Original Research Paper

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A PROSPECTIVE STUDY ON CORRELATION OF MAGNETIC RESONANCE SPECTROSCOPY WITH HISTOPATHOLOGICAL EXAMINATION IN SUPRATENTORIAL BRAIN TUMORS

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KEYWORDS :

INTRODUCTION

Magnetic Resonance Spectroscopy [MRS] is an advanced imaging modality that enables the study of metabolites within the normal brain parenchyma or neoplastic tissue that reflect the nature of lesions, helps in characterisation and grading of brain tumours[1].

MR spectroscopy is a sequence in Magnetic Resonance Imaging which provides a measure of brain chemistry, a means of non-invasive imaging that measures relative levels of various tissue metabolites[2].

Hence, this study will help us identify the specificity and the sensitivity of MRS in diagnosing supratentorial brain lesions and its accuracy to correlate with histopathological diagnosis pre-operatively, which can be considered a great tool in armamentarium for neurosurgeons because characterisation based on metabolic contents and grading of tumours especially tumours with infiltrative nature like gliomas helps in better surgical planning, devising better management protocols – whether requirement of post op radiotherapy / chemotherapy in present or not, and also helps in follow-up of patients as a diagnostic imaging modality.

The important metabolites evaluated in long TE proton spectra are Choline, N-acetyl aspartate (NAA), Creatine, Lactate & in short TE proton spectra are Glutamate /Glutamine, Gamma-amino butyric acid (GABA), Myo-Inositol, Alanine, Lipid[3].

AIMS AND OBJECTIVES

To analyze the MR spectroscopy of the supratentorial brain tumors, correlate with the post operative histopathology and try to find out reliability of MRS in making a pathological diagnosis pre operatively.

To analyze the spectroscopic diagnosis along with parent images like CT brain (Plain & contrast) and conventional MRI (T1W, T2W, DWI & contrast) before giving the final imaging diagnosis.

Review Of The Literature

Meyer et al. in their series of 27 patients with biopsy confirmed brain tumours, showed that the combination of lac/water and choline/water ratio obtained from regions of contrast enhancing brain tumours permitted differentiation of low-grade astrocytoma from anaplastic astrocytoma and Glioblastoma Multiforme (GBM)[4].

In a multi-centre study involving 86 cases of glial tumours, **Negendank et al.** showed that all tumours demonstrated abnormally decreased NAA/Cr and increased Cho/Cr ratios with respect to normal brain parenchyma.[5]

Butcher et al. have described a series of 26 intracranial tumours in which MRS allowed differentiation of infiltrative processes from circumscribed lesions but did not allow differentiation of different types of lesions with in each category.[6]

Kinoshi et al. suggested that glycine levels were markedly elevated in GBMs, high-grade astrocytoma, ependymomas and medullo blastomas, whereas they were low in metastatic tumors.[7]

Grand and co-workers in their study series of 34 cystic intracranial lesions, showed that with a TE 0f 136 msec, the presence of an amino acid peak resonating at 0.9 ppm in bacterial abscess allows differentiation from necrotic neoplasms, which do not show this spectral peak.[8]

Patients & Methods

Study Design:

This is a prospective analytical study conducted over a period of 2 years from July 2021 to June 2023 in the Department of Neurosurgery, Kurnool Medical College and Government General Hospital which is a tertiary care centre in Andhra Pradesh.

The patients who presented with neurological symptoms were initially evaluated radiologically by CT Head and those found to have intracranial space occupying lesion / suspicious of brain tumors were further investigated with MRI.

Only patients with ambiguity in diagnosis based on CT and MRI plain sequences were considered for further evaluation with Magnetic Resonance Spectroscopy (MRS) were included in the study

MRS studies were performed on 1.5 tesla whole body MR system with standard imaging head coil (PHILIPS INGENIA 1.5T) using single voxel and multi voxel spectroscopic imaging techniques.

MRS probable pathological diagnosis was correlated with postoperative histopathological diagnosis of the lesion.

