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Role of MR Spectroscopy in Evaluation of Intraaxial Brain Tumors

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ABSTRACT

To define biochemical markers of intraaxialbrain tumors by means of MRspectroscopy.To estimate role of MR spectroscopy in diagnosing and grading of intraaxialbrain tumors with histopathologicalco-relation.To estimate role of MR spectroscopy in determining the infiltrative nature of the intra axial braintumor.

Keywords:
MR spectroscopy,axial braintumor

1. Introduction

Intra axial brain masses are a noteworthy health problem and present numerous imaging challenges. These lesions comprise of primary neoplasm, secondary neoplasm, tumefactive demyelinating lesions, lymphoma, encephalitis and abscesses. [1-3]In intracranial tumor management, imaging plays vital integral role. Magnetic resonance (MR) imaging in specific has developed as the imaging modality most often used to assess intracranial tumors. Importance of MR imaging in the examination of intraaxial tumors can be split into tumor diagnosis with classification, treatment planning and post treatment scrutiny. The advanced MR techniques have developed which offer more than the anatomic information provided by the conventional MR imaging sequences. [4] They produce physiologic data and information on chemical composition. The current advanced techniques comprise of perfusion imaging, diffusion-weighted imaging, MR spectroscopy, blood oxygen level–dependent (BOLD) imaging and molecularimaging.[5]With only anatomic imaging, distinction between extra axial and intra axial brain tumors is simple; though, the major diagnostic task isnoninvasively and precisely differentiate intraaxial tumors to avoid biopsy and follow-up imaging studies. Incorporation of diagnostic information from advanced magnetic resonance (MR) imaging techniques can further enrich the classification accuracy of conventional anatomic imaging.[6]

MR spectroscopy permits the non-invasive calculation of selected biological compounds in vivo. Proton spectroscopy has been acknowledged as a secure and noninvasive diagnostic method. Proton spectroscopy when combined with MRI techniques, [7-9] permits for the association of anatomical and physiological variation in the metabolic and biochemical processes taking place within the previously determined volumes in the brain. MR spectroscopy provides information about the likely extent and nature of changes on a routine MRI scan by examining the presence or ratio of tissue metabolites such as NAA, creatine, choline, and lactateetc.[10]

Extensive usage of quicker MR spectroscopy applications with higher signal-to-noise ratio (SNR) and spatial resolution, allows us to detect functional metabolic changes, which provides more data to recognize the precise nature of the tumor and the morphological and physiological changes occurring in the adjacent brain parenchyma. Longitudinal studies have established that MRS is useful in monitoring disease evolution and treatment effects. MR spectroscopy also has a prognostic implication.[11-13]

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2. Methodology

The study was carried out at the Department of Radiodiagnosis, Sri Lakshmi Narayana Institute of Medical Sciences from December 2018 to July 2020 with aim to evaluate role of MR spectroscopy in intraaxial braintumors.

Source of data:
Patients with clinical features suggestive of intra cranial space occupying lesion referred for MRI study to the Department of the Radiodiagnosis, Sri Lakshmi Narayan Institute of Medical Sciences wereincludedinstudy.TheMRIwasdoneontheadviceofthereferring doctor and no patient was made to undergo MRI for the sole purpose of thisstudy.
STUDY PERIOD: 18 months.
STUDY DESIGN: Observational
Inclusion criteria:
The study includes

- All patients with clinical features suggestive of intra cranial space occupyinglesion.
- All patients with incidentally diagnosed intraaxial brain tumor byCT.

Exclusion criteria:
The study will exclude
- Cases with benign lesions after histopathologyconfirmation.

- Patient having history ofclaustrophobia.

- Patient having history of metallic implants insertion, cardiac pacemakers and metallic foreign body insitu.
- Patient clinically unstable.

SAMPLING AND SAMPLE SIZE: The study is time bound study with sample size of 60 cases.

Data acquisition:
Patients with clinically suspected intra cranial lesion referred for MRI study, underwent the examination after contraindications for MRI were excluded and consent was taken. All the MRI scans in this study were performed using Siemens 1.5 T MAGNETOM ESSENZA MRI scanner.

Mri protocol:
MRI protocol consisted of thefollowing
- Post-contrast T1W-FS axial, Coronal andsagittal.

	TR	TE	NO. OF SLICES	GAP IN mm	MATRIX	FOV
T1WI	500	9.7	20-23	1	288	230
T2WI	4000	101	20-23	1	480	230

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FLAIR	9000	105	20-23	1	240	230
DWI	3800	107	20-23	1	128	230
T2 GRE	68000	20	20-23	1	288	230

Single voxel spectroscopy; multi voxel spectroscopy was performed at TE of 135 ms, TR was at 1500 ms. In single voxel studies the voxel is placed on the lesion so that it covers the maximum area of the solid tumoral area. In multivoxel spectroscopy, the voxel was extendedtocoverperilesionalareainselectivecasesofhighgradetumors, avoiding areas of cysts or necrosis and with minimal contaminationfromthe surrounding non-tumoral tissue.
Ascomparedtoamultivoxelmagneticresonancespectroscopy,the operation is quicker and simpler in single voxel magnetic resonance spectroscopy. As compared to a multi voxel magnetic resonance spectroscopy where it is difficult to space over the total area of interest, a limited volume of interest in a single voxel magnetic resonance spectroscopy allows an admirable space. In case of a single voxel magnetic resonance spectroscopy, there is brilliant spectral quality and peak separation with high signal to noise quantification when equated to amultivoxelmagneticresonancespectroscopywhichshowslowersignal to noise and poses problems with quantification. Due to partial volume and chemical shift displacement effects from adjacent tissues, there is spectral contamination in case of a single voxel MRS. The chemical shift aliasing in a multi voxel MRS is due to the bleeding of spectra from the adjacent voxel. The multi voxel magnetic resonance spectroscopy which takes about 6-8 minutes for 2D imaging and 10-15 minutes for 3D imaging is time consuming as compared to single voxel magnetic resonance spectroscopy which consumes about 3-5 minutes pervoxel.

