International Journal Dental and Medical Sciences Research
Volume 4, Issue 4, July-Aug 2022 pp 275-290 www.ijdmsrjournal.com ISSN: 2582-6018

Magnetic Resonance Spectroscopyand Diffusion Weighted Imaging In Suspicious Intracranial Space Occupying Lesions And Its Association With Histopathological Findings.

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Submitted: 15-07-2022 Accepted: 27-07-2022

STRUCTURED ABSTRACT
Objectives -
Primary Objective
To study the diagnostic accuracy of MRS and DWI in diagnosing brain tumours with histopathological co-relation.
Secondary Objective
1)To evaluate the role of MRS, DWI in differentiating between benign and malignant lesions.
2)To evaluate the role of MRS, DWI in differentiating between radiation necrosis and tumor recurrence.
3) To evaluate the role of MRS and DWI as diagnostic tool for diagnosing various intracranial lesions.
Material and methods:
Conventional MRI, MRS, DWI of 51 patients with brain tumors was done using 1.5T Siemens machine using standard protocols. It was correlated with histopathology findings to determine the accuracy of MRS, DWI in diagnosing brain tumors, their grade and analysis was done using PASW 18 software.
Results and discussion
The tumors showed decreased NAA and Cr contents and a high Chosignal. The Lac-Lip signal was high in abscess. Reports that Cho/Cr ratio and cho/NAA ratio increases with glioma's grade whereas NAA/Cr decreases wereconfirmed with histopathological correlation.
Conclusions:
1) MRS and DWI plays key role and has a significant added value to conventional MRI in diagnosing and grading various brain tumors.
2) MRS and DWI has high diagnostic accuracy in differentiating between benign and malignant brain tumors, radiation necrosis and tumor recurrence, plays key role in follow up of patients after treatment.

Key words: Magnetic Resonance Spectroscopy, Diffusion Weighted Imaging,brain tumors, radiation necrosis, choline, creatine, N-acetylcysteine.

I. INTRODUCTION

Intracranial space occupying lesions (ICSOL) are a significant health problem and present several imaging challenges.The annual incidence of intracranial tumors according to published western data ranges from 10 to 17 per 100,000 persons.[1]ICSOL is defined as a mass lesion in the cranial cavity with diverse etiology and includes primary neoplasm(benign or malignant), metastatis, lymphoma, abscesses, tuberculoma,encephalitis, arteriovenous malformation, haematoma, inflammatory lesions, and parasitic lesions.[1]ICSOL can present with seizures, focal neurological deficits, raised intracranial pressure (ICP) or endocrine dysfunction or can be incidental findings.ICP can present as headache, vomiting, impaired vision and changes in consciousness.[2]Brain and other nervous system cancer is the 10th leading cause of death for men and women. It is estimated that 18,020 adults (10,190 men and 7,830 women) die from primary cancerous brain and CNS tumors per year. The 5-year survival rate for people with a cancerous brain or CNS tumor is almost 36%. The 10-year survival rate is almost 31%. Survival rates decrease with age.[3]Establishing an accurate neoplastic etiology is essential in timely diagnosis and neurosurgical intervention.

Magnetic Resonance(MR) imaging plays an important role in diagnosing neoplastic nature of these lesions, anatomic localization, and to differentiate them from other ICSOL. Conventional MR imaging provides anatomical information and advanced MR imaging modalities can provide physiological and biochemical information about these tumours.[4]The current advanced techniques include perfusion imaging, diffusion-weighted imaging (including diffusion tensor imaging), MR spectroscopy, blood oxygen

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level–dependent (BOLD) imaging.[1]MR imaging has emerged as the imaging modality most frequently used to evaluate intracranial tumours with an ever expanding multifaceted role. The role of MR imaging in the workup of tumours can be broadly divided into tumour diagnosis and classification, treatment planning, identification of active tumour and tumourinvasion delineation of the target volume for radiation therapy, monitoring of therapy and post-therapy evaluation.

Magnetic resonance spectroscopy allows the non-invasive measurement of selected biological compounds in vivo. Proton spectroscopy has been recognized as a safe and non-invasive diagnostic method. When coupled with conventional magnetic resonance imaging techniques, proton spectroscopy allows for the correlation of anatomical and physiological changes in the metabolic and biochemical processes occurring within previously determined volumes in the brain. Magnetic resonance spectroscopy (MRS) provides information about the possible extent and nature of changes on a routine MRI scan by analyzing the presence of tissue metabolites such as NAA, creative, choline,lactate etc.[4]

Widespread usage of faster MRS applications with higher signal to-noise ratio (SNR) and spatial resolution allows in better detection of functional metabolic changes, this provides more data to understand the exact nature of the tumour, morphological and physiological changes occurring in the surrounding brain parenchyma. Longitudinal studies have demonstrated that MR spectroscopy(MRS) is useful to monitor disease progression and treatment effects. MRS done at frequent intervals of time during the course of treatment is helpful to assess the extent of response of disease to treatment. This is useful to adjust the treatment regimen, to add new treatment modality or to change the course of treatment. MR spectroscopy also has a prognostic implication which is especially applied in evaluation of infarct area, infiltrative nature of neoplastic disease and extent of involvement of demyelinating disease.[4]

Advanced MR imaging has a wide role in tumor management. For example- identification of exact extension of tumor and its precise surgical excision with margins free of neoplastic tissue.They play an important role in providing information on various parameters of the tumor like infiltrative nature, biochemical component, grade of differentiation which is vital in choosing the treatment regimen, follow up and predicting the survival rate and prognosis. They play vital role in differentiating between radiation necrosis and tumor recurrence. [5]

Diffusion weighted imaging (DWI) is a standard tool in in oncologic imaging. Computed DWI refers to synthesising of arbitrary b value DW images from a set of measured b value images by voxel wise fitting. Computed DW imaging is advantageous as it generates DW images with a higher diffusion effect than that can be achievable by using conventional MR imaging.[6]

DWI has many applications in oncologic imaging like in tumour detection and characterization, assessment of prediction and response to treatment. DWI is analysed along with Apparent Diffusion Coefficient (ADC) mapping and aids in diagnosing malignancy, early identification of ischaemic stroke,differentiation of stroke from stroke mimics, arachnoid cyst from epidermoid cyst, abscess from necrotic tumours.[7]

II. AIMS AND OBJECTIVES

Primary Objective

To study the diagnostic accuracy of MRS and DWI in diagnosing brain tumours with histopathological co-relation.