Inclusion Criteria:

Patients admitted in neurosurgery department with diagnosis of supratentorial brain tumors and for whom MRS was done after taking prior consent to be included in the study, willing for radiological evaluation and surgery were included in the study.

Exclusion Criteria :

1. Patients with contraindication for MR imaging (patients with metallic implants, cardiac pacemakers, IUDs, aneurysmal clips, previous gunshot wounds, cochlear implants etc.)
2. Patients with coagulopathies
3. Patients not willing to give consent
4. Pregnant women
5. Non operative patients

OBSERVATIONS AND RESULTS

Present study was a prospective observational study which was conducted to study correlation of magnetic resonance spectroscopy (MRS) with histopathological examination (HPE) in the diagnosis of supratentorial brain tumours. The study was carried out at the Department of Neurosurgery, Kurnool Medical College and General hospital, Kurnool, Andhra Pradesh.

A total of 105 patients that satisfied inclusion/exclusion criteria were included in the study after obtaining their informed consent.

The following section shows the detailed statistical analysis along with interpretation and the graphical representation of the available data.

Table 1) Distribution of magnetic resonance spectroscopy (MRS)

diagnosis of supratentorial brain tumours among the cases studied.

MRS diagnosis	Number of cases	Percentage (%) of cases
Glioma	75	71.4
Abscess	12	11.4
Lymphoma	3	2.9
Epidermoid	3	2.9
Inconclusive	12	11.4
Total	**105**	**100.0**

Out of 105 cases studied, 75 cases (71.4%) had Glioma, 12 cases (11.4%) had Abscess, 3 cases (2.9%) had Lymphoma, 3 cases (2.9%) had Epidermoid and 12 cases (11.4%) had no specific or inconclusive diagnosis on magnetic resonance spectroscopy (MRS) in the study group.

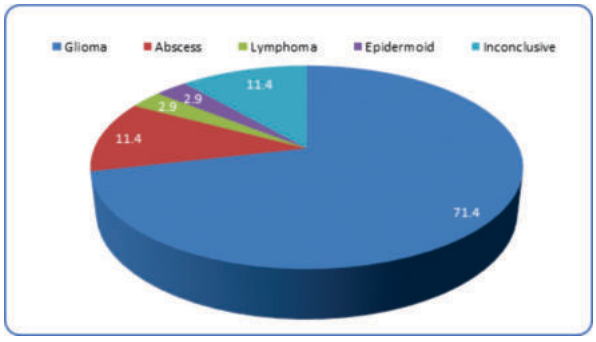

Chart :1) Distribution of magnetic resonance spectroscopy (MRS) diagnosis of supratentorial brain tumours among the cases studied.

Table 2) Distribution of histopathological examination (HPE) diagnosis of supratentorial brain tumours among the cases studied.

HPE diagnosis	Number of cases	Percentage (%) of cases
Glioma	63	60.0
Meningioma	12	11.4
Abscess	9	8.6
Lymphoma	6	5.7
Tuberculoma	3	2.9
Epidermoid	3	2.9
Metastasis	3	2.9
Neurocytoma	3	2.9
Ganglioglioma	3	2.9
Total	**105**	**100.0**

Out of 105 cases studied, 63 cases (60.0%) had Glioma, 12 cases (11.4%) had Meningioma, 9 cases (8.6%) had Abscess, 6 cases (5.7%) had Lymphoma, 3 cases (2.9%) had Tuberculoma, 3 cases (2.9%) had Epidermoid, 3 cases (2.9%) had Metastases, 3 cases (2.9%) had Neurocytoma, 3 cases(2.9%) had Ganglioglioma using histopathological examination (HPE) in the study group.

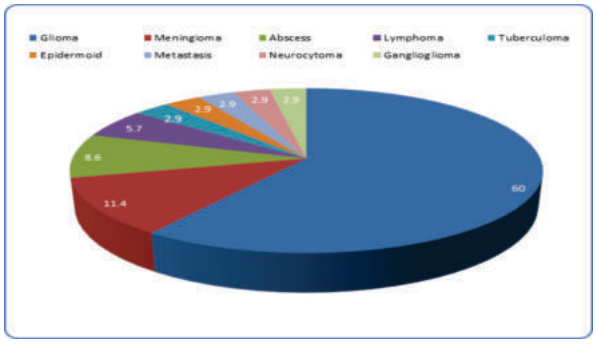

Chart: 2) Distribution of histopathological examination (HPE) diagnosis of supratentorial brain tumours among the cases studied.