Study definition:
MRspectroscopyisusedasdiagnostictestfordiagnosingintraaxial brain tumors. An increase choline peak at 3.2ppm, myoinositol peakat3.6ppm, lipid peak at 0.9-1.4ppm, lactate peak at 1.3ppm and reduced NAA peak at 2.0ppm, creatinine peak at 3.0,3.9ppm was considered significant for diagnosing brain tumors. We reported brain tumor as high grade if there was increase in choline/creat ratio of more than 2.3, choline/NAA ratio of more than 1.9, reduced NAA/creatinine of less than1.5.Wereportedbraintumorsaslowgradeifcholine/creatinineratio was less than 2.3, this value was used as a threshold value in order to increase the specificity of detecting brain tumors. Astrocytoma tumors were divided as low grade and high grade by using threshold value for myoinositol/creatinineratioof0.82+/-0.25forlowgradetumorsand0.33
+/- 0.16 for high grade tumors.

Statistical analysis:
In Microsoft excel, data was entered and data sheet and analysis was done. Descriptive statistics, frequencies and proportions were calculated and tabulated. Sensitivity, specificity, negative predictive value,positivepredictivevalueanddiagnosticaccuracytotestthevalidity of MR Spectroscopy with respect to histopathological examination were calculated. Fisher exact test was the test of significance for categorical data. $p < 0.05$ was considered as statisticallysignificant.

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3. Results

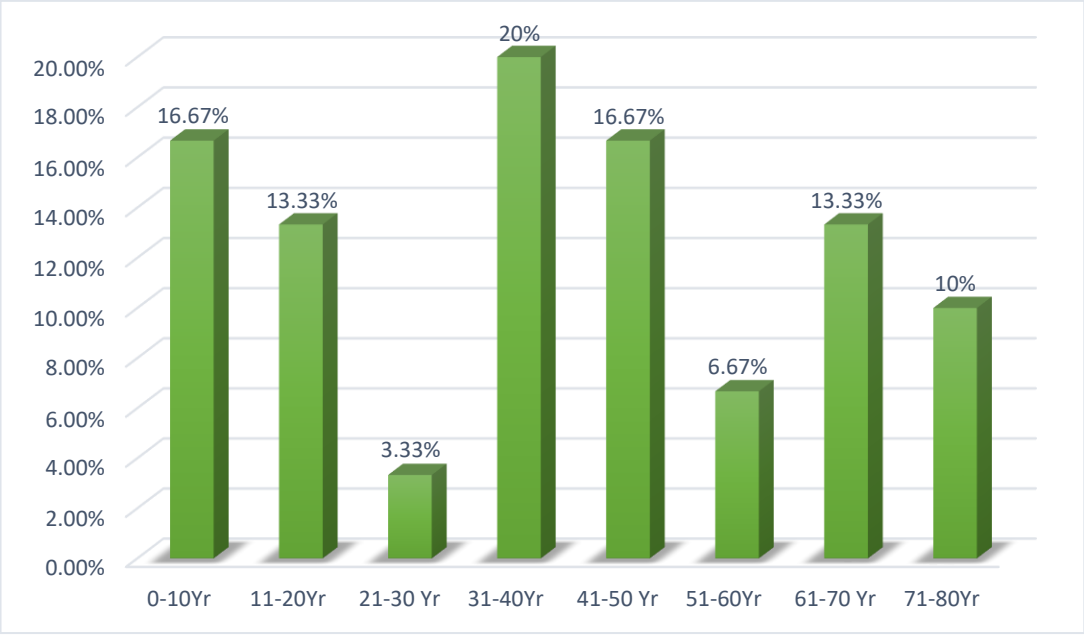
In the study, it was observed that majority of the patients with intra-axial brain tumors were between 31 to 40 years of age. They constitute 20%of totalstudysample.Theyoungestpatientwas10monthsoldandtheoldest was 78 years old female.

TABLE – 1: AGE DISTRIBUTION OF SAMPLE

AGE (years)	NO. OF CASES	PERCENTAGE
0-10	10	16.67%
11-20	8	13.33%
21-30	2	3.33%
31-40	12	20%
41-50	10	16.67%
51-60	4	6.67%
61-70	8	13.33%
71-80	6	10%
TOTAL	**60**	**100%**

Graph – 1: Bar Diagram showing Age distribution of the subjects

In the study it was observed that majority i.e. 73.33% of the patients with intraaxial brain tumors



were males. It is evident that there is male preponderance in intraaxial braintumors.