Secondary Objective

1) To evaluate the role of MRS, DWI in differentiating between benign and malignant lesions.
2) To evaluate the role of MRS, DWI in differentiating between radiation necrosis and tumor recurrence.

III. METHODOLGY

Source of data

The main source ofdata for the study are patients from Government ThirumalaDevaswomMedical College hospital, Vandanam, Alappuzha.

Methods of collection of data

All patients referred to the department of Radiodiagnosiswith suspicion of brain tumors in a period of one and half years from January 2020 to December 2021 wereconsidered for the study. Conventional MR findings and MRS, DWI features were studied and correlated with HPR reports. Statistical analysis was done to identify the accuracy of MRS, DWI in diagnosing and grading brain tumors.

STUDY DESIGN–

Cross sectional study – Test tool evaluation.

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STUDY PERIOD-
For duration of one and halfyears from January 2020 to December 2021

STUDY SETTING-
Department of Radiodiagnosis, Government T. D. Medical College Alappuzha, Kerala.

STUDY POPULATION-
The hospital patient population is usually from district of Alappuzha.All patients referred to the department of Radio diagnosis from other departments particularly neuromedicine,neurosurgery and paediatric surgery department with suspected intracranial space occupying lesionin a period of one and halfyears from Jan 2020 to December 2021 were consideredfor this study.All the patients with clinical suspicion, CT imaging features suggestive of ICSOL, previous similar history with suspicion of recurrence, post chemo-radiation therapy patients wereconsidered in the study.

INCLUSION CRITERIA
The study includes
-All patients referred to the department of Radiodiagnosis with suspicion of intracranial space occupying lesion.
-All the biopsy proven cases of brain tumours.
- Patients of all age group and sex are included in the study.

EXCLUSION CRITERIA
The study will exclude
- Patient having history of claustrophobia.
- Patient having history of metallic implants insertion, cardiac pacemakers
metallic foreign body in situor any contraindication to undergo MRI.
- Patient clinically unstable.
- All those patients who are not willing to participate in the study.

SAMPLE SIZE - The sample size required for the study is calculated by using the formula**n= 4PQ/d2** where P is sensitivity of the study obtained by considering previous similar studies, Q is 100- P, d is the precision usually 15-20% of P.
Considering P-85%, Q= 100-85=15 and d-20% of P, P= 17. n = 4×85×15/17n= 18. **This study requires atleast 18 histopathologically proven cases of brain tumours.** As many patient with suspicious intracranial space occupying lesions are included in the study till eighteen histopathologically proven case of brain tumour is obtained. If available more samples will be included over the entire thesis period.

EQUIPMENT AND TECHNIQUE USED : The MRI scan was performed MR SIEMENS. It possesses a Ultra-compact, superconducting, active shielded superconducting magnet with a magnetic field strength of 1.5 T, sense coils are used for acquisition of images.The contrast material used in the study is gadolinium-DTPA (Magnevist) at a dose of 0.2 ml/kg body weight.The standard head coil was used as the receiver coil. The cMRI examination included the following: precontrast series that included axial, sagittal, andcoronal T1 WI [550/15 ms (TR/TE)] spin echo, axialand coronal T2WI (3000/120 ms) turbo spin-echo,and fast fluid attenuation inversion recovery (FLAIR) [8000/140/2800 ms (TR/TE/TI)] was obtained usingsections of 3 mm thickness. Postcontrast series includedaxial, coronal, and sagittal T1 WI spin echo sequences.We evaluated the cMRI with regard to lesion signalcharacteristics and the presence of hemorrhage, necrosis, peritumoral edema, mass effect, and contrast enhancement.

Diffusion imaging with apparent diffusion coefficient calculation of brain lesions DWI was performed for all patients in the axial planeusing single shot echo-planar spin-echo sequence EPI[3.400/100 ms (TR/TE)], matrix 192 × 192, slicethickness 5 mm, gap 1.5 mm with a duration of 120s, and b = 0, b = 500, and b = 1000 applied in the X, Y, andZ directions. [46]Postprocessing of ADC maps was doneusing the standard software supplied on the machine console to obtain the ADC value and map; the lowestADC values were measured usingregion of interest in the solid portion of the lesion, while preferably avoidingcystic and necrotic areas. Standard mean ADC valueswere calculated automatically and expressed in $10^{-3}mm^2/s$. [47] **A cutoff value of$0.9\times10^{-3}mm^2/s$ was used todifferentiate between high garde lesion and low grade lesion.**
After the conventional MRI volume of interest from the lesion (VOI) was selected from T1post-contrast images, VOI was selected from the solid part of lesion with edges of the voxelwell within the mass and in most of the cases perilesional edema was included within theVOI. VOI was carefully selected so that it will not include areas of hemorrhage or calcificationand unintended areas like ventricles, calvarium, and so on. In our institution,we used Multivoxel MR spectroscopy technique (chemical shift method) at intermediate TE of 135 ms.