Table 3) Distribution of concordance or accuracy (true positive and true negatives) of MRS with reference to HPE diagnosis for each type of diagnosis among the cases studied.

	Accuracy of MRS with reference to HPE	
Diagnosis	Number of cases (TP+TN)	Percentage (%) of cases - (% Accuracy)
Glioma	81	77.1
Meningioma	93	88.6
Abscess	102	97.1
Lymphoma	102	97.1
Tuberculoma	102	97.1
Epidermoid	105	100.0
Metastasis	102	97.1
Neurocytoma	102	97.1
Ganglioglioma	102	97.1
Overall	--	91.7

The accuracy of MRS with reference to (or gold standard) HPE for each type of diagnosis such as Glioma, Meningioma, Abscess, Lymphoma, Tuberculoma, Epidermoid, Metastasis, Neurocytoma and Ganglioglioma was 77.1%, 88.6%, 97.1%, 97.1%, 97.1%, 100.0%, 97.1%, 97.1%, 97.1% respectively.

The overall accuracy of MRS with reference to (or gold standard) HPE was 91.7% in the study group.

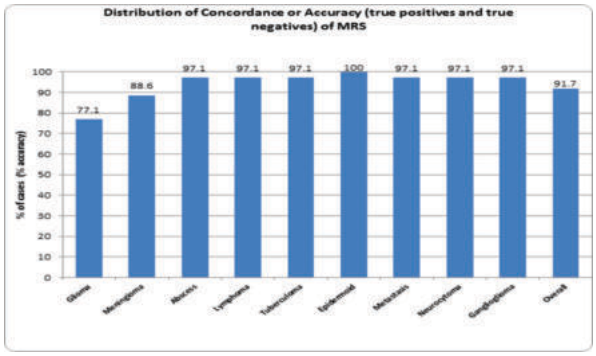

Chart 3) Distribution of concordance or accuracy (true positive and true negatives) of MRS with reference to HPE diagnosis for each type of diagnosis among the cases studied.

Table 4) Diagnostic efficacy measures of MRS with reference to HPE as a Gold standard for each type of diagnosis.

	Diagnostic efficacy measures (%)				
Diagnosis	Sensitivity	Specificity	Positive predictive value (PPV)	Negative predictive value (NPV)	Accuracy
Glioma	90.5	57.1	76.0	80.0	77.1
Meningioma	0.0	100.0	NA	88.6	88.6
Abscess	100.0	96.9	75.0	100.0	97.1
Lymphoma	50.0	100.0	100.0	97.1	97.1
Tuberculoma	0.0	100.0	NA	97.1	97.1
Epidermoid	100.0	100.0	100.0	100.0	100.0
Metastasis	0.0	100.0	NA	97.1	97.1
Neurocytoma	0.0	100.0	NA	97.1	97.1
Ganglioglioma	0.0	100.0	NA	97.1	97.1

The above table shows the diagnostic efficacy measures of magnetic resonance spectroscopy with reference to histopathological examination (HPE) as a gold standard for each diagnosis.

The diagnostic efficacy measures such as sensitivity, specificity, PPV, NPV and accuracy of MRS with reference to HPE for the diagnosis of Glioma was 90.5%, 57.1%, 76.0%, 80.0% and 77.1% respectively.

The diagnostic efficacy measures such as sensitivity, specificity, PPV, NPV and accuracy of MRS with reference to HPE for the diagnosis of Meningioma was 0.0%, 100.0%, NA, 88.6% and 88.6% respectively.