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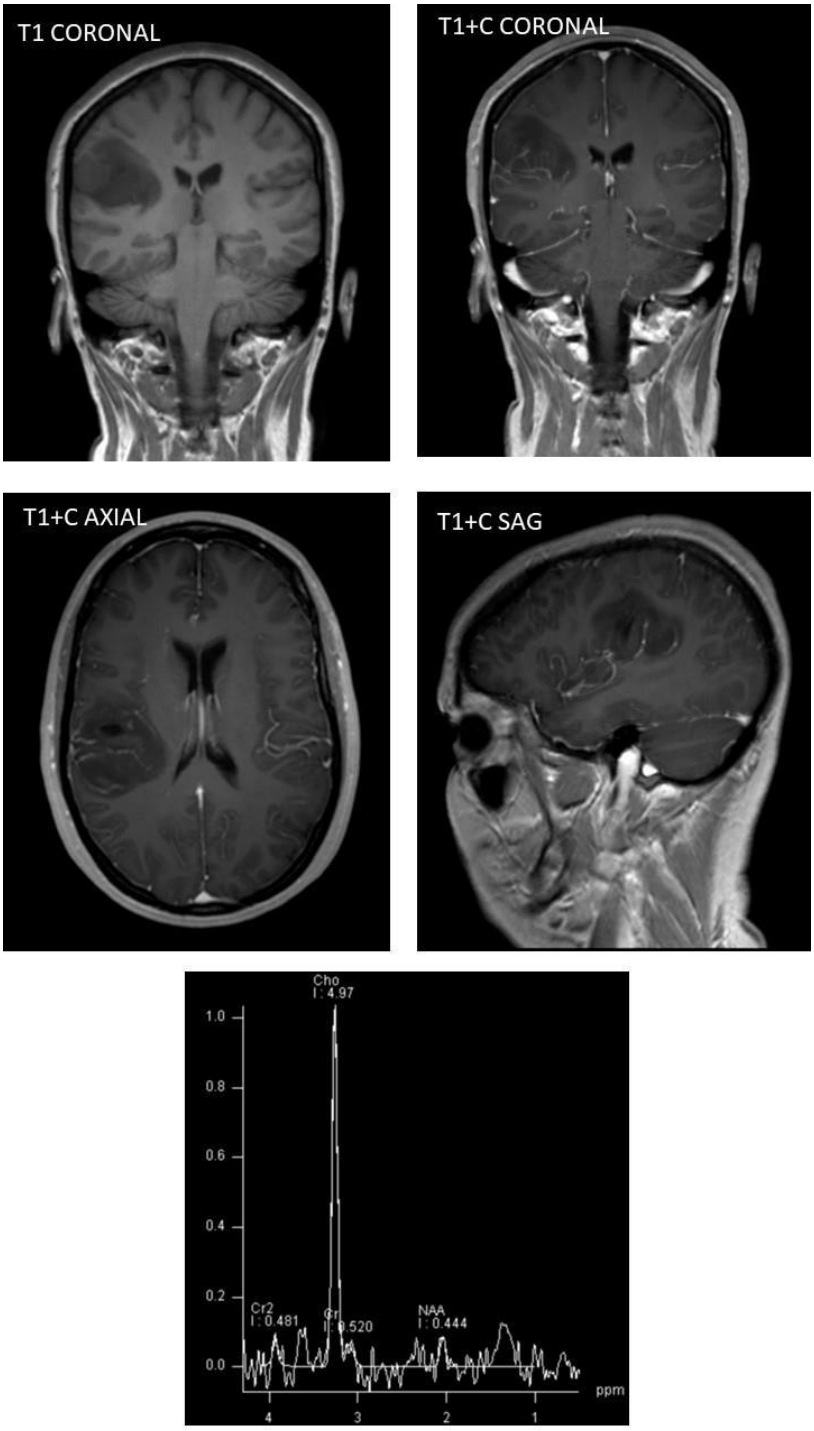

Figure 1 - Anaplastic astrocytoma.

T1axial,sagittalandcoronalshowlargeheterogeneouslyhypointenselesioninrighttemporo-parietalregion.
T2/FLAIR axial show heterogeneously hyperintense lesion with small cystic area in right temporo-parietal region with moderate perilesional edema.
DWI and ADC show no restricted diffusion in the lesion.

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T1 post-contrast axial, sagittal and coronal show few areas of enhancement within the lesion.
In this study it was observed that majority i.e. 73.33% of the patients were having intraaxial brain tumors in supratentorial location. It was observed that most common location for intraaxial brain tumor is supratentorial

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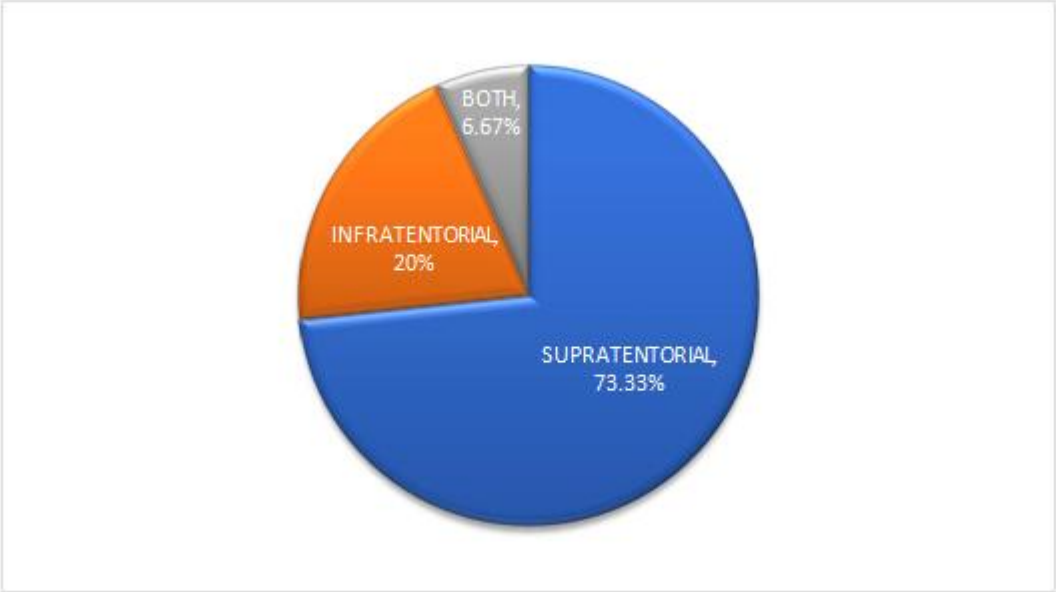
TABLE – 3 : DISTRIBUTION OF SAMPLE BASED ON LOCATION

	NO. OF CASES	**PERCENTAGE**
SUPRATENTORIAL	44	73.33%
INFRATENTORIAL	12	20%
BOTH	4	6.67%
TOTAL	**60**	**100%**

Graph-3 : Pie Diagram showing distribution of sample based on location



In this study majority of the patients i.e., 43.33% had hypointense signal on T1.