A typical VOI consisted of an 8 × 8 cm region placed within a 16 × 16 cm field of view on

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a 1.5-cm transverse section. A 16 × 16 phase-encoding matrix was used to obtain 8 × 8 arrays of spectra in the VOI, with an in-plane resolution of 1 × 1 cm and a voxel size of 1 × 1 × 1.5 cm3.[39]The time taken to acquire spectra was around 8-10 min.The metabolite peaks were assigned as follows: Cho-3.22 ppm; Cr-3.02 ppm; NAA-2.02ppm; lactate was identified at 1.33 ppm by its characteristic doublet and inversion at intermediate TE. [57] Lipid peak was demonstrated at 0.9–1.3 ppm without inversion at intermediateTE. Metabolite ratios were obtained for Cho/Cr, Cho/NAA, NAA/Cr, and lactate/Cr. MaximalCho/Cr, Cho/NAA and lactate/Cr and minimum NAA/Cr ratios were obtained from spectral maps. Lactate/Cr was used instead of lipid-lactate/Cr used by other studies in literaturebecause lipid peak was not consistently seen in most of the cases at intermediate TE. [41]

Final diagnosis was reached either by surgical findingsand histopathological examination, bypost-treatment radiological and clinical follow-up, or by a consensus of clinical and imaging modalities.

Patients with MR features of malignant brain tumors are treated surgically or chemoradiation. Operated cases are sent to department of pathology for histopathological examination. The resected gross specimen of brain tumor is stored in 10% formalin solution container and its histological features are studied after proper staining and immunochemistry techniques. HPR is considered gold standard in confirming diagnosis and type of brain tumors

Picture of our MRI machine Siemens 1.5T

SEQUENCES:

Conventional spin echo sequences, axial T1, T2, FLAIR, Coronal T2;Sagittal T1; Post contrast T1 FFE axial, coronal and sagittal; DWI; T2 FFE;SV short TE 35ms Single voxel spectroscopy; multi voxel intermediate TE 135ms spectroscopy was performed. In single voxel studies the voxel is placed on the lesion so that itcovers the maximum area of the solid tumoral area. In multivoxel spectroscopy,the voxel was extended to cover perilesional area in selective cases of high gradetumors, avoiding areas of cysts or necrosis and with minimal contamination from thesurrounding non-tumoral tissue. Volume of interest size ranged between 1.5X1.5X1.5cm3 (3.4ml) and 2X2X2 cm3 (8ml). We used PRESS and T1 FFE post contrastsequence as localization sequence with 5 mm thickness. Spectroscopy wasavoided in small lesions close to the bone and sinuses. GadobenateDimeglumine contrast was used with dosage being 0.1 mmol/kg bodyweight.

IV. STATISTICAL ANALYSIS:

Data wasentered in Microsoft Excel data sheet and analysis was done by usingPASW statistics 18 software. Descriptive statistics, frequencies and proportions werecalculated and tabulated. Continuous variables were expressed as mean (SD) and categorical variables as frequency counts and proportions. PASW softwarewas used to calculate sensitivity,specificity, negative predictive value, positive predictive value and diagnosticaccuracy to test the validity of MR Spectroscopy, DWI with respect to histopathologicalexamination. An Area under Receiver Operator Characteristic (AUROC) curve was used to determine the discriminative ability of MR Spectroscopy. Point estimates and 95% confidence intervals around point estimates were determined for the measures of diagnostic effectiveness. A Fisher's exact test was used to the test of significance for categorical data. $p < 0.05$ was considered as statistically significant.

The diagnostic performance of the calculated ADC values in glioma grading wasevaluated using receiver operating characteristic curve analysis. Comparison between groups was made using the Student t-test for independent samples for quantitative data when normally distributed and the Mann–Whitney U-test for independent samples when not normally distributed. The c2-test was computed or 2 × 2 tables when the row and column variables were independent, without indicating the strength or direction of the relationship.

Example case - Tectal Plate glioma

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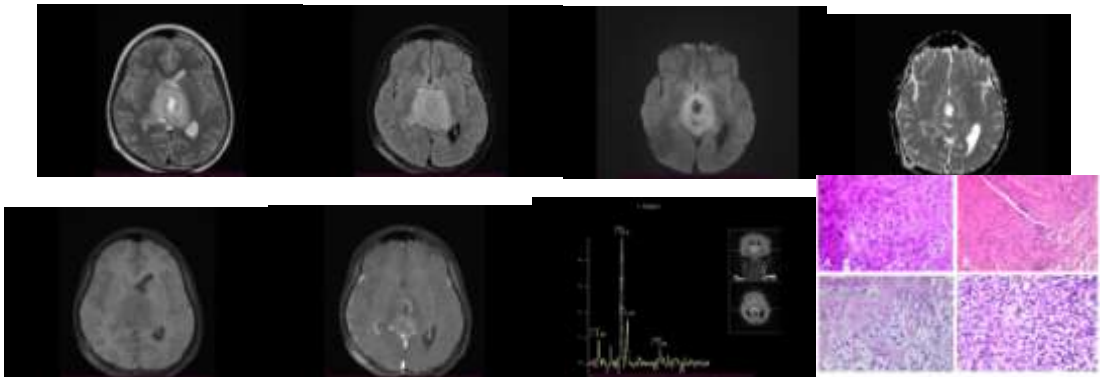
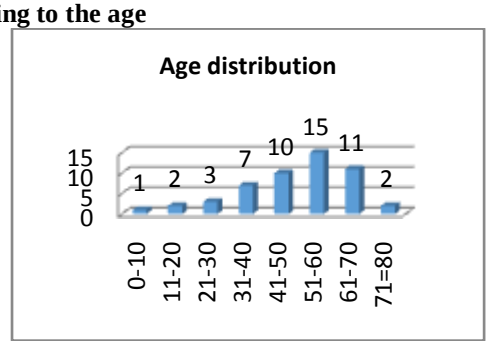