The diagnostic efficacy measures such as sensitivity, specificity, PPV,

NPV and accuracy of MRS with reference to HPE for the diagnosis of Abscess was 100.0%, 96.9%, 75.0%, 100.0% and 97.1% respectively. The diagnostic efficacy measures such as sensitivity, specificity, PPV, NPV and accuracy of MRS with reference to HPE for the diagnosis of Lymphoma was 50.0%, 100.0%, 100.0%, 97.1% and 97.1% respectively.

The diagnostic efficacy measures such as sensitivity, specificity, PPV, NPV and accuracy of MRS with reference to HPE for the diagnosis of Tuberculoma was 00.0%, 100.0%, NA, 97.1% and 97.1% respectively. The diagnostic efficacy measures such as sensitivity, specificity, PPV, NPV and accuracy of MRS with reference to HPE for the diagnosis of Epidermoid was 100.0%, 100.0%, 100.0%, 100.0% and 100.0% respectively.

The diagnostic efficacy measures such as sensitivity, specificity, PPV, NPV and accuracy of MRS with reference to HPE for the diagnosis of Metastasis was 00.0%, 100.0%, NA, 97.1% and 97.1% respectively.

The diagnostic efficacy measures such as sensitivity, specificity, PPV, NPV and accuracy of MRS with reference to HPE for the diagnosis of Neurocytoma was 00.0%, 100.0%, NA, 97.1% and 97.1% respectively.

The diagnostic efficacy measures such as sensitivity, specificity, PPV, NPV and accuracy of MRS with reference to HPE for the diagnosis of Ganglioglioma was 00.0%, 100.0%, NA, 97.1% and 97.1% respectively.

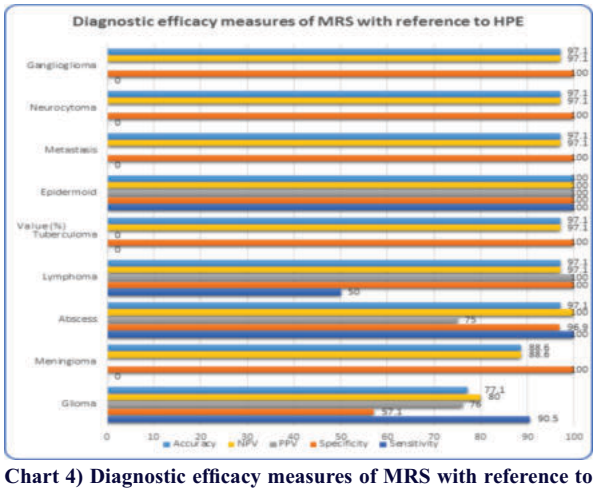

Chart 4) Diagnostic efficacy measures of MRS with reference to HPE as a Gold standard for each type of diagnosis.

Table 5) Distribution of true positive (TP), true negative (TN), false positive (FP) and false negative (FN) cases by MRS with reference to HPE as a Gold standard for each type of diagnosis.

	Diagnosis by MRS with reference to HPE					
Diagnosis	True Positive (TP)	True Negative (TN)	False Positive (FP)	False Negative (FN)	Cohen-Kappa value	P-value
Glioma	57 (90.5%)	24 (57.1%)	18 (42.9%)	6 (9.5%)	0.500	0.001***
Meningioma	--	93 (100.0%)	--	12 (100.0%)	--	--
Abscess	9 (100.0%)	93 (96.9%)	3 (3.1%)	0	0.842	0.001***
Lymphoma	3 (50.0%)	99 (100.0%)	0	3 (50.0%)	0.653	0.001***
Tuberculoma	--	102 (100.0%)	--	3 (100.0%)	--	--
Epidermoid	3 (100.0%)	102 (100.0%)	--	--	1.000	0.001***
Metastasis	--	102 (100.0%)	--	3 (100.0%)	--	--
Neurocytoma	--	102 (100.0%)	--	3 (100.0%)	--	--
Ganglioglioma	--	102 (100.0%)	--	3 (100.0%)	--	--

P-value by Chi-Square test. P-value<0.05 is considered to be statistically significant. ***P-value<0.001.