TABLE – 4 : DISTRIBUTION OF SAMPLE BASED ON SIGNAL CHARACTERISTICS ON T1W

	NO. OF CASES	**PERCENTAGE**
ISOINTENSE	12	20%

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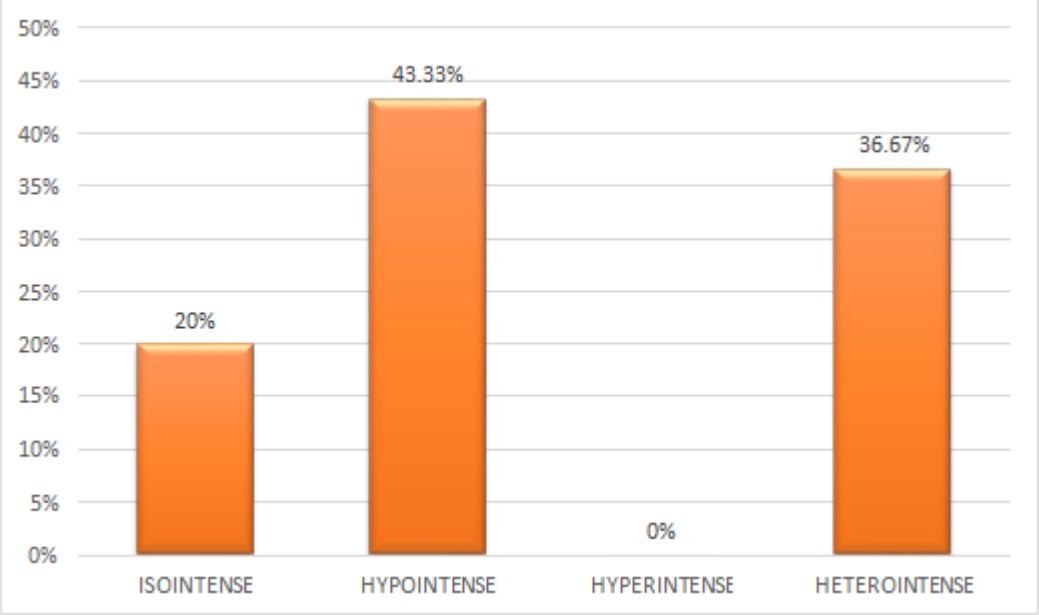
HYPOINTENSE	26	43.33%
HYPERINTENSE	-	0%
HETEROINTENSE	22	36.67%
TOTAL	**60**	**100%**

Graph-4 : Bar diagram showing distribution of sample based on signal characteristics on T1



In this study majority of the patients i.e., 60% had heterogenous signal on T2.

TABLE – 5 : DISTRIBUTION OF SAMPLE BASED ON SIGNAL CHARACTERISTICS ON T2W

	NO. OF CASES	**PERCENTAGE**
ISOINTENSE	4	6.67%
HYPOINTENSE	-	-
HYPERINTENSE	20	33.33%
HETEROINTENSE	36	60%
TOTAL	**60**	**100%**

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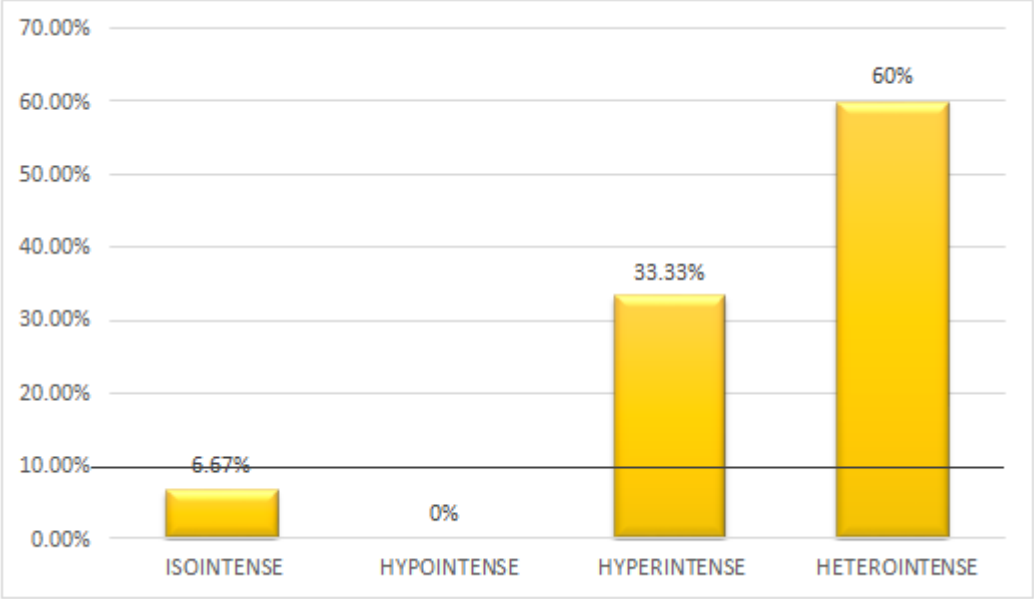
Graph-5 : Bar diagram showing distribution of sample based on signal characteristics on T2



In this study majority of brain tumors i.e., 53.33% had no blooming on gradient and 46.67% showed blooming, out of which most common cause was bleed i.e., 92.8% and the rest 7.14% was due to calcification within the tumor.