- T2WI shows an ill defined hyperintense lesion involving bilateral thalami and tectal plate with cystic component.
- It appears hyperintense on FLAIR images, isointense on T1WI.
- There are areas of mild diffusion restriction with ADC values are not very low.
- Following contrast administration there is mild and heterogenous postcontrast enhancement.
- MRS at intermediate TE- 135 shows significantly elevated choline and significantly reduced NAA levels with chol/ NAA ratio – 8.1, Chol/cr- 3.2, NAA/cr – 0.4.
- Biopsy of Tectal glioma: A and B: Due to the small amount of tumor sample, the pathology could not confirm the type of tumor, and the patients were diagnosed with gliosis. The tumor cells are diffusely and strongly positive for GFAP and Olig2. Ki67 labeling is minimal. C: Typical morphologic features of pilocytic astrocytoma: Rosenthal fibers, sclerotic vessels, and an alternating loose and more compact architecture. The tumor cells are diffusely and strongly positive for GFAP and Olig2. Ki67 labeling is minimal. D: The pathology revealed anaplastic oligodendroglioma (WHO grade III). Tumor cells are extremely abundant, with a diverse morphology, increased nuclear and cytoplasmic proportions, and common mitotic signs. Tumor vascular endothelial hyperplasia is obvious, and there is tumor necrosis. The tumor cells are diffusely and strongly positive for GFAP and Olig2. Ki67 labeling is 40%.

V. RESULTS AND ANALYSIS

Distribution of samples according to the age



In this study it was observed that ICSOL are common in age group of 51-60 years followed by 61-70years and 41-50 years.

Distribution of sample according to sex

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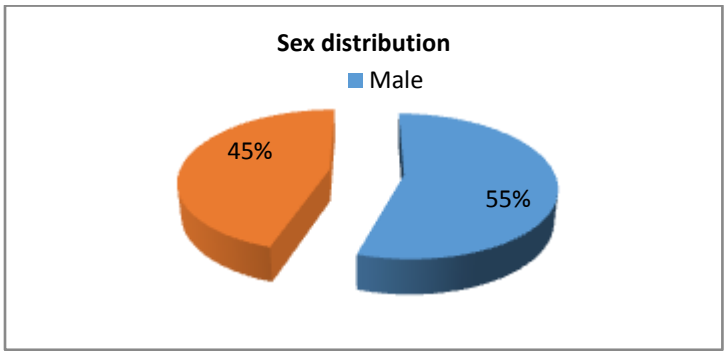
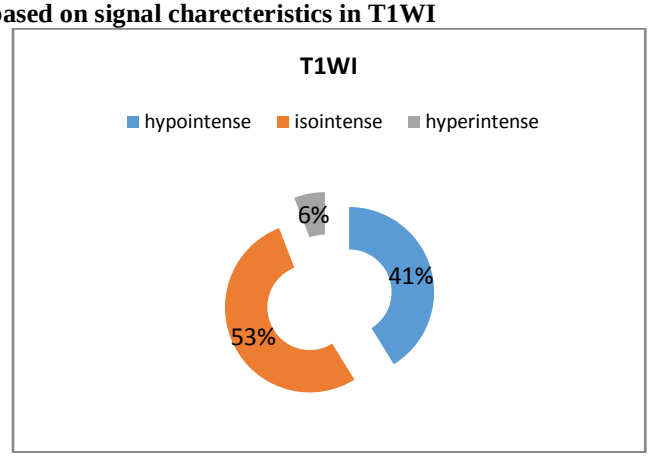


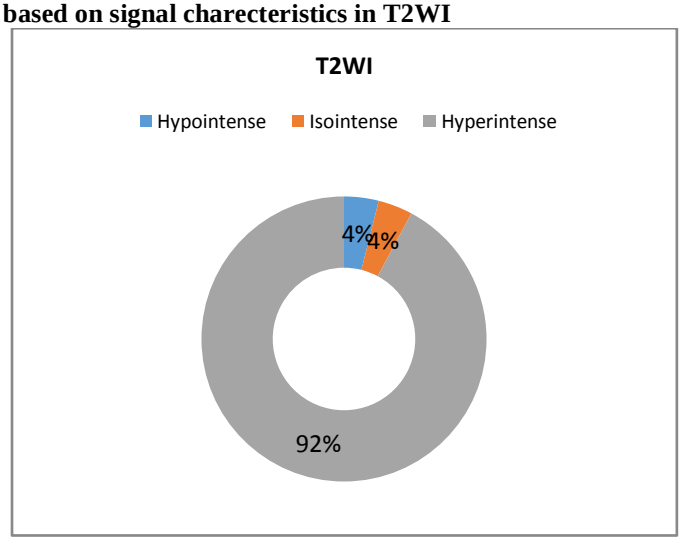
In this study it was observed that ICSOL are common in males – 55% than compared to females – 45%

Distribution of sample based on signal charecteristics in T1WI



In this study it was observed that majority of the lesions appear hypointense and isointense on T1WI.

Distribution of sample based on signal charecteristics in T2WI



In this study it was observed that 92% of the lesions appear hyperintense on T2WI and the rest appears isontense (4%) and hypointense (4%) on T2WI.

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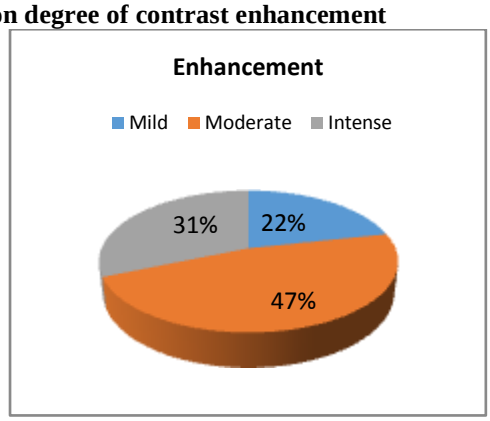
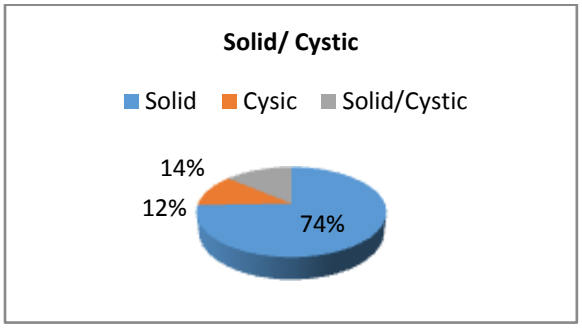
Distribution of samples based on degree of contrast enhancement