Out of 105 cases, 57 were positive by both MRS and HPE and 24 were negative by both MRS and HPE and 18 cases were positive by MRS and negative by HPE and 6 cases were negative by MRS and positive by HPE for Glioma, the Cohen-Kappa value was 0.500 and P-value<0.001. It indicates that, there was a statistically significant moderate agreement between MRS and HPE for the diagnosis of Glioma.

Out of 105 cases, 9 were positive by both MRS and HPE and 93 were negative by both MRS and HPE and 3 cases were positive by MRS and negative by HPE for Abscess, the Cohen-Kappa value was 0.842 and P-value<0.001. It indicates that, there was a statistically significant higher to perfect agreement between MRS and HPE for the diagnosis of Abscess.

Out of 105 cases, 3 were positive by both MRS and HPE and 99 were negative by both MRS and HPE and 3 cases were negative by MRS and positive by HPE for Lymphoma, the Cohen-Kappa value was 0.653 and P-value<0.001. It indicates that, there was a statistically significant moderate to higher agreement between MRS and HPE for the diagnosis of Lymphoma. Out of 105 cases, 3 were positive by both MRS and HPE and 102 were negative by both MRS and HPE for Epidermoid, the Cohen-Kappa value was 1.000 and P-value<0.001. It indicates that, there was a statistically significant perfect agreement between MRS and HPE for the diagnosis of Epidermoid. The statistical agreement for the diagnosis such as Meningioma, Tuberculoma, Metastasis, Neurocytoma and Ganglioglioma cannot be studied due insufficient data.

Table 6) Distribution of Glioma grading by MRS according to Glioma grading by HPE

	Glioma Grades (HPE)							
	High		Low		Total		Cohen-Kappa	p-value
Glioma Grades (MRS)	n	%	n	%	n	%		
High	39	100.0	3	16.7	42	73.7	0.872	0.001***
Low	0	0.0	15	83.3	15	26.3		
Total	39	100.0	18	100.0	57	100.0		

P-value by Chi-Square test. Cohen-Kappa for statistical agreement between two modalities. P-value<0.05 is considered to be statistically significant. ***P-value<0.001.

Distribution of Glioma grading by MRS according to Glioma grading by HPE :

Of 39 cases with Glioma High grade by HPE, all had high grade on MRS. Of 18 cases with Low grade on HPE, 15 (83.3%) had Low grade on MRS and 3 (16.7%) had High grade on MRS. Distribution of grading of Glioma by MRS is significantly associated with grading of Glioma by HPE (P-value<0.05) with Higher to Perfect Cohen Kappa value of 0.872. There is a higher to perfect statistically significant agreement between Glioma grading by MRS and Glioma grading by HPE in the study group.

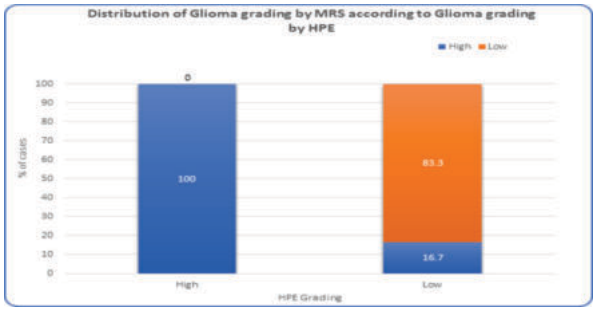

Chart: 5) Distribution of Glioma grading by MRS according to Glioma grading by HPE.

CONCLUSION

- When diagnostic dilemmas present themselves, MR spectroscopy considered in perspective with MRI and clinicopathologic features can be useful in certain situations. MRS helps in improving our ability to predict pre operative histological diagnosis.
- MRS can help to increase the ability to predict the grade of the Glioma. As the grade increases NAA and creatine decreases and choline, lipids and lactate increases[9].
- The overall diagnostic accuracy of MRS with reference to (or gold standard) HPE was 91.7% in our study in predicting the preoperative histopathological diagnosis. After correlating with the clinical features, CT and other MR imaging sequences further increases accuracy of predicting the probable pathological diagnosis.

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