In this study it was observed that majority of tumors i.e., 80% showed perilesional edema. It is evident that most of the brain tumors present with perilesional edema..

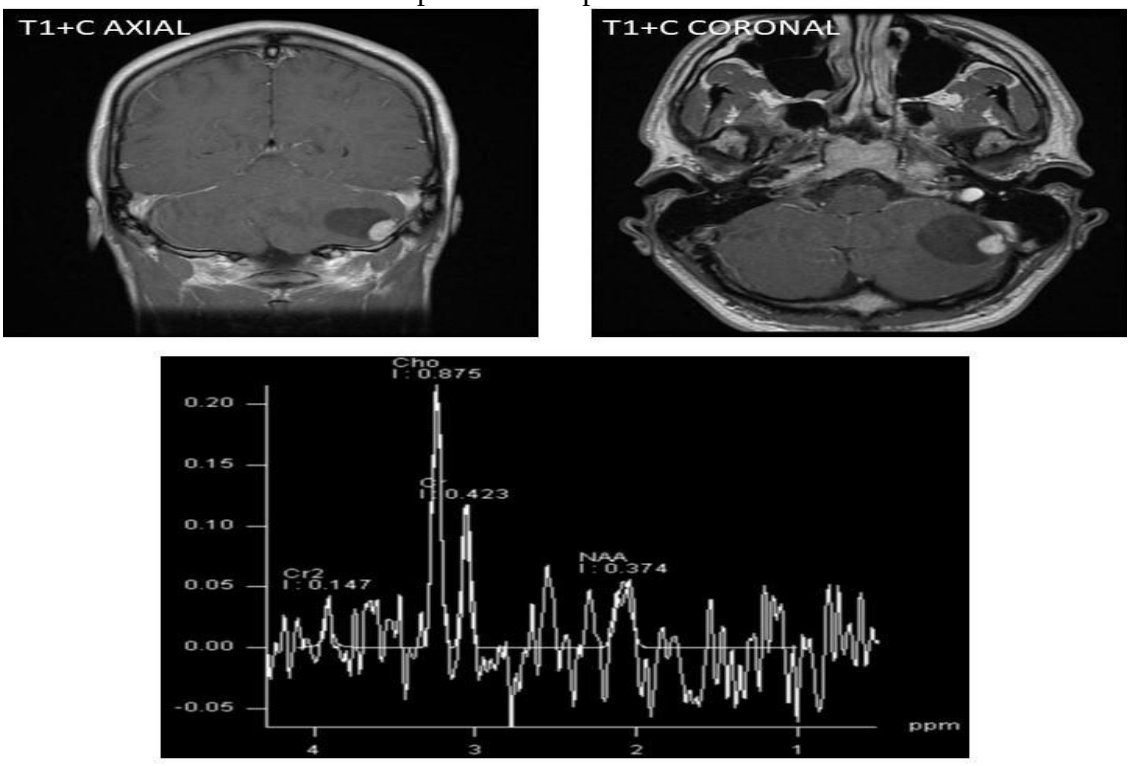


Figure 2 – Hemangioblastoma

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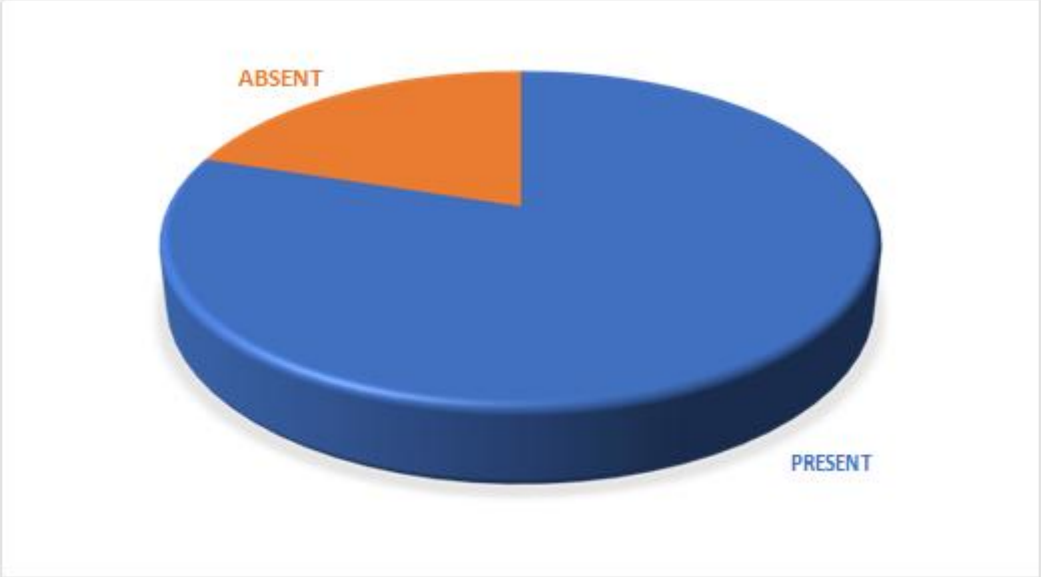
T1 axial and sagittal show hypointense cystic lesion with isointense nodule in posterior fossa. T2/FLAIR axial show hypointense cystic lesion with hypertense nodule in posterior fossa with no perilesional edema.
DWI and ADC show no restricted diffusion in the lesion.
T1 post-contrast axial and coronal show homogeneous enhancement of mural nodule. MRS shows increased Choline and reduced NAA

TABLE – 7 DISTRIBUTION OF SAMPLE BASED ON PERILESIONAL EDEMA

	NO. OF CASES	**PERCENTAGE**
PRESENT	48	80%
ABSENT	12	20%
TOTAL	**60**	**100%**

Graph-8 : Pie diagram showing distribution of sample based on perilesional edema.