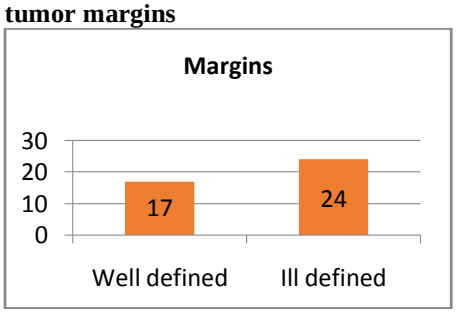
In this study it was observed that 47% of the lesions shows moderate enhancement , 31% shows intense enhancement , 22% shows mild patchy enhancement

Distribution of samples based on solid and cystic component of brain tumors



In this study it was observed that 74% of the lesions appear solid, 12% shows cystic components, 14% shows solid and cystic appearance.

Distribution of samples based on tumor margins



In this study it was observed that 33.3% of lesions are well defined and the rest majority are ill defined lesions.

Distribution of samples based on MR- Spectroscopy findings

Choline	No of cases	Percentage
Increased	48	94.1 %
Decreased/ Normal	3	5.9 %
Total cases	51	100 %

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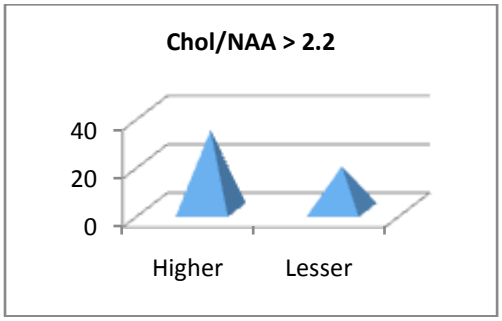
NAA	No of cases	Percentage
Normal	2	3.9 %
Decreased	49	96.0 %
Total	51	100 %

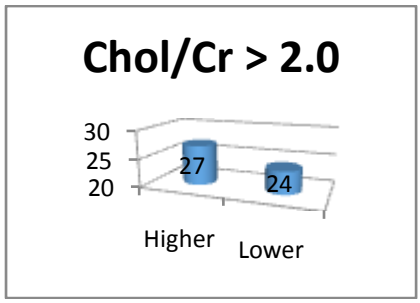
Creatinine	No of cases	Percentage
Normal	7	13.7 %
Decreased	44	86.2 %
Total cases	51	100 %

Chol/ NAA	No of cases	Percentage
Lower	18	35.2 %
Higher	33	64.7 %
Total	51	100 %



In this study it was observed that 33 lesions (64.7%) lesions showedchol/NAA >2.2 and hence characterised as high grade lesions and the rest 18 cases (35.3%) as low grade lesions.

Chol/Cr	No of case	Percentage
Higher	15	29.4 %
Lower	36	70.6 %
Total	51	100 %



In this study it was observed that 27 cases (52.9%) shows Chol/Cr >2.0 and characterised as high grade lesions and rest 24 cases (27.1%) shows lower value and hence as low grade lesions.

NAA/Cr	No of cases	Percentage
Higher	20	39.3 %
Lesser	31	60.7 %
Total	51	100 %

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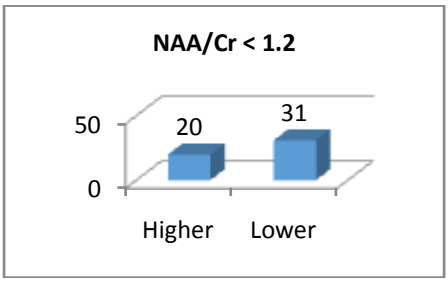
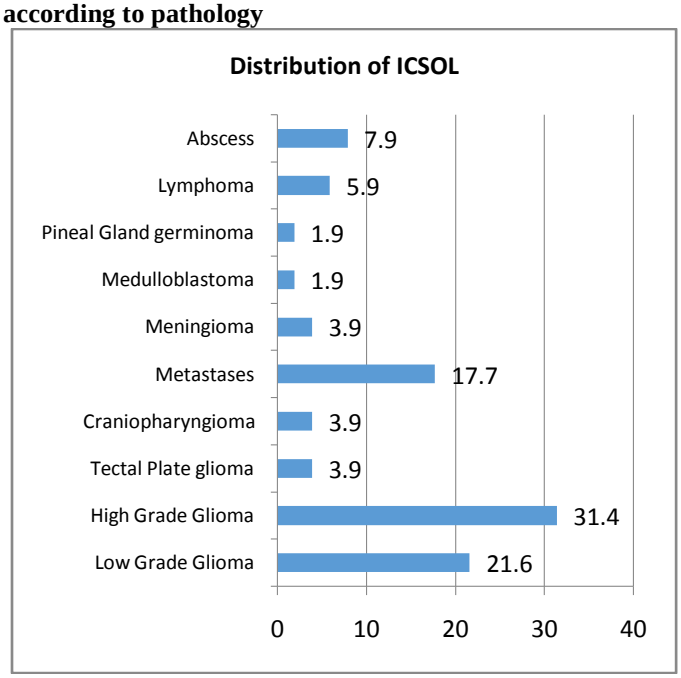


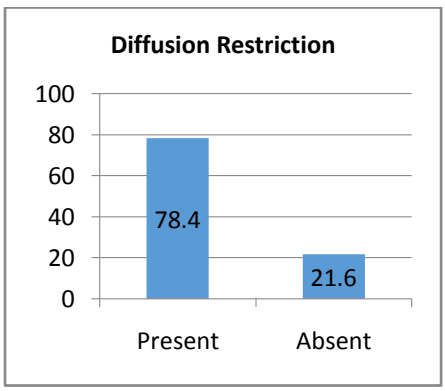
In this study it was observed that 31 cases (60.7%) shows reduced NAA/Cr <1.2 and hence as high grade lesions and rest of the 20 cases (39.3%) as low grade lesions.

