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ROLE OF MAGNETIC RESONANCE SPECTROSCOPY IN CHARACTERIZATION OF SUPRATENTORIAL BRAIN LESIONS

Original Research

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ABSTRACT

Background: Supratentorial brain tumors present complex diagnostic challenges, often necessitating differentiation between neoplastic and non-neoplastic lesions. While magnetic resonance imaging (MRI) offers detailed anatomical insights, it sometimes lacks the specificity required for tumor characterization. Magnetic resonance spectroscopy (MRS) has emerged as a promising non-invasive adjunct, enabling metabolic evaluation of intracranial lesions. Understanding metabolite alterations through MRS may improve early tumor detection, aid in precise grading, and enhance therapeutic decision-making, potentially minimizing the need for invasive procedures.

Objective: This study aimed to assess the diagnostic efficacy of magnetic resonance spectroscopy (MRS) in evaluating patients with suspected intracranial lesions, highlighting its role in improving early detection, tumor grading, treatment planning, and overall patient outcomes.

Methods: A prospective observational study was conducted at Armed Forces Institute of Radiology and Imaging (AFIRI), Rawalpindi, from August 2024 to April 2025. Thirty patients fulfilling inclusion criteria were enrolled. Magnetic resonance spectroscopy was performed using a 1.5 Tesla MRI scanner with multi-voxel acquisition in spin-echo sequence mode. Metabolites assessed included choline (Cho) at 3.2 ppm, creatine (Cr) at 3.0 ppm, N-acetylaspartate (NAA) at 2.0 ppm, lactate at 1.33 ppm, lipid within 0.7–1.3 ppm, and myoinositol at 3.56 ppm. Cho/NAA and Cho/Cr ratios were calculated for both intralesional and perilesional regions. Statistical analysis was performed using SPSS version 25.0, considering a p-value <0.05 as significant.

Results: Among 30 patients, 19 (63.33%) were male and 11 (36.67%) were female. Age distribution revealed 8 patients (26.67%) aged 20–29 years, 6 (20.00%) aged 30–39 years, 5 (16.67%) each in 40–49 and 50–59 years, and 6 (20.00%) above 60 years. Intralesional Cho/Cr ratios ranged between 0.50–5.00 for primary tumors and 0.80–3.00 for metastases, whereas Cho/NAA ratios ranged from 0.60–7.50 for primary tumors and 2.00–10.00 for metastases. Perilesional Cho/Cr ratios varied from 0.50–7.00 in primary tumors and 0.80–2.00 in metastases, while perilesional Cho/NAA ratios ranged from 0.80–8.00 in primary tumors and 0.62–2.00 in metastases. Statistically significant differences ($p<0.05$) were observed in both Cho/NAA and Cho/Cr ratios when differentiating between tumor grades and tumor types.

Conclusion: The study validates the diagnostic utility of magnetic resonance spectroscopy as a non-invasive tool for evaluating supratentorial brain lesions. Intralesional Cho/Cr ratios effectively differentiated tumor grades, while perilesional Cho/NAA ratios distinguished primary tumors from metastases. The significant alterations in metabolite profiles underscore the potential of MRS in enhancing tumor characterization, aiding early diagnosis, and optimizing treatment planning.

Keywords: Brain Neoplasms, Diagnostic Imaging, Magnetic Resonance Spectroscopy, Neoplasm Grading, Supratentorial Neoplasms, Tumor Biomarkers, Tumor Diagnosis.

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INTRODUCTION

Brain tumors are broadly classified into supratentorial and infratentorial types, with primary malignant brain tumors occurring at an incidence of approximately 3.0% in males and 2.1% in females per 100,000 individuals worldwide (1). Despite advances in imaging, distinguishing low-grade from high-grade tumors, and neoplastic from non-neoplastic brain lesions, remains a significant diagnostic challenge. Conventional magnetic resonance imaging (MRI), though indispensable, often falls short in reliably characterizing these lesions, necessitating invasive procedures such as biopsy or repeated imaging follow-ups (2). Gadolinium-enhanced MRI has improved the visualization of malignant brain lesions, yet limitations persist, particularly in differentiating between various types of supratentorial tumors based solely on imaging characteristics (3). Although biopsy continues to serve as the gold standard for definitive diagnosis, its invasive nature carries inherent risks and discomfort for patients. Historically, biopsy was the only means to obtain tissue samples from brain lesions for histopathological evaluation. However, emerging non-invasive imaging modalities like magnetic resonance spectroscopy (MRS) are transforming the diagnostic landscape by providing metabolic insights into brain lesions without the need for tissue sampling (4). MRS enhances the diagnostic precision of MRI by evaluating the chemical composition of brain tissues, offering crucial information about tumor grade, type, and treatment response (5,6).

Magnetic resonance spectroscopy functions by detecting and quantifying specific metabolites within the brain or tumor tissue, thus reflecting underlying biochemical changes associated with various pathological states. It operates as a multiparametric molecular imaging tool that complements structural MRI, enabling the detection of metabolic patterns linked to tumor biology (7). Through the analysis of the electromagnetic spectrum emitted by brain tissue, MRS generates a spectrum where the frequency (chemical shift) and amplitude (concentration) of various metabolites such as N-acetyl aspartate (NAA), choline, creatine, lactate, lipid, and myo-inositol are represented (8,9). Two primary techniques for spectral localization exist: single-voxel and multivoxel spectroscopy, each providing valuable data for clinical interpretation. Given the critical need for non-invasive diagnostic tools that can improve accuracy while minimizing patient risk, this study aims to explore the role of magnetic resonance spectroscopy in the detection of brain tumors, using histopathological examination as the reference standard. The objective is to rationalize MRS as a non-invasive, adjunctive tool that enhances diagnostic confidence, facilitates treatment planning, and potentially reduces the dependence on invasive biopsy procedures.

METHODS

A prospective observational study was conducted at the Armed Forces Institute of Radiology and Imaging (AFIRI), Rawalpindi, after obtaining ethical approval from the Institutional Review Board (IRB), spanning from August 2024 to April 2025. Written informed consent was secured from all participants prior to inclusion. The sample size was determined using the WHO sample size calculator, based on a 95% confidence interval, a 5% margin of error, and an anticipated prevalence of 1.89% for supratentorial brain lesions. Patients presenting with probable supratentorial space-occupying brain lesions and willing to provide legal informed consent were eligible for inclusion. Exclusion criteria comprised individuals with a history of significant head trauma, medical conditions contraindicating MRI—such as the presence of aneurysmal clips, cardiac pacemakers, cochlear implants, or other incompatible devices—and those unwilling to participate. Prior to MRI scanning, all patients underwent thorough screening to exclude ferromagnetic materials, cardiac implants, or any other contraindications. Participants were positioned supine with head immobilization to minimize motion artifacts. An initial topogram of the head was performed to plan the imaging sequences systematically. Standardized MRI protocols were applied, including axial, coronal, and sagittal T1- and T2-weighted sequences, with a slice thickness uniformly set at 5 mm.

For magnetic resonance spectroscopy (MRS), a spin-echo sequence with long and short echo times (144 ms and 35 ms, respectively) was utilized to perform multi-voxel MRS. Water suppression was achieved using the chemical shift selective (CHESS) technique. Voxels were carefully positioned over the lesional and perilesional regions, avoiding contamination from cerebrospinal fluid or scalp fat to ensure spectral accuracy. Metabolites assessed included N-acetyl aspartate (NAA) at 2.0 parts per million (ppm), creatine (Cr) at 3.0 ppm, choline (Cho) at 3.2 ppm, lactate at 1.33 ppm, lipid components between 0.7–1.3 ppm, and myo-inositol at 3.56 ppm. Cho/NAA and Cho/Cr ratios were calculated both within the lesion and in adjacent perilesional tissue to aid in diagnostic evaluation. Data analysis was carried out using the Statistical Package for Social Sciences (SPSS) software version 25.0. Quantitative variables were expressed

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as means and standard deviations (Mean ± SD), while qualitative variables were presented as frequencies and percentages. Statistical significance was defined at a p-value threshold of less than 0.05.

RESULTS

A total of 30 patients were included in the study, comprising 19 males (63.33%) and 11 females (36.67%), indicating a male predominance in supratentorial brain tumors. The distribution across age groups revealed that 8 patients (26.67%) were aged between 20–29 years, 6 patients (20.00%) between 30–39 years, 5 patients (16.67%) between 40–49 years, 5 patients (16.67%) between 50–59 years, and 6 patients (20.00%) were aged above 60 years. Histopathological evaluation showed that Grade I pilocytic astrocytoma and Grade IV glioblastoma multiforme (GBM) were the most frequently encountered tumor types, each diagnosed in 9 patients (30.00%). Grade II diffuse astrocytoma was identified in 4 patients (13.33%), metastasis in 4 patients (13.33%), and meningioma in 3 patients (10.00%), while one case (3.33%) was categorized as others. No cases of Grade III anaplastic astrocytoma were observed. Regarding tumor classification based on imaging, primary low-grade tumors were identified in 16 patients (53.33%), primary high-grade tumors in 10 patients (33.33%), and metastasis in 4 patients (13.33%). The mean choline/creatine (Cho/Cr) ratios within intralesional areas were found to be 1.23±0.30 for primary low-grade tumors, 3.58±1.26 for primary high-grade tumors, and 2.07±1.11 for metastatic lesions, with a statistically significant difference observed (p-value <0.05). In the perilesional areas, the mean Cho/Cr ratios were 1.23±0.36 for primary low-grade tumors, 3.21±1.51 for primary high-grade tumors, and 1.35±0.49 for metastatic tumors, also demonstrating a statistically significant difference (p-value <0.05). Similarly, the mean choline/N-acetyl aspartate (Cho/NAA) ratios in intralesional regions were 1.46±0.74 for primary low-grade tumors, 4.05±1.54 for primary high-grade tumors, and 4.88±3.52 for metastatic lesions, with statistical significance noted (p-value <0.05). In perilesional areas, the mean Cho/NAA ratios were 1.31±0.33 for primary low-grade tumors, 3.84±1.97 for primary high-grade tumors, and 1.31±0.57 for metastases, also achieving statistical significance (p-value <0.05).

Table 1: Gender and age distribution of brain tumor cases (n = 30)

Gender	**Value; n (%)**
Male	19 (63.33 %)
Female	11 (36.67 %)
Total	30 (100.00 %)
Age (years)	
20-29	8 (26.67 %)
30-39	6 (20.00 %)
40-49	5 (16.67 %)
50-59	5 (16.67 %)
>60	6 (20.00 %)
Total	30 (100.00 %)

Table 2: Distribution by histopathological grade or type

Histopathological grade/type	**Number of patients; n (%)**
Grade I (Pilocytic Astrocytoma)	9 (30.00 %)
Grade II (Diffuse Astrocytoma)	4 (13.33 %)
Grade III (Anaplastic Astrocytoma)	-
Grade IV (Glioblastoma Multiforme or GBM)	9 (30.00 %)
Meningioma	3 (10.00 %)
Metastasis	4 (13.33 %)
Others	1 (3.33 %)
Total	30 (100.00 %)

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Table 3: Mean Choline/Creatine (Cho/Cr) ratios of intralesional and perilesional areas (n = 30)

Tumor Type	Range	Mean±S.D.	P-value
Intralesional Area			
Primary Tumor			
Low Grade	0.50 - 1.60	1.23±0.30	<0.05
Hight Grade	1.70 - 5.00	3.58±1.26	
Metastasis	0.80 - 3.00	2.07±1.11	
Perilesional Area			
Primary Tumor			
Low Grade	0.50 - 1.80	1.23±0.36	<0.05
Hight Grade	1.70-7.00	3.21±1.51	
Metastasis	0.80-2.00	1.35±0.49	

Table 4: Mean Choline/N-acetyl aspartate (Cho/NAA) ratios of intralesional and perilesional areas (n = 30)

Tumor Type	Range	Mean±S.D.	P-value
Intralesional Area			
Primary Tumor			
Low Grade	0.60-4.00	1.46±0.74	
Hight Grade	2.00-7.50	4.05±1.54	<0.05
Metastasis	2.00-10.00	4.88±3.52	
Perilesional Area			
Primary Tumor			
Low Grade	0.80-1.90	1.31±0.33	
Hight Grade	2.00-8.00	3.84±1.97	<0.05
Metastasis	0.62-2.00	1.31±0.57	

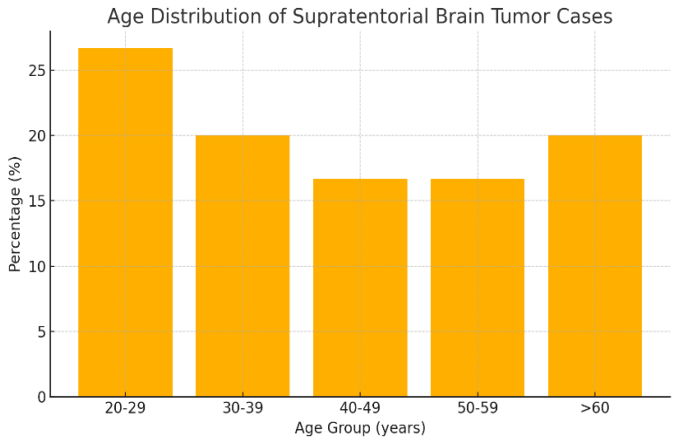


Figure 1 Age Distribution of Supratentorial Brain Tumor Cases

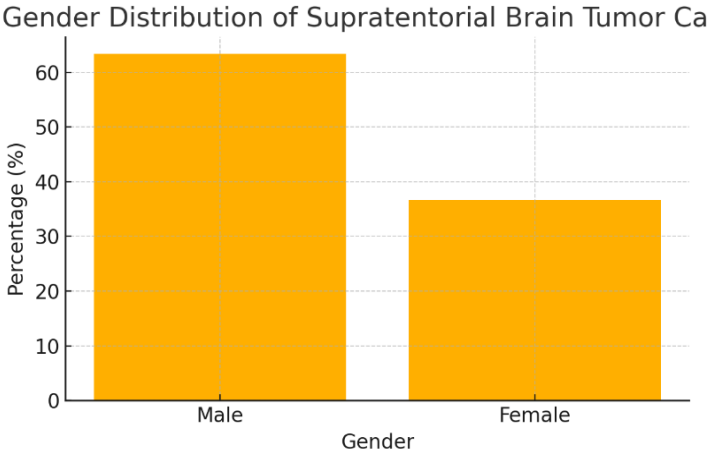
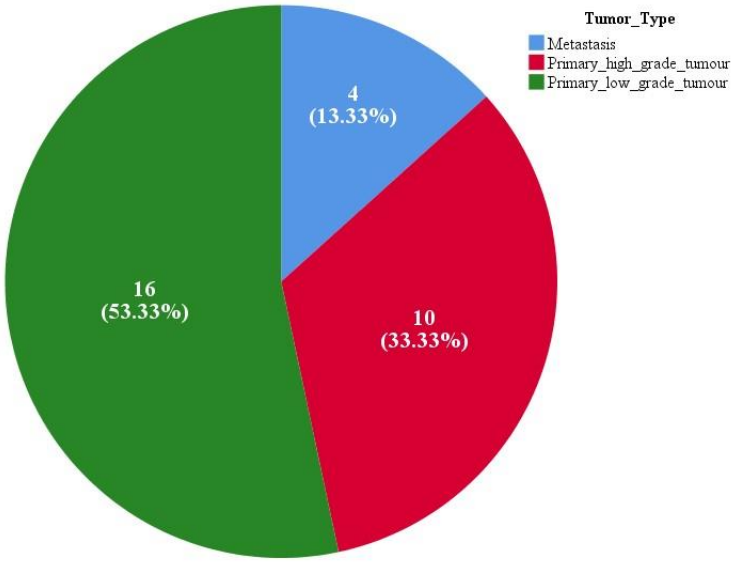


Figure 2 Gender Distribution of Supratentorial Brain Tumor Cases



DISCUSSION

Conventional MRI remains the primary imaging modality for the initial evaluation of brain tumors, providing crucial anatomical information including the presence of edema, mass effect, and enhancement patterns (10). While MRI offers valuable structural insights, magnetic resonance spectroscopy (MRS) serves as an important non-invasive adjunct, offering biochemical information that traditionally could only be obtained through invasive brain biopsies. MRS enables the qualitative assessment of brain metabolites, reflecting processes such as cellular proliferation, neuronal integrity, energy metabolism, and necrotic transformation within neoplastic or adjacent tissues (11). In the present study, a higher prevalence of supratentorial brain tumors was observed among male patients compared to females (63.33% versus 36.67%), a finding that aligns with previous epidemiological observations reporting male predominance in intracranial neoplasms (12). This gender distribution emphasizes a consistent demographic pattern across various geographic regions and may reflect underlying biological or environmental risk factors. The histopathological distribution revealed that Grade I (pilocytic astrocytoma) and Grade IV (glioblastoma multiforme) tumors were most prevalent, each accounting for 30.00% of cases, while lower frequencies were observed for Grade II diffuse astrocytoma, meningioma, and metastases. In contrast, other studies reported a wider variety of tumor types, including pituitary adenomas and pineal region tumors, reflecting differences in study populations, inclusion criteria, and possibly diagnostic practices (13). These variations underscore the importance of localized data in understanding regional tumor epidemiology.

In the metabolic profiling conducted through MRS, significant escalation of Cho/Cr ratios was noted from low-grade to high-grade tumors, suggesting that elevated choline levels correlate with increasing tumor aggressiveness (14). However, no substantial metabolic difference was observed between primary brain tumors and metastases in terms of Cho/Cr ratios, indicating overlapping biochemical properties between these lesion types (15,16). These findings emphasize the strength of Cho/Cr ratios in tumor grading but also highlight their limitation in differentiating between primary and metastatic malignancies. Perilesional analysis further indicated that Cho/Cr ratios did not significantly differ between primary and metastatic tumors, supporting previous observations that perilesional metabolic changes may be subtle or non-specific. In line with earlier research, all cancers exhibited elevated Cho peaks and increased Cho/NAA ratios, though the magnitude of these changes varied. A notably greater elevation of Cho/NAA ratios was detected within high-grade primary tumors, reinforcing the potential of this ratio as a marker for malignancy (17,18). The current study demonstrated fluctuations in Cho/Cr ratios within tumor voxels, with values escalating in proportion to tumor grade. A significant divergence between low-grade and high-grade primary tumors based on Cho/Cr ratios was revealed, suggesting that Cho/Cr measurement may serve as a predictive biomarker for tumor grading. This finding strengthens the utility of MRS as a supportive tool for non-invasive brain tumor characterization (19,20).

One of the strengths of this study lies in its prospective design and the application of multi-voxel MRS for both intralesional and perilesional assessment, providing a comprehensive metabolic evaluation. The use of histopathology as the reference standard adds credibility to the diagnostic comparisons. However, certain limitations must be acknowledged. The relatively small sample size may limit the generalizability of the findings. Additionally, the absence of advanced spectroscopic techniques, such as high-field MR systems

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or multi-parametric imaging fusion, restricted the depth of metabolic analysis. Further, the lack of evaluation of sensitivity, specificity, and predictive values of MRS parameters represents a missed opportunity to quantify diagnostic performance. Future studies should aim for larger, multicentric cohorts and incorporate advanced imaging methodologies, including machine learning-assisted spectroscopic interpretation and integrated imaging biomarkers. Comparative analyses between MRS and emerging non-invasive imaging technologies, such as positron emission tomography-magnetic resonance imaging (PET-MRI), could also provide richer diagnostic frameworks. Improvements in voxel placement techniques and standardization of spectral interpretation criteria would further enhance the reproducibility and clinical application of MRS in brain tumor evaluation. Overall, the findings reinforce the pivotal role of MRS in enhancing the diagnostic capabilities of conventional MRI, supporting its integration into routine neuro-oncological imaging protocols, while emphasizing the need for continued research to overcome current limitations.

CONCLUSION

This study underscores the diagnostic significance of magnetic resonance spectroscopy (MRS) in the evaluation and characterization of supratentorial brain lesions. By providing metabolic insights beyond what conventional MRI offers, MRS facilitates the differentiation of lesions with overlapping radiological features. The findings highlight the influence of gender, age, and histopathological grade on tumor distribution, while also reinforcing the role of choline as a key biomarker in distinguishing between tumor types. Elevated intralesional Cho/Cr ratios effectively differentiated low-grade from high-grade primary tumors, and perilesional Cho/NAA ratios proved valuable in distinguishing primary brain tumors from metastatic lesions. The demonstrated variations in metabolite ratios affirm MRS as a promising, non-invasive tool that can aid in the early diagnosis, accurate grading, and informed treatment planning of supratentorial brain tumors, supporting its integration into routine neuro-oncological imaging protocols.

AUTHOR CONTRIBUTION

Author	Contribution
Sarah Nathaniel*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Khwaja Baqar Hassan	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
Rabia Haq	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Anum Ibrahim	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Momina Siddiqui	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Nigar Ayesha	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published

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