In this study it was observed that majority of brain tumors i.e. 63.33% had intense post contrast enhancement. It is evident that most of brain tumors show intense enhancement on post contrast study.

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Graph-12 : Bar diagram showing distribution of sample based on MR SPECTROSCOPY findings of intraaxial brain tumors.

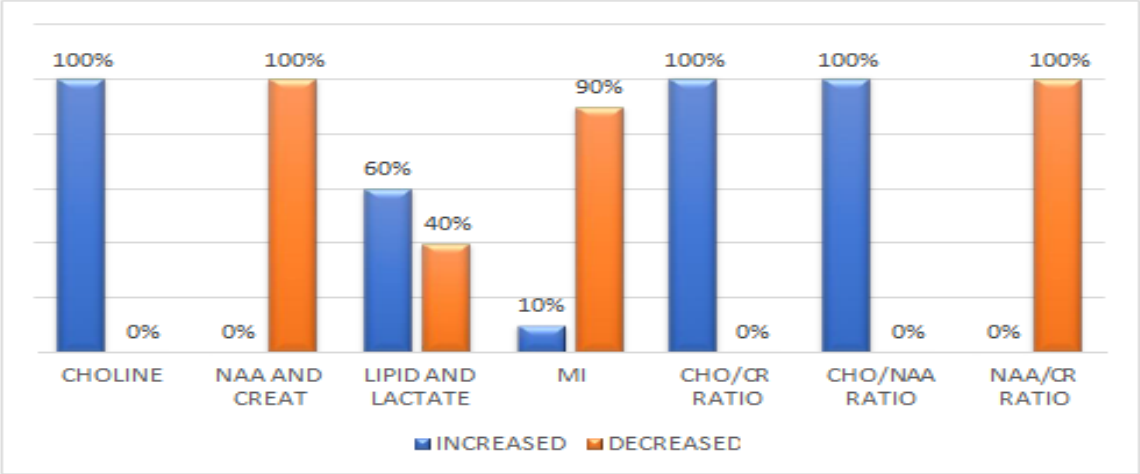

TABLE – 12 : DISTRIBUTION OF CASES ACCORDING TO PATHOLOGY

SERIAL NO.	INTRAAXIAL BRAIN TUMOR	NO. OF CASES	PERCENTAGE
1.	HIGH GRADE GLIOMA (GRADE3 AND GRADE4 GLIOMA)	28	51.85%
2.	LOW GRADE GLIOMA (GRADE1 AND GRADE2 GLIOMA)	4	7.41%
3.	OLIGODENDROGLIOMA	4	7.41%
4.	GLIOMATOSIS CEREBRI	4	7.41%
5.	EPENDYMOMA	4	7.41%
6.	MEDULLOBLASTOMA	4	7.41%
7.	METASTASIS	2	3.70%
8.	CHOROID PLEXUS PAPILLOMA	2	3.70%
9.	LYMPHOMA	2	3.70%
TOTAL		**54***	

*OUT OF 60 CASES, HISTOPATHOLOGY WAS NOT DONE IN 6 CASES.

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Graph – 13 : Distribution of cases according to pathology

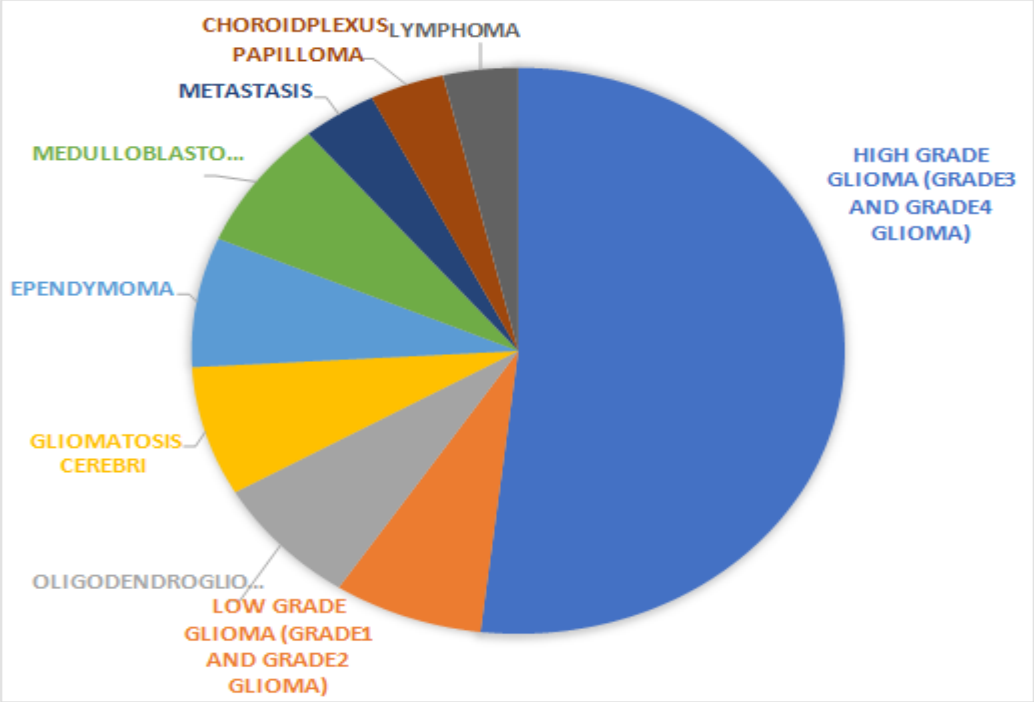

TABLE – 13 : DISTRIBUTION OF CASES BASED ON MRI DIAGNOSIS IN CORELATION WITH HISTOPATHOLOGICAL DIAGNOSIS

SL. NO.	INTRAAXIAL BRAIN TUMOR	HISTOPATHOLOGICAL DIAGNOSIS	MRI DIAGNOSIS
1.	GBM (Grade 4)	22	24
2.	High Grade Glioma (Grade 3)	4	6
3.	Low Grade Glioma (Grade 2)	6	4
4.	Oligodendroglioma	4	2
5.	GliomatosisCerebri	4	4
6.	Ependymoma	4	2
7.	Medulloblastoma	4	4
8.	Metastasis	2	2
9.	Choroid Plexus Papilloma	2	2
10.	Lymphoma	2	2
11.	Neurocytoma	-	2
	TOTAL	**54**	**54**

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Graph-14 : Intraaxial brain tumors

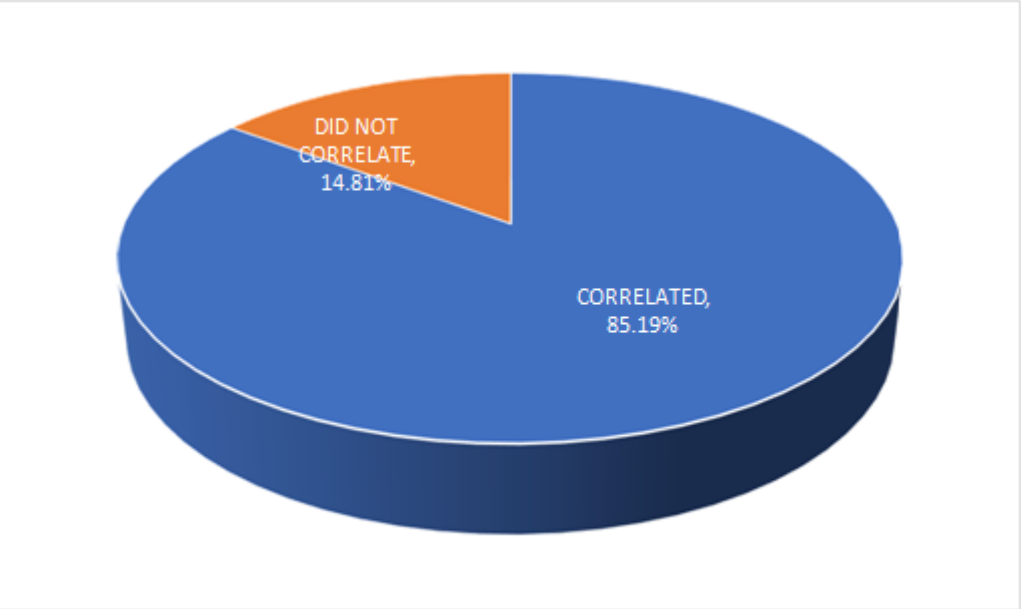

TABLE – 14 : VALIDITY OF MR SPECTROSCOPY WITH HISTOPATHOLOGY AS A DIAGNOSTIC TEST

GlioblastomaMultiforme

		Histopathology			
		GBM	**Others**	**Total**	**Fisher Exact Test**
MR Spectroscopy	GBM	20	4	24	p = 0.00000001
	Others	2	28	30	
	Total	**22**	**32**	**54**	

There is significant association between MR Spectroscopy findings and Histopathological findings for Glioblastoma Multiforme

		95% Confidence Limit
Sensitivity	90.91%	70.84% to 98.88%
Specificity	87.5%	71.01% to 96.49%
Positive Predictive Value	83.33%	66.45% to 92.66%
Negative Predictive Value	93.33%	78.77% to 98.14%
Diagnostic Accuracy	88.89%	77.37% to 95.81%

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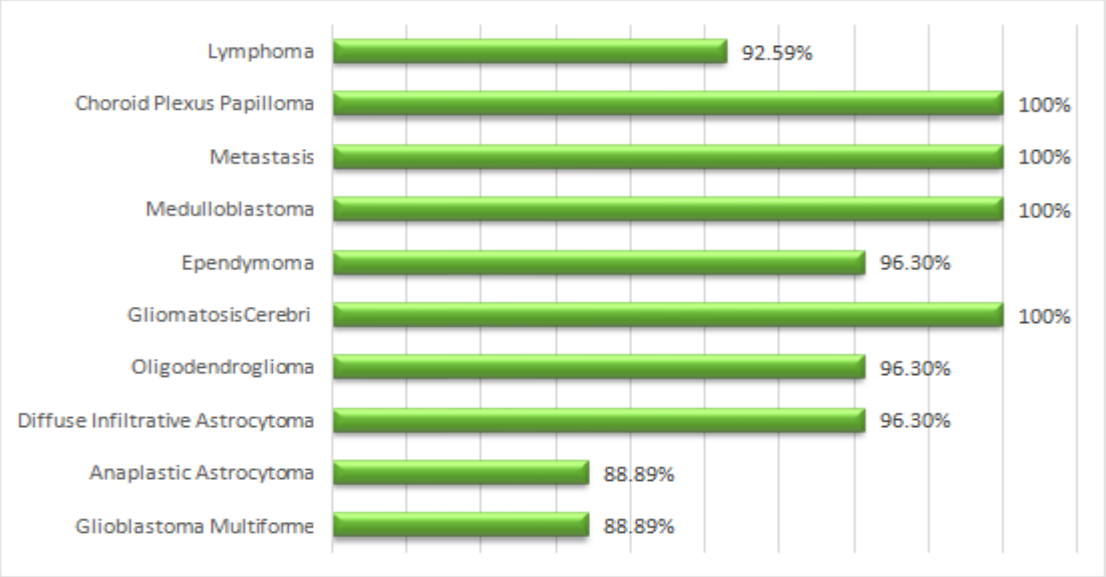
Graph-19 : Bar Diagram Showing Diagnostic Accuracy of MR Spectroscopy in diagnosing various Brain Tumors



4. Discussion

In our study, all age group patients were included. Brain neoplasms were most commonly found in 31-40 (n=12) years age group followed by 41-50 (n=10) years age group and 0-10 (n=10) years age group. (Refer Table-1, Graph-1). P A McKinney studied the incidence of brain neoplasms in all age group and found that primary brain neoplasms occur most commonly in 7thdecade. In our study, difference is due to small samplesize.[14-16]Out of 60 patients in our present study, incidence of brain neoplasms was more in males 73.33% (n=44). (Refer Table-2, Graph- 2)In our study of 60 cases, 73.33% (n=44) neoplasms were supratentorial, 20%(n=12) were infratentorial and 6.67%(n=4) were both supra and infratentorial in location. Infratentorial tumors were less common than supratentorial tumors in our study.

In our study, glioma cases were reported as low grade (diffuse infiltrative astrocytoma) or high grade astrocytoma (anaplastic astrocytoma and glioblastoma multiformae), oligodendroglioma,ependymomaand gliomatosiscerebriaccording to the MR characterization of tumors. Both conventional sequences and different parameters of MR spectroscopy was used to optimize for better results.[17,18]Glioma constituted 70% (n=42) out of the total 60 cases in our study. It was the most frequent brain neoplasm found in our study.Out of 42 gliomas cases diagnosed on Magnetic Resonance Imaging, 24 were GBM, 6 were anaplastic astrocytoma, 4 were diffuse infiltrative astrocytoma, 2 case of oligodendroglioma, 4 cases of gliomatosiscerebri and 2 case ofependymoma.[19]

In our study 40 out of 42 (95%) cases of glioma had perilesional edema. The only two case which did not show perilesional edema were ependymoma(n=2). Intense enhancement was showed by all GBM. Moderate enhancement was showed by anaplastic astrocytoma. Minimal enhancement was showed by diffuse infiltrative astrocytoma cases. [20] Intense enhancement was showed by oligodendroglioma, ependymomaand two case of gliomatosiscerebri. Mild enhancement wasshowedbytheothertwocasesofgliomatosiscerebri. Ourfindings are in agreement with study conductedby R Felix, W Schörneretal.[21]

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In our study, all anaplastic astrocytoma and glioblastoma multiformecases and 2 case of oligodendrogliomawere heterogenouslesion withnecrotic and solid component together. The 4 casesof
diffuse infiltrative astrocytoma and 2 cases of ependymoma were solid lesions without any necrotic center. In cases of gliomatosiscerebri, two case were solid and the other two were heterogenous with solid and necroticcomponent.[22] hypointense on T1W and hyperintense on T2W. Lesions were solid to solid and cystic. They showed minimal enhancement. No blooming were observed on T2 GRE sequence.Two cases did not correlate histopathologically, it was diagnosed as anaplastic astrocytoma. Howeverwe got diagnostic accuracy of 96.3% and a significant association between MRS and histopathology findings with p=0.00004743 ($p<0.05$ being significant). We got 100% sensitivity and 96% specificity. Our findings were similartostudydoneMauricioCastilloaetal.[23]Therewas increased cho/creatratio of 2.03(±0.42), increased cho/NAA ratio of 1.9(±0.34) and reduced NAA/creatpeak at 0.9(±0.33). mI/creatratio was lower at 0.80(±0.25). Both cases showed no choline MRSI all tumors showed increased choline peak, reduced NAA, reduced mIpeak at 3.6 ppm and reduced creat. There was increased cho/creatratio of 6.5(±0.55), increased cho/NAA ratio of 3.5(±0.22) and reduced NAA/creatpeak at 0.8(±0.33). mI/creatratio was lower at 0.15(±0.15). All the cases showed increased choline peak with raised cho/creatratio in perilesional edema probably due to tumoralinfiltration.[24-27]
In our study we evaluated four patients witholigodendroglioma, two of which were misdiagnosed as GBM on MRI. All cases were histopathologicallyproven as anaplastic oligodendroglioma. All the tumors were found in adults in 2ndand 4thdecade. [28]
On conventional MR sequences, lesion appeared heterogeneous to hypointense mass on T1W and heterogeneous to hyperintense on T2W. Two out of four cases showed ill-defined margins, having necrotic and solid component together. Cortical bone thinning was noted in all the cases. Foci of blooming were observed on T2 GRE sequence due to calcification.
Our study has certain limitations. First being, Perfusion MRI was not done, it may have been useful in preoperative assessment of tumor grade. [28] Second being misclassification of oligodendrogliomawith anaplastic astrocytoma, ependymomawith neurocytomaand misgradingof anaplasticastrocytoma with diffuse infiltrative astrocytoma. This can be because of faulty allocation of volume of interest due to tumor heterogeneity and small sample study in the limitedtime.

5. Conclusions

On the basis of MRS alone, accurate grading of gliomas may be difficult. Combining MRS withconventional andother advancedMR imaging techniques, grading becomes moreprecise.Some features of tumors on conventional MRI (e.g. contrast enhancement, surrounding edema, signal heterogeneity, necrosis, hemorrhage and midline crossing) suggest a high grade. MRS is complementary and helpful for glioma grading. High grade gliomas demonstrate marked elevation o f Cho, decreased NAA and presence of Lactate and Lipid. Myoinositol is raised in low grade gliomas and reduced with increasing grades of tumors.
Our study also demonstrates that spectroscopic MR measurements in the region surrounding the tumor can be used to demonstrate differences in solitary metastases and high-grade gliomas and also peritumoralinfiltrative nature of certain intraaxialbrain tumor.
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Ethical approval: The study was approved by the Institutional Ethics Committee

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Conflict of interest
The authors declare no conflict of interest.

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