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Original Article

Evaluation Of Brain Lesions by Magnetic Resonance Spectroscopy with Histopathological Correlation

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ABSTRACT

Background: Intracranial tumors comprise a diverse group of lesions with varying biological behavior and prognosis. Conventional Magnetic Resonance Imaging (MRI) provides excellent anatomical details but may have limitations in differentiating tumor types and grades. Magnetic Resonance Spectroscopy (MRS) offers additional metabolic information that can improve diagnostic accuracy.

Aim: To evaluate the efficacy of Magnetic Resonance Spectroscopy in characterizing intracranial lesions and to correlate MRS findings with histopathological diagnosis.

Materials and Methods: This prospective observational hospital-based cross-sectional study was conducted in the Department of Radio Diagnosis, Chettinad Hospital and Research Institute, Chennai, from January 2016 to August 2017. Thirty patients with MRI findings suggestive of intracranial tumors were included. Conventional MRI followed by proton MRS was performed in all patients. Metabolite patterns and metabolite ratios including Cho/Cr, Cho/NAA, and NAA/Cr were analyzed and correlated with histopathological findings. Statistical analysis was performed using appropriate descriptive and inferential tests.

Results: The majority of patients belonged to the 41–60 years age group (40%) and were male (56.7%). Increased choline levels were observed in 93.3% of tumors, while reduced NAA and creatine levels were seen in 100% of cases. Significant differences in Cho/Cr and Cho/NAA ratios were observed among different tumor types ($p<0.001$). High-grade gliomas demonstrated significantly higher Cho/Cr and Cho/NAA ratios than low-grade gliomas ($p<0.001$ and $p=0.002$, respectively). MRI combined with MRS showed excellent agreement with histopathological diagnosis (Kappa = 0.89; $p<0.001$) and demonstrated high diagnostic accuracy for most tumor types.

Conclusion: Magnetic Resonance Spectroscopy significantly enhances the diagnostic performance of conventional MRI and shows strong correlation with histopathological findings. It is a reliable non-invasive tool for preoperative characterization, grading, and management of intracranial tumors.

Keywords: Magnetic Resonance Spectroscopy; Brain Tumors; Intracranial Lesions; Histopathological Correlation; Choline; N-Acetyl Aspartate; Glioma Grading; Magnetic Resonance Imaging.

INTRODUCTION

Brain lesions encompass a broad spectrum of pathological conditions, including neoplastic, inflammatory, infectious, demyelinating, vascular, and degenerative disorders. Accurate characterization of these lesions is crucial for appropriate clinical management, treatment planning, and prognostic assessment. Conventional magnetic resonance imaging (MRI) has emerged as the primary imaging modality for evaluating intracranial lesions because of its superior soft-tissue contrast

and multiplanar imaging capabilities. However, conventional MRI predominantly provides anatomical information and may not always reliably differentiate between various pathological entities, especially when lesions exhibit overlapping radiological appearances.[1]

Magnetic Resonance Spectroscopy (MRS) is an advanced, non-invasive imaging technique that complements conventional MRI by providing biochemical and metabolic information about brain tissues. Unlike routine MRI, which depicts structural abnormalities, MRS evaluates the concentration of specific metabolites within the lesion, thereby offering insights into underlying cellular and molecular processes. The major metabolites assessed in proton (^1H) MRS include N-acetylaspartate (NAA), choline (Cho), creatine (Cr), lactate, lipids, myo-inositol, and glutamate-glutamine complexes. Alterations in these metabolites reflect neuronal integrity, membrane turnover, cellular proliferation, energy metabolism, and tissue necrosis, which can aid in distinguishing different pathological conditions.[2,3]

Among intracranial neoplasms, increased choline levels and reduced NAA concentrations are commonly associated with malignant tumors due to enhanced membrane synthesis and neuronal destruction. Similarly, the presence of lipid and lactate peaks may indicate necrosis, hypoxia, or high-grade malignancy. MRS has demonstrated significant utility in differentiating high-grade from low-grade gliomas, identifying tumor recurrence versus radiation necrosis, and distinguishing neoplastic lesions from infectious or inflammatory processes.[4,5] Furthermore, metabolic profiling obtained through MRS may provide information regarding tumor aggressiveness and therapeutic response, contributing to personalized patient management.