Distribution of sample according to pathology



In this study it was observed that majority of the ICSOL were glioma (56.9%), followed by metastasis, abscess.

Distribution of sample based on diffusion restriction



In this study it was observed that diffusion restriction is seen in 78.4% of the lesions.

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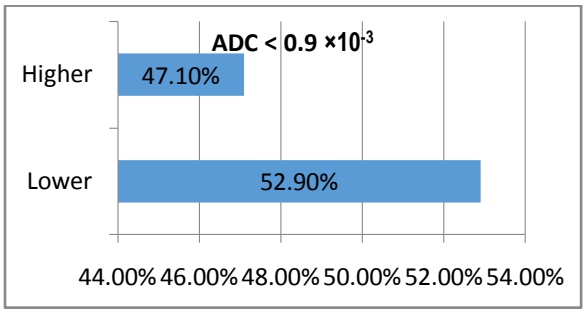
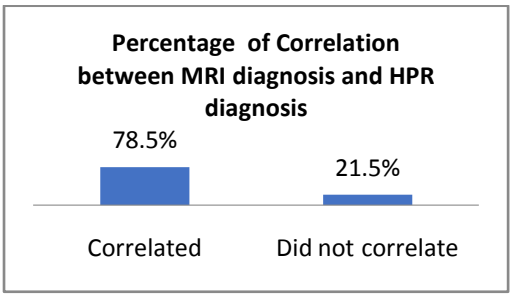


Distribution of samples based on ADC values

In this study it was observed that out of 78.% of the lesions which shows diffusion restriction 52.9% shows ADC values < 0.9× 10^{-3} mm^2/s and hence a high grade lesions.

Distribution of cases based on MRI diagnosis in correlation with histopathological diagnosis

Sl No.	ICSOL	MRI diagnosis	HPR diagnosis
1	Low grade Glioma	15	13
2	High Grade Glioma	8	6
3	GBM	12	11
4	Metastases	5	7
5	Lymphoma	3	3
6	Craniopharyngioma	2	2
7	Diffuse Midline glioma	1	2
8	Abscess	2	3
9	Meningioma	2	2
10	Schwannoma	1	0
11	Pineal Parenchymal tumor	2	1
12	Medulloblastoma	1	1



In this study it was observed that 78.5% of the cases shows correlation between MRI diagnosis and histopathological diagnosis.

Bar Diagram showing sensitivity of MR in diagnosing ICSOL

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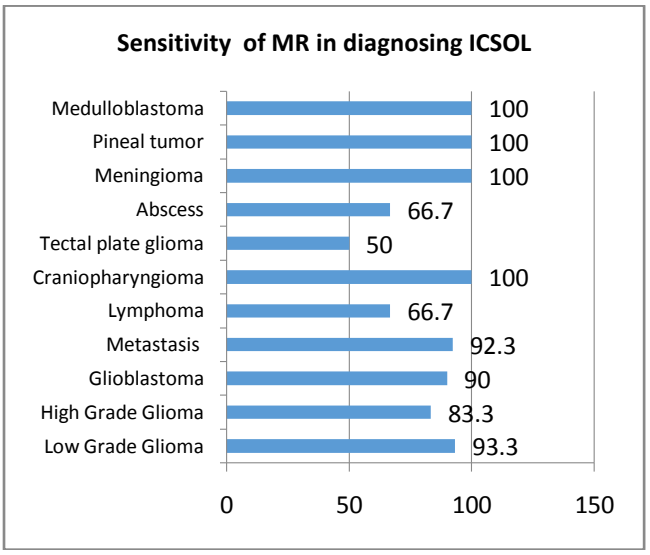
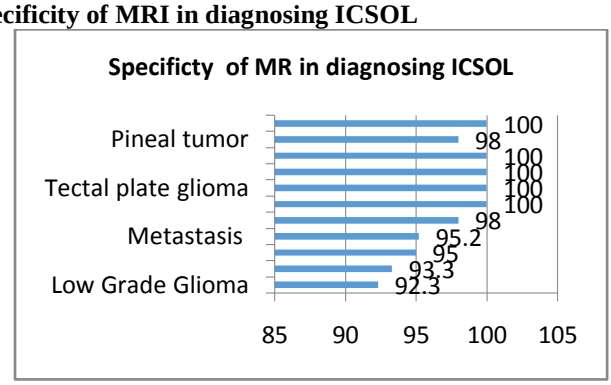


In this study it was observed that sensitivity of MRI in diagnosing various ICSOL is high except in few conditions like abscess, midline glioma. This may be because of small sample size.

Bar Diagram showing specificity of MRI in diagnosing ICSOL



In this study it was observed that specificity of MRI in diagnosing various ICSOL is high with comparatively on lower end for gliomas.

Bar Diagram showing diagnostic accuracy of MR in diagnosing ICSOL

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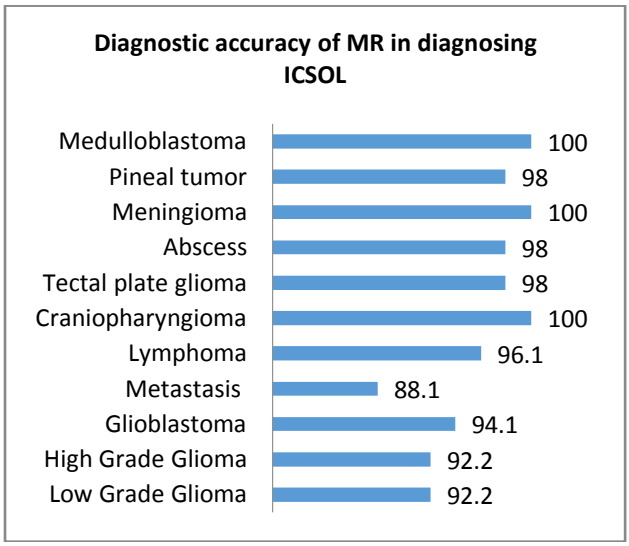

In this study it was observed that accuracy of MRI in diagnosing various ICSOL is high and for most of them it is > 90%

VI. DISCUSSION

Age distribution-Patients from all age group were included in our study. Brain neoplasmswere most commonly found in 51-60(n-15) years age group. The second mostcommon age group was 61-70 (n=11) and 41-50 (n=10) years age group.

Sex distribution Out of 51 patients in our present study, incidence of brain neoplasmswas more in males 55% (n=28).

Gliomas :

In our study, glioma cases were reported as low grade (diffuseinfiltrative astrocytoma) or high grade astrocytoma (anaplastic astrocytoma andglioblastoma multiforma), oligodendroglioma, ependymoma and gliomatosiscerebri according to the MR characterization of tumors. Glioma constituted 63.6 % (n=32) out of the total 51 cases inour study, and was the most common brain neoplasm found in our study. Out of28 cases of gliomas diagnosed on MRI, 11 were GBM, 6 were anaplastic astrocytoma, 13 were diffuse astrocytoma, 2 cases of Diffuse Midline glioma.In our study 30 out of 32 (93.75%) cases of glioma had perilesional edema.Two case of low grade gliomas did not show edema. All GBM showed intense enhancement, anaplastic astrocytoma showedmoderate enhancement, and diffuse infiltrative astrocytoma cases had minimal enhancement.Histopathology was done in all cases of glioma.MRI findings werecorrelated with histopathology of the tumor in 26 out of 32 cases. First casewhich did not correlate was of diffuse infiltrative astrocytoma which onhistopathology turned out to be anaplastic astrocytoma. Second case was pineal parenchymal tumor of intermediate differentiation which on histopathological diagnosis turned out to be midline tectal glioma. Twocases wasof high grade glioma , which on histopathology turned out to be metastases

Low grade gliomas

Low grade glioma or diffuse infiltrative astrocytoma are grade 2 astrocytomas. There werefifteen patients with low grade gliomas in our study. On conventional MR sequences, lesions were hypointense on T1W andhyperintense on T2W. Lesions were solid to solid and showedminimal enhancement. No blooming were observed on T2 FFE sequence.On MRSI the three tumors showed increased choline peak, reducedNAA, increased mI peak and reduced creat peak. There was increased cho/creat ratio of 2.2(±0.42), increased cho/NAA ratio of 2.1(±0.34) and reducedNAA/creat peak at 1.2 (±0.33). mI/creat ratio was higher at 0.80(±0.25). Bothcases showed no choline peak in perilesional edema outside the tumor margin. (Refer Table-11.3)One of the case did not correlate histopathologically, it was diagnosedas high grade anaplastic glioma. However we got diagnostic accuracy of 96.3% and asignificant association between MRS and histopathology findings withp=0.00854 ($p<0.05$ being significant). We got 93.3% sensitivity and 93.3% specificity. Our findings were similar to study done Mauricio Castilloa et al.

We had two case of midline glioma. It was in a 10 year old girl and 18year old girl. Onconventional MR sequences it appeared as a well defined T1 hypointense lesionand T2/FLAIR hyperintense lesion. No blooming on T2 FE. Moderate contrastenhancement. On MRSI we observed increased choline peak, reduced NAA,increased mI peak and reduced creat peak.

International Journal Dental and Medical Sciences Research
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There was increased cho/creat ratio of 2.2(±0.42), increased cho/NAA ratio of 2.1(±0.34) and reduced NAA/creatpeak at 1..2(±0.33). mI/creat ratio was lower at 0.80(±0.25). Both cases showedno choline peak in perilesional edema outside the tumor margin. (Refer to case of tectal glioma). Our findings were similar to study done by Broniscer A et al.

High Grade Glioma

High grade gliomas or anaplastic astrocytomas are grade 3 astrocytomas. Eight patients with high grade gliomas were evaluated in our study. On conventional MR sequences, lesion was hypointense to isointense on T1W andhyperintense on T2W imaging. Six cases showed blooming on T2 FFEsuggestive of bleed.On MRSI both the tumors showed increased choline peak, reducedNAA, reduced mI peak and reduced creat peak. There was increased cho/creat ratio of 4.8(±0.55), increased cho/NAA ratio of 3.2(±0.22) and reducedNAA/creat peak at 1.0(±0.33). mI/creat ratio was lower at 0.33(±0.15). Six ofthe cases showed increased choline peak with raised cho/creat ratio inperilesional edema probably due to tumoral infiltration. (Refer Table-11.2).Our findings were similar to study done by Magalhaes A, Godfrey W et al and Mauricio Castilloa et al. Two of the case did not correlate on histopathology, which turned out tobe glioblastoma and another one as metastases. We got sensitivity of 83%, specificity of 93% and diagnostic accuracy of 92.2%. There is significantassociation between MR spectroscopy findings and histopathological findings, with p=0.0001 (p<0.05 being significant). (Refer to table 14.2)

GLIOBLASTOMA MULTIFORMAE

GBM are grade 4 astrocytomas. 12 patients with Glioblastomamultiformae were evaluated in our study. All GBM cases were found in adults between 4th to 8th decade.On conventional MR sequences, all cases were heterogeneouslyhypointense on T1W and heterogeneously hyperintense on T2W imaging. Blooming, necrosis, diffuse infiltrative nature and tumor heterogenietywas a prominent feature observed in all cases.On MRSI all tumors showed increased choline peak, reduced NAA,reduced mI peak at 3.6ppm and reduced creat. There was increased cho/creatratio of 7.5(±0.55), increased cho/NAA ratio of 3.8(±0.22) and reducedNAA/creat peak at 0.7(±0.33). mI/creat ratio was lower at 0.15(±0.15). All thecases showed increased choline peak with raised cho/creat ratio in perilesionaledema probably due to tumoral infiltration.One cases of GBM did not correlate on histopathology. It was diagnosed as metastasis on histopathology.However we found a sensitivity 91%, specificity of 96% and diagnostic accuracy of 94%. Significant associationbetween MR spectroscopy findings and histopathological findings withp=0.00001 (p<0.05 being significant). Our study was similar to study done byMagalhaes A, Godfrey W et al63 and Mauricio Castilloa et al.(16) We had got three postoperative patient of GBM, who had come for follow up after treatment. They werein 6^{th}- 7^{th}decade. Onconventional MR sequences T1 and T2 shows an irregular mixed densityheterogeneous mass lesion in right frontotemporal lobe and other two in left fronto temporoparietal lobes with perilesionalextensive edema and mass effect. The mass was seen extending and infiltratingthe genu of corpus callosum and right internal capsule. On post contrast,heterogeneous post contrast enhancement with stellate shape non enhancingcentral area suggestive of possible necrosis was observed. T2 FFE showedlinear gradient blooming. On MRSI showed increased choline peak, reducedNAA peaks, increased cho/creat ratio of 4.5(±0.55), increased cho/NAA ratioof 2.5(±0.22) and reduced NAA/creat peak at 0.9(±0.33) ratio in theperilesional white matter edema and in enhancing portion of the mass. Ourfindings were similar to study done by Taylor JS, Langston JW, Reddick WE, et al.

Diffuse Midline gliomas

Diffuse Midline glioma are type of diffuse midline glioma, usually H3K27mutated types. They are commonly seen in paediatric population. They carry poor prognosis. In our study we evaluated two patients with diffuse midline glioma. It was seen in two girls aged 10 and 18 years. One was misdiagnosed as Pineal parenchymal tumor of intermediate differentiation on MRI. Both were histopathologically proven as diffuse midline glioma. On conventional MR sequences, lesion appeared diffuse ill defined heterogeneous tohypointense mass on T1W and heterogeneous to hyperintense on T2W. One ofthe cases showed was having both solid and cystic component. Mild diffusion restriction areas were also seen.On MRSI the three tumors showed increased choline peak, reducedNAA, increased lipid lactate peak and reduced creat peak. There was increasedcho/creat ratio of 2.38(±0.42), increased cho/NAA ratio of 1.9(±0.34) andreduced NAA/creat peak at 0.9(±0.33). Both cases showed choline peak inperilesional edema outside the tumor margin.We got specificity of 100% and sensitivity of 50%.

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Diagnostic accuracy of 98%. (Refer Table-11.7). Our study is inagreement with the study done by Spampinato MV, Smith JK, Kwock L et al [25]

Craniopharyngioma

Craniopharyngioma are common sellar and suprasellar mass lesions. They are of two types – papillary type- solid tumors, adamantinomatous type – sommon in adults with cystic components. It shows bimodal age distribution. We had twopatients with craniopharyngioma and they were in 3rd decade of life.On conventional MR sequences the lesions were T1 hypo to isointense, T2hyperintense. They were illdefined lesions showing intense contrastenhancement on T1 FFE. One of the cases showed bloomingon T2 FFE in the periphery due to calcification. On MRSI both the tumors showed increased choline peak, reduced

NAA, increased mI peak and reduced creat peak, cystic components showed elevated lipid levels due to its cholesterol rich contents. There was increased cho/creatratio of 2.3(±0.55), increased cho/NAA ratio of 2.1(±0.22) and reduced NAA/creat ratio of 1.39(±0.33). We got sensitivity of 100%, specificity of 100%, diagnostic accuracy of 100% with significant associationbetween MR Spectroscopy findings and Histopathological findings for craniopharyngioma p=0.00084 ($p<0.05$ being significant).Our study is in agreement with previous studies done by Mohana-Borges etal (65), Galanaud D et al66 and Peretti-Viton P et al.(67)

LYMPHOMA

Lymphomas can be of two types – primary CNS lymphoma and secondary CNS lymphoma in patients with known case of systemic lymphoma. We had two patient with lymphoma and another one misdiagnosed as abscess which onhistopathology was diagnosed as lymphoma. Patients were in age group from30-40 years.On conventional MR, the lesions showed homogenously hypo to isointenseon T1 and heterogeneously hyperintense on T2. The lesion was well defined with intense post contrast enhancement on T1 FFE. No blooming on T2 FFE. Lesion showed uniform diffusion restriction with low ADC values. On MRSI both the tumors showed increased choline peak, reduced NAA and reduced creat peak. There was increased cho/creat ratio of 2.03(±0.42), increased cho/NAAratio of 1.9(±0.34) and reduced NAA/creat peak at 0.9(±0.33).We got sensitivity of 67%, specificity of 98%, diagnostic accuracy of 96.1%. Our study shows similar results obtained in study done by Fouladi M et al (68)

MEDULLOBLASTOMA

Medulloblastoma has been graded as grade 4 brain tumor by WHO. We had one patient with medulloblastoma. Patient was12years old.They have been classified into SHH type, WNT type, Group 3, Group 4 types.On conventional MR, the lesions appeared isointense to grey matter onboth T1 and T2. They were well defined lesions seen in roof of IV ventricle and showed significant amount ofcontrast enhