mean age was 51.71 ± 11.57 years. Males were 82.2% and females 17.8%. On spectroscopy 75.60% lesions were neoplastic while histopathology confirmed 82.20% as neoplastic. True positive rate was 75.60%.

Conclusion

Magnetic resonance spectroscopy shows good diagnostic accuracy and is helpful non-invasive tool in differentiating neoplastic from non-neoplastic brain lesions.

INTRODUCTION:

Focal brain lesion refers to discrete abnormalities of the brain parenchyma, which may be neoplastic or non-neoplastic in origin.1 These are most commonly detected using various neuroimaging techniques such as computed tomography or magnetic resonance imaging of patients who complain of various symptoms such as headache, seizures, focal neurological signs, vomiting, or altered sensorium.2 The various etiologies of focal brain lesion include primary or metastatic tumors, abscesses, granulomas, demyelinative diseases, infarction, and radiation encephalopathy.3 In addition, in developing countries, infectious processes such as tuberculoma and cerebral abscesses are common.4

The characterization of focal brain lesions includes the precise nature of the lesion, whether neoplastic or non-neoplastic, and the grade or aggressiveness of the lesion. The size of the lesion, its anatomical location, its margins, associated edema, mass effect, and enhancement characteristics are typically obtained from routine imaging with conventional Magnetic Resonance Imaging (MRI).5 Lesion characteristics such as irregular margins and heterogeneous enhancement with associated edema may suggest a high-grade lesion; however, these characteristics are nonspecific.6 Non-neoplastic processes such as abscesses or demyelinating diseases may mimic neoplastic processes on routine imaging. Histopathology represents the gold standard for lesion characterization as it provides detailed information on cellular atypia, mitotic activity, and necrosis. 7

Magnetic Resonance Spectroscopy (MRS) is an advanced imaging technique where the biochemical content of the brain is studied instead of its structural features.8 It is capable of measuring the amount of various metabolites, including N-acetylaspartate (NAA), choline (Cho), creatine (Cr), and lactate.9 Their ratios help differentiate the various pathologies. In the case of neoplastic lesions, the levels of choline are elevated due to increased membrane turnover, while NAA is decreased due to the loss of neurons, causing a reversal of Hunter's angle.10 In the case of radiation necrosis, the levels of metabolites are decreased, while in abscess or infection, lactate and other metabolites may be elevated.11

With regard to the current local population, brain lesion cases due to focal brain lesions are frequently encountered in neurosurgical and radiological practice, but data regarding the accuracy of Magnetic Resonance Spectroscopy in differentiating neoplastic from non-neoplastic brain lesions, based on indigenous studies, is limited. In addition, delayed presentation of cases is common, and infectious conditions, such as tuberculoma and abscess, which may mimic neoplastic brain lesions, are frequently encountered, making it imperative to examine the accuracy of MRS, which is non-invasive, as opposed to surgical option which invasive and not available in a timely manner.

Methodology:

This cross sectional study was conducted at the Radiology department of Shifa International Hospital, Islamabad. Approval was obtained from the IRB department of the hospital before commencement of the study. The sample size was calculated by WHO 1.1 Calculator by taking percentage of lesions diagnosed among focal brain lesions on MRS as well as on histopathology as 86.8%,12 confidence level 95% and absolute precision 10%. The calculated sample size was 45 patients. All adult patients of either gender, aged 18 to 60 years, admitted under neurosurgery department with focal brain lesions identified on conventional MRI and having MRS performed in hospital before surgery were included. Focal brain lesion was taken as any localized abnormality within brain parenchyma detected on conventional MRI and reported by consultant Radiologist categorized as neoplastic or non-neoplastic in nature. Patients who did not undergo histopathological examination and

lesions not technically suitable for spectroscopy because of location were excluded from study. Written informed consent was obtained from every patient before inclusion in the research.

Detailed clinical history and relevant physical examination findings were documented. All patients first underwent conventional MRI followed by Magnetic Resonance Spectroscopy. After imaging assessment, patients underwent neurosurgical intervention in neurosurgery department. During surgery biopsy specimen was obtained and sent to histopathology department for microscopic evaluation. Patients were followed postoperatively until histopathology report was received. After completion of surgical procedure and availability of histopathology report interpretation criteria were applied. On MRS, lesion was labeled as neoplastic when elevated choline peak was present with NAA-creatinine ratio less than 1.6 and choline-creatinine ratio more than 1.5 causing reversal of Hunter's angle, suggestive of glial origin. Radiation necrosis was considered when decreases were seen in N-acetylaspartate, choline, and creatine peaks. Ischemia and infarction were considered when an increased lactate peak was seen. Infection was considered when NAA was absent with increased lactate, alanine, cytosolic acid, and acetate peaks. Under histopathology, the brain lesion was considered neoplastic when numerous abnormal cells with irregular nuclear contours and tumor nuclei with varying nuclear atypia were seen under the microscope. True positive was considered when a focal brain lesion gave the same diagnosis with both magnetic resonance spectroscopy and histopathology results. The outcome of interest was the proportion of true positive results among patients with focal brain lesions who underwent magnetic resonance spectroscopy and histopathology examination.

All collected data were entered and analyzed using SPSS version 23. Quantitative variable such as age was presented as mean ± Standard Deviation. Qualitative variables including gender, diagnosis on MRS and diagnosis on Histopathology were presented as frequencies and percentages. Effect modifiers like age and gender were controlled by stratification. Post stratification Chi-Square test was applied to determine statistical significance. P-value less than 0.05 was taken as significant.

RESULTS

The study comprised a total of 45 patients with mean age of 51.71±11.57 years. The distribution of gender showed male predominance where 37 (82.2%) patients were males and only 8 (17.8%) were females (Table-I). When magnetic resonance spectroscopy findings were analyzed, it was found that 34 (75.60%) lesions were classified as neoplastic while 11 (24.40%) lesions were classified as non-neoplastic. On the other hand, histopathology results demonstrated that 37 (82.20%) lesions were neoplastic and 8 (17.80%) lesions were non-neoplastic. The true positive results showed that 34 (75.60%) cases were correctly identified as positive while 11 (24.40%) cases were not correctly identified (Table-II). The association between true positive results and demographic factors were examined through stratified analysis (Table-III). For age groups, patients who were ≤40 years showed 7 (77.8%) true positive cases and 2 (22.2%) non-true positive cases, whereas patients who were >40 years demonstrated 27 (75.0%) true positive cases and 9 (25.0%) non-true positive cases, with p-value of 1.000 using Fischer Exact Test which indicated no statistically significant difference. Regarding gender stratification, males had 30 (81.1%) true positive results and 7 (18.9%) non-true positive results, while females showed 4 (50.0%) true positive results and 4 (50.0%) non-true positive results, with p-value of 0.085 using Fischer Exact Test which suggested that difference was not statistically significant (Table-III)

Table-I: Patient Demographics

Demographics	Mean ± SD / n (%)
Age (years)	51.71±11.57
Gender	
Male n (%)	37 (82.2%)
Female n (%)	8 (17.8%)

Table-II: Frequency of Neoplastic and Non-Neoplastic Lesions by MRS, Histopathology and True Positive Results

Characteristic	Frequency	%age
Magnetic Resonance Spectroscopy		
Neoplastic	34	75.60%
Non-Neoplastic	11	24.40%
Histopathology		
Neoplastic	37	82.20%
Non-Neoplastic	8	17.80%
True Positive		
Yes	34	75.60%
No	11	24.40%

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Table-III: Association of True Positive Results with Demographic Factors

Demographic Factors		True Positive		p-value
		Yes n(%)	No n(%)	
Age Group (years)	≤40	7 (77.8%)	2 (22.2%)	1.000*
	>40	27 (75.0%)	9 (25.0%)	
Gender	Male	30 (81.1%)	7 (18.9%)	0.085*
	Female	4 (50.0%)	4 (50.0%)	

*Fischer Exact Test

DISCUSSION:

The average age of the participants of the current study was found to be 51.71 ± 11.57 years, which suggests an increased occurrence of focal brain lesions in the middle and older ages of the human lifespan. This may be due to the increased occurrence of neoplastic processes and degenerative changes in the brain tissue, which may be due to the accumulation of genetic mutations, exposure to various environmental factors, and decreased immune surveillance mechanisms in the human body over the course of the lifespan. In the current

study, it was observed that males were predominant, with 37 (82.2%) males and 8 (17.8%) females. This suggests an increased susceptibility of males to focal brain lesions. Various factors may be responsible for this increased susceptibility, including hormonal, occupational exposure to carcinogens, and lifestyle factors, which may be prevalent in the male gender. The true positive rate of magnetic resonance spectroscopy was found to be 75.60%, which suggests the high diagnostic accuracy of MRS in detecting neoplastic lesions when compared to histopathology. The ability of MRS to detect neoplastic lesions may be due to the ability of MRS to analyze the metabolic content of the brain tissue, where neoplastic tissues show increased levels of choline, decreased N-acetylaspartate, and the presence of the lactate peak, which are characteristics of neoplastic tissues.

The present study evaluated role of magnetic resonance spectroscopy in characterization of focal brain lesions by comparison with histopathology and found mean age of patients was 51.71±11.57 years which is comparable with findings of Alam et al. 13 who reported mean age of 40±18 years and Manzoor et al. 14 who found mean age of 47.17±16.46 years. However, this was higher than age reported by Gulalai et al. 15 with mean age 39.10±20.60 years and Jesrani et al.16 who reported mean age of 35.45±10.36 years. The higher mean age in current study can be explained by fact that neoplastic lesions are showing increased incidence with advancing age due to accumulation of genetic mutations and cellular damage over time.

Gender distribution in present study showed male predominance with 37 (82.2%) males and 8 (17.8%) females which is in agreement with findings of Alam et al. 13 who reported 75.5% males and also consistent with Jesrani et al. 16 who found 60.78% males. Similarly, Sarfraz et al. 17 and Farzana et al. 18 both reported 56.7% males in their studies. However, these findings are contrasting with results of Manzoor et al. 14 who found female predominance with 55.5% females and Danassegarane et al. 19 who reported 75% females in their study population. The male predominance in current study may be attributed to higher exposure to environmental risk factors and occupational hazards in male population. On magnetic resonance spectroscopy, present study identified 34 (75.60%) neoplastic lesions while histopathology confirmed 37 (82.20%) neoplastic lesions. These findings are showing similarity with Alam et al. 13 who reported 81% neoplastic lesions on histopathology. However, Jesrani et al. 16 found lower percentage with only 47.1% neoplastic lesions on histopathology which may be due to their specific focus on ring enhancing lesions only. Gulalai et al. 15 reported 58.7% neoplastic lesions on histopathology while Farzana et al. 18 and Sarfraz et al. 17 both found 66.7% positive cases for brain tumors on histopathology. The variation in percentage of neoplastic lesions across different studies can be explained by differences in patient selection criteria, referral patterns and types of lesions being evaluated.

The true positive rate of MRS in current study was 75.60% which indicates good diagnostic performance. This finding is supported by high diagnostic accuracy reported in other studies where Alam et al. 13 found diagnostic accuracy of 88.67% with sensitivity of 93.02% and specificity of 70%. Jesrani et al. 16 reported even higher accuracy of 92.1% with sensitivity of 87.5% and specificity of 93.3%. Similarly, Manzoor et al. 14 found diagnostic accuracy of 88.39% with sensitivity of 90.79% and specificity of 86.08%. Gulalai et al. 15 reported diagnostic accuracy of 90.48% with sensitivity of 89.19% and specificity of 92.31%. Farzana et al. 18 and Sarfraz et al.17 both found accuracy of 91.3% with sensitivity of 89.0% and specificity of 96.0% for MRS. Sande et al. 20 demonstrated that addition of MRS to MRI improved diagnostic agreement from 78.9% to 86.3%. These consistently high accuracy rates across multiple studies are confirming that

MRS is having robust diagnostic capability in differentiating neoplastic from non-neoplastic brain lesions because of its ability to detect metabolic alterations in tumor tissue.

The limitations of the present study must be considered, and it must be noted that this study was carried out at one center, which might be considered as one institution, and this might limit the study's applicability to other healthcare facilities and settings. Moreover, the study's sample size was considered to be small, as it included 45 patients, which might influence the study's ability to demonstrate statistically significant correlations and relationships, especially when considering subgroups of the study's sample. Lastly, the study's sample was dominated by males, as only 8 females (17.8%) were included, compared to 37 males (82.2%).

Conclusion:

It is the conclusion of the current study that magnetic resonance spectroscopy (MRS) is an effective diagnostic tool for characterizing focal brain lesions when measured against histopathology as a gold standard. The current study found that the diagnostic accuracy of MRS in differentiating neoplastic from non-neoplastic lesions was satisfactory, with an acceptable true positive rate.

Disclaimer:

There is nothing to declare.

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Ethical Approval:

Permission for conducting this research was taken from the Institutional Ethical Committee before starting the study. All procedures was carried out in agreement with committee guidelines and principles of the Declaration of Helsinki.

Informed Consent:

Written consent was obtained from every participant before inclusion. They were informed clearly that their personal data will remain confidential and they have full right to withdraw from study at any time without any issue.

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CONFLICT OFF INTEREST:

THE AUTHOR DECLARE THAT THEY HAVE NO COMPETING INTEREST RELATED TO THIS RESEARCH.