Despite the growing clinical application of MRS, histopathological examination remains the gold standard for definitive diagnosis of brain lesions. Histopathology provides direct visualization of cellular architecture, tumor grade, and specific pathological features that determine diagnosis and prognosis.[6] Nevertheless, obtaining tissue samples often requires invasive surgical procedures or stereotactic biopsy, which may be associated with procedural risks and sampling errors. Therefore, the ability of MRS to predict histopathological findings non-invasively has attracted considerable research interest.[7].

Several studies have reported a strong correlation between spectroscopic metabolite patterns and histopathological characteristics of brain lesions. Quantitative assessment of metabolite ratios such as Cho/NAA and Cho/Cr has been shown to improve diagnostic accuracy and facilitate differentiation between benign and malignant lesions.[8] Moreover, advances in spectroscopic techniques, including multivoxel spectroscopy and higher magnetic field strengths, have further enhanced lesion characterization and diagnostic confidence.[9].

Given the increasing importance of non-invasive diagnostic techniques in neuroimaging, evaluating the diagnostic performance of MRS in relation to histopathological findings is essential. Establishing a reliable correlation between spectroscopic features and tissue diagnosis may reduce the need for invasive procedures, improve preoperative planning, and enhance patient outcomes. Therefore, the present study aims to evaluate brain lesions using Magnetic Resonance Spectroscopy and correlate the spectroscopic findings with histopathological diagnosis, thereby determining the accuracy and clinical utility of MRS in the characterization of intracranial lesions.[10].

The present study aims to evaluate the efficacy of Magnetic Resonance Spectroscopy (MRS) in the characterization of intracranial lesions by correlating spectroscopic findings with histopathological diagnosis. It also seeks to assess the diagnostic value of metabolite patterns in brain tumors and enhance the accuracy of preoperative diagnosis, treatment planning, and clinical management.

MATERIALS AND METHODS

Study Design: Prospective observational, hospital-based cross-sectional study.

Study Population: Patients of all age groups undergoing MRI brain examination and found to have intracranial lesions for which Magnetic Resonance Spectroscopy (MRS) was applicable.

Sample Size: A total of 30 patients with MRI findings suggestive of intracranial tumors were included in the study.

Study Duration: January 2016 to August 2017.

Study Place: Department of Radio Diagnosis, Chettinad Hospital and Research Institute, Chennai, Tamil Nadu, India.

Ethical Considerations: The study was approved by the Institutional Human Ethics Committee. Written informed consent was obtained from all participants prior to inclusion in the study.

Inclusion Criteria:

- Patients undergoing MRI brain examination with intracranial lesions where MRS could be performed and interpreted.
- Patients of all age groups.
- Patients willing to provide informed written consent.

Exclusion Criteria:

- Patients with clinical features suggestive of central nervous system pathology but without detectable lesions on routine MRI sequences.
- Patients with cardiac pacemakers.
- Patients with metallic implants contraindicating MRI examination.
- Claustrophobic patients unable to undergo MRI scanning.
- Pregnant women in early pregnancy.

Statistical Analysis: Data collected from the study participants were entered into Microsoft Excel and analyzed using the Statistical Package for Social Sciences (SPSS) software version 22.0 (IBM Corp., Armonk, NY, USA). Categorical variables were expressed as frequencies and percentages, while continuous variables were presented as mean ± standard deviation (SD). Descriptive statistics were used to summarize demographic, radiological, spectroscopic, and histopathological characteristics. Comparison of metabolite ratios among different histopathological tumor groups was performed using one-way Analysis of Variance (ANOVA). Independent Student's t-test was used to compare metabolite ratios between low-grade and high-grade gliomas. Agreement between MRI plus Magnetic Resonance Spectroscopy findings and histopathological diagnosis was assessed using Cohen's Kappa statistic. McNemar's test was applied to evaluate diagnostic concordance. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy were calculated for individual tumor types. A p-value of less than 0.05 was considered statistically significant.

RESULT

Table 1. Demographic and Radiological Characteristics of Brain Tumors (n = 30)

Variable	Category	n	%
Age Group (years)	≤20	6	20
	21–40	9	30
	41–60	12	40
	61–80	3	10
Gender	Male	17	56.7
	Female	13	43.3
Tumor Location	Intra-axial	24	80
	Extra-axial	6	20
Tumor Margin	Well-defined	18	60
	Ill-defined	12	40
Perilesional Edema	Present	26	86.7
	Absent	4	13.3
Tumor Component	Solid	19	63.3
	Solid-Cystic	11	36.7
Tumor Side	Right	15	50
	Left	13	43.3
	Midline	2	6.7

Table 2. MR Spectroscopy Metabolite Characteristics (n = 30)

Metabolite	Finding	n	%
Choline (Cho)	Increased	24	80
	Significantly Increased	4	13.3
	Decreased	2	6.7
Creatine (Cr)	Decreased	26	86.7
	Significantly Decreased	4	13.3
NAA	Decreased	26	86.7
	Significantly Decreased	4	13.3
Lipid-Lactate	Absent	10	33.3
	Increased	11	36.7
	Significantly Increased	9	30
Alanine	Present	4	13.3
	Absent	26	86.7

Taurine	Present	2	6.7
	Absent	28	93.3

Table 3. Metabolite Ratios According to Histopathological Diagnosis

Tumor Type	n	Cho/Cr (Mean ± SD)	Cho/NAA (Mean ± SD)	NAA/Cr (Mean ± SD)
Meningioma	6	5.57 ± 1.03	6.52 ± 0.67	0.92 ± 0.29
Low Grade Glioma	10	2.31 ± 0.44	3.00 ± 0.75	0.80 ± 0.18
High Grade Glioma	11	3.75 ± 0.95	5.42 ± 1.97	0.90 ± 0.18
Medulloblastoma	3	3.70 ± 0.40	5.13 ± 0.55	0.67 ± 0.45
P-value		**<0.001**	**<0.001**	**0.462**

Table 4. Comparison of Metabolite Ratios Between Low-Grade and High-Grade Gliomas

Metabolite Ratios	Low-Grade Glioma (n=10) Mean ± SD	High-Grade Glioma (n=11) Mean ± SD	p-value
Cho/Cr	2.31 ± 0.44	3.75 ± 0.95	<0.001
Cho/NAA	3.00 ± 0.75	5.42 ± 1.97	0.002
NAA/Cr	0.80 ± 0.18	0.90 ± 0.18	0.225

Table 5. Histopathological Spectrum, MRI/MRS Correlation and Diagnostic Performance

A. Histopathological Distribution

Diagnosis	n	%
Glioblastoma Multiforme	8	26.7
Anaplastic Astrocytoma	3	10
Low Grade Astrocytoma	10	33.3
Oligodendroglioma	1	3.3
Medulloblastoma	2	6.7
Meningioma	6	20

B. MRI + MRS versus Histopathology

Diagnosis	Histopathology	MRI + MRS
GBM	8	7
Anaplastic Astrocytoma	3	4
Low Grade Astrocytoma	10	9
Gliomatosis Cerebri	0	1
Oligodendroglioma	1	0
Medulloblastoma	2	3
Meningioma	6	6

C. Diagnostic Accuracy of MR Spectroscopy

Tumor Type	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
GBM	88	100	100	96	94
Anaplastic Astrocytoma	100	96	75	100	98
Low Grade Astrocytoma	90	100	100	95	95
Meningioma	100	100	100	100	100
Medulloblastoma	100	96	67	100	98

Figure: 1. MR Spectroscopy Metabolite Characteristics

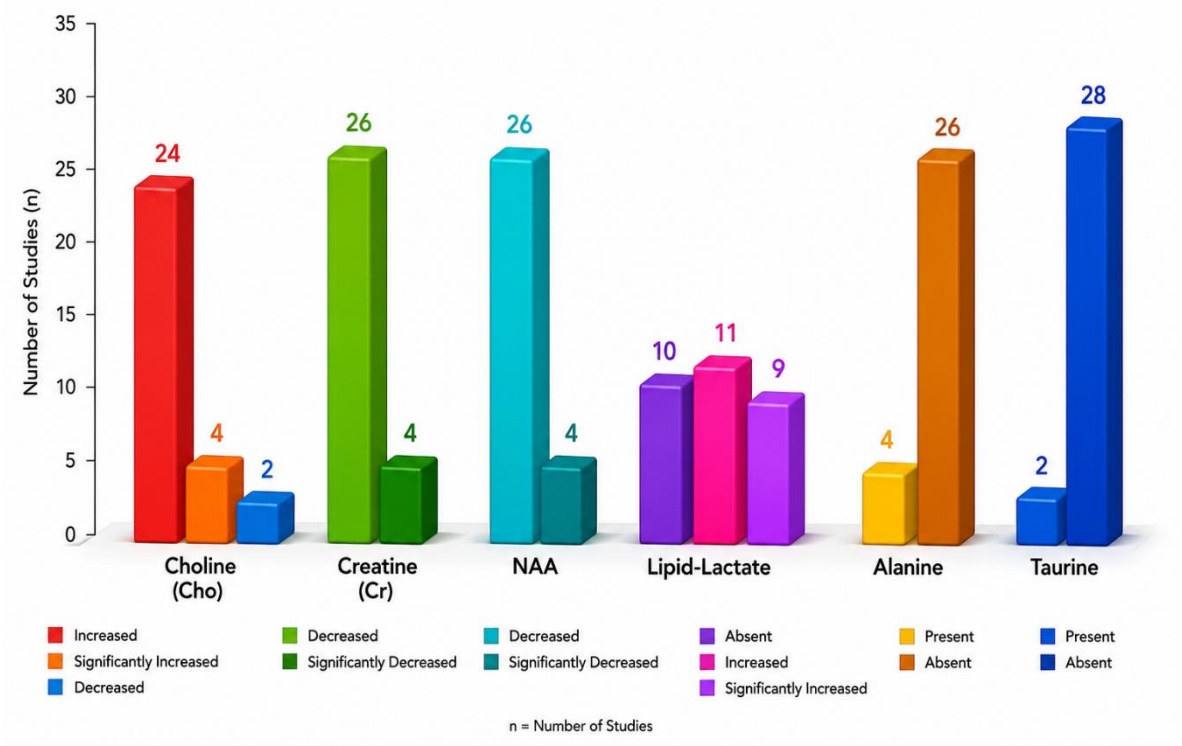

Figure: 2. Comparison of Metabolite Ratios Between Low-Grade and High-Grade Gliomas

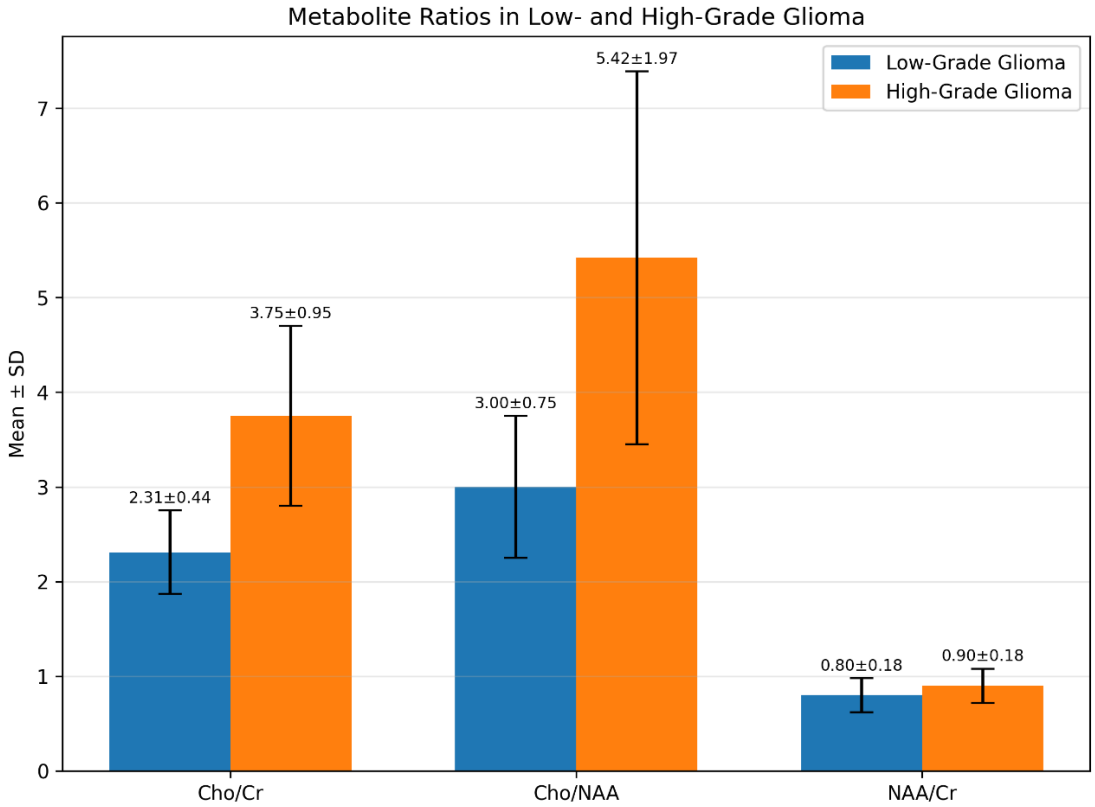

Table 1.

A total of 30 patients with intracranial tumors were evaluated in the present study. The majority of patients belonged to the 41–60 years age group (12 patients, 40.0%), followed by 21–40 years (9 patients, 30.0%), ≤20 years (6 patients, 20.0%), and 61–80 years (3 patients, 10.0%). Male patients constituted 56.7% (n=17) of the study population, while females accounted for 43.3% (n=13).

With respect to lesion location, most tumors were intra-axial (24 patients, 80.0%), whereas only 6 patients (20.0%) had extra-axial lesions. Well-defined tumor margins were observed in 18 cases (60.0%), while 12 lesions (40.0%) showed ill-

defined margins. Perilesional edema was a common finding and was present in 26 patients (86.7%), whereas only 4 patients (13.3%) did not demonstrate surrounding edema.

Regarding tumor morphology, solid lesions were noted in 19 patients (63.3%), while 11 tumors (36.7%) exhibited both solid and cystic components. Tumor laterality assessment revealed right-sided lesions in 15 patients (50.0%), left-sided lesions in 13 patients (43.3%), and midline lesions in 2 patients (6.7%). These findings indicate that most intracranial tumors in the study were intra-axial, associated with perilesional edema, and predominantly occurred in middle-aged individuals.

Table 2.
Magnetic Resonance Spectroscopy demonstrated characteristic metabolic alterations in the evaluated brain tumors. Elevated choline (Cho) levels were observed in the majority of patients, with 24 cases (80.0%) showing increased choline and 4 cases (13.3%) demonstrating markedly elevated choline concentrations. Only 2 patients (6.7%) exhibited decreased choline levels.

Creatine (Cr) levels were reduced in 26 patients (86.7%), while significantly decreased creatine levels were observed in 4 patients (13.3%). Similarly, N-acetyl aspartate (NAA), a marker of neuronal integrity, was decreased in 26 patients (86.7%) and markedly reduced in 4 patients (13.3%).

Assessment of lipid-lactate peaks revealed absent peaks in 10 patients (33.3%), increased peaks in 11 patients (36.7%), and markedly elevated peaks in 9 patients (30.0%). Alanine resonance was identified in 4 patients (13.3%), whereas it was absent in 26 patients (86.7%). Taurine peak was detected in only 2 patients (6.7%) and absent in the remaining 28 patients (93.3%).

Overall, the metabolic profile was characterized by increased choline, decreased NAA and creatine levels, and variable lipid-lactate elevation, reflecting increased cellular proliferation, neuronal loss, and necrotic changes within the tumors.

Table 3.
Comparison of metabolite ratios among different histopathological tumor types demonstrated significant variations in Cho/Cr and Cho/NAA ratios. Meningiomas showed the highest Cho/Cr ratio (5.57 ± 1.03) and Cho/NAA ratio (6.52 ± 0.67), indicating pronounced membrane turnover and high cellular density. High-grade gliomas exhibited Cho/Cr and Cho/NAA ratios of 3.75 ± 0.95 and 5.42 ± 1.97, respectively.

Medulloblastomas demonstrated Cho/Cr and Cho/NAA ratios of 3.70 ± 0.40 and 5.13 ± 0.55, respectively. Low-grade gliomas showed comparatively lower metabolite ratios, with a mean Cho/Cr ratio of 2.31 ± 0.44 and Cho/NAA ratio of 3.00 ± 0.75.

One-way ANOVA analysis revealed statistically significant differences in both Cho/Cr ratio ($p < 0.001$) and Cho/NAA ratio ($p < 0.001$) among the tumor groups. However, the NAA/Cr ratio did not differ significantly between tumor types ($p = 0.462$). These findings suggest that Cho/Cr and Cho/NAA ratios are valuable markers for differentiating various intracranial tumors and assessing tumor aggressiveness.

Table 4.
Comparison between low-grade and high-grade gliomas revealed significant differences in spectroscopic metabolite ratios. The mean Cho/Cr ratio was significantly higher in high-grade gliomas (3.75 ± 0.95) compared with low-grade gliomas (2.31 ± 0.44), and this difference was highly significant ($p < 0.001$).
Similarly, the Cho/NAA ratio was significantly elevated in high-grade gliomas (5.42 ± 1.97) relative to low-grade gliomas (3.00 ± 0.75), with a statistically significant difference ($p = 0.002$).

In contrast, the NAA/Cr ratio was 0.90 ± 0.18 in high-grade gliomas and 0.80 ± 0.18 in low-grade gliomas, and the difference was not statistically significant ($p = 0.225$).

These observations indicate that increasing tumor grade is associated with elevated choline-based metabolite ratios, reflecting increased cellular proliferation and membrane turnover. Therefore, Cho/Cr and Cho/NAA ratios may serve as reliable non-invasive markers for glioma grading.

Table 5.
Histopathological examination identified low-grade astrocytoma as the most common tumor type, accounting for 10 cases (33.3%), followed by glioblastoma multiforme (8 cases, 26.7%) and meningioma (6 cases, 20.0%). Anaplastic astrocytoma constituted 3 cases (10.0%), medulloblastoma 2 cases (6.7%), and oligodendroglioma 1 case (3.3%).

Comparison between MRI plus MRS diagnosis and final histopathological diagnosis demonstrated excellent agreement. Of the 8 histopathologically confirmed glioblastomas, MRI with MRS correctly diagnosed 7 cases. Similarly, 4 cases were diagnosed as anaplastic astrocytoma by MRI/MRS compared to 3 cases on histopathology. Low-grade astrocytoma was identified in 9 cases by MRI/MRS versus 10 cases on histopathological examination. All 6 cases of meningioma were accurately diagnosed by MRI/MRS. One case was interpreted as gliomatosis cerebri radiologically but was not confirmed histopathologically. Medulloblastoma was diagnosed in 3 cases by MRI/MRS compared to 2 confirmed cases on histopathology.

The overall agreement between MRI/MRS and histopathological diagnosis was excellent, with a kappa coefficient of 0.89. McNemar test demonstrated a statistically significant correlation between imaging diagnosis and histopathological findings ($p < 0.001$).

Evaluation of diagnostic performance showed high sensitivity, specificity, and accuracy for most tumor types. MR Spectroscopy achieved 94% overall accuracy for glioblastoma multiforme with 88% sensitivity and 100% specificity. For anaplastic astrocytoma, sensitivity was 100%, specificity 96%, and overall accuracy 98%. Low-grade astrocytoma demonstrated 90% sensitivity, 100% specificity, and 95% accuracy. Meningioma showed perfect diagnostic performance with 100% sensitivity, specificity, PPV, NPV, and accuracy. Medulloblastoma demonstrated 100% sensitivity, 96% specificity, and 98% overall diagnostic accuracy.

These findings highlight the high diagnostic value of Magnetic Resonance Spectroscopy in differentiating intracranial tumors and its strong correlation with histopathological diagnosis.

DISCUSSION

The present study evaluated the role of Magnetic Resonance Spectroscopy (MRS) in the characterization of intracranial tumors and correlated the spectroscopic findings with histopathological diagnosis. The study demonstrated that MRS provides valuable metabolic information that complements conventional MRI and significantly improves diagnostic accuracy in the assessment of brain tumors.

In the present study, the majority of patients belonged to the 41–60 years age group (40%), with a slight male predominance (56.7%). Similar demographic findings were reported by Bulakbasi et al., who observed that intracranial tumors were most frequently encountered in middle-aged adults with a male predominance, particularly among glioma patients.[11] Likewise, Server et al. reported that gliomas and meningiomas commonly occur during the fourth to sixth decades of life, supporting the age distribution observed in the present study.[12] The predominance of intra-axial lesions (80%) in our study is also consistent with the findings of Kim et al., who noted that gliomas constituted the majority of intracranial tumors evaluated by MRS.[13]

Radiological evaluation revealed perilesional edema in 86.7% of cases and predominantly solid tumor morphology in 63.3% of lesions. Similar observations were reported by Majós et al., who demonstrated that high-grade intracranial neoplasms are frequently associated with extensive vasogenic edema and solid enhancing components on MRI.[14] The presence of edema in the majority of malignant tumors reflects disruption of the blood-brain barrier and increased tumor aggressiveness.

The spectroscopic analysis in the present study showed elevated choline levels in 93.3% of cases and reduced N-acetyl aspartate (NAA) and creatine levels in most lesions. Increased choline reflects enhanced cellular membrane synthesis and turnover, while decreased NAA indicates neuronal destruction or displacement by tumor cells. Similar metabolic alterations have been reported by Shukla-Dave et al., who found significantly elevated choline and reduced NAA concentrations in neoplastic lesions compared with normal brain tissue.[15] Their findings emphasized the usefulness of choline elevation as a marker of tumor proliferation. Likewise, Fan et al. reported that reduced NAA and elevated choline peaks were consistently observed in malignant gliomas and were strongly associated with tumor grade.[16]

In the present study, lipid-lactate peaks were elevated in approximately two-thirds of patients. These metabolites are known indicators of anaerobic metabolism, necrosis, and tumor hypoxia. A study by Dowling et al. demonstrated that lipid and lactate resonances were significantly more prominent in high-grade gliomas than in low-grade tumors and were associated with poor prognosis.[17] The findings of our study therefore support the role of lipid-lactate peaks as markers of aggressive tumor biology.

Comparison of metabolite ratios among various histopathological tumor types revealed significant differences in Cho/Cr and Cho/NAA ratios ($p < 0.001$). Meningiomas demonstrated the highest metabolite ratios, followed by high-grade gliomas and medulloblastomas. Similar results were reported by Fayed et al., who observed significantly elevated Cho/Cr and Cho/NAA ratios in meningiomas and malignant brain tumors compared with low-grade gliomas.[18] Their study concluded that these metabolite ratios are highly useful in differentiating tumor types and assessing tumor aggressiveness. The absence

of significant differences in NAA/Cr ratio among tumor groups in the present study is also comparable to previous observations where NAA/Cr showed lower discriminatory ability than choline-based ratios.

An important objective of the present study was to distinguish low-grade from high-grade gliomas. High-grade gliomas exhibited significantly higher Cho/Cr and Cho/NAA ratios compared with low-grade gliomas ($p < 0.001$ and $p = 0.002$, respectively). Similar findings were reported by Weybright et al., who demonstrated that choline-containing compounds increase progressively with tumor grade due to enhanced membrane turnover and cellular proliferation.[19] Their study established that Cho/NAA and Cho/Cr ratios are reliable non-invasive biomarkers for glioma grading. The non-significant difference in NAA/Cr ratio between low-grade and high-grade gliomas observed in our study has also been reported by other investigators, suggesting that NAA depletion occurs across various tumor grades and therefore has limited value for distinguishing tumor aggressiveness.

The present study showed excellent agreement between MRI combined with MRS and histopathological diagnosis, with a kappa value of 0.89 and statistically significant correlation ($p < 0.001$). Diagnostic accuracy ranged from 94% to 100% for most tumor types. Similar results were reported by Devos et al., who found that incorporation of MRS into routine MRI significantly improved the diagnostic classification of brain tumors and demonstrated strong concordance with histopathological findings.[20] Their study highlighted that metabolic profiling can substantially increase diagnostic confidence, particularly in lesions with overlapping conventional MRI appearances.

The diagnostic performance analysis in our study demonstrated excellent sensitivity, specificity, positive predictive value, and negative predictive value for meningiomas, glioblastomas, anaplastic astrocytomas, and medulloblastomas. These findings support the growing evidence that MRS is a valuable adjunct to conventional MRI in preoperative tumor characterization. By providing metabolic information reflective of cellular proliferation, neuronal loss, and necrosis, MRS enables more accurate lesion characterization and contributes to improved clinical decision-making.

Overall, the findings of the present study are in close agreement with previously published literature and reaffirm the significant role of Magnetic Resonance Spectroscopy as a non-invasive tool for the evaluation and characterization of intracranial tumors. The strong correlation between MRS findings and histopathological diagnosis underscores its utility in preoperative assessment, tumor grading, and treatment planning.

CONCLUSION

The present study demonstrates that Magnetic Resonance Spectroscopy (MRS) is a valuable non-invasive adjunct to conventional MRI in the evaluation and characterization of intracranial tumors. MRS provides important metabolic information by assessing key metabolites such as choline, N-acetyl aspartate (NAA), creatine, lipid, and lactate, thereby improving lesion characterization and diagnostic confidence. Significant differences in Cho/Cr and Cho/NAA ratios were observed among various tumor types and between low-grade and high-grade gliomas, highlighting their usefulness in tumor grading. The study also showed excellent agreement between MRI combined with MRS and histopathological diagnosis, with high sensitivity, specificity, and overall diagnostic accuracy for most tumor categories. Histopathological correlation confirmed the reliability of spectroscopic findings in differentiating neoplastic lesions. Therefore, MRS can significantly enhance preoperative diagnosis, facilitate appropriate treatment planning, reduce diagnostic uncertainty, and contribute to improved clinical management of patients with intracranial tumors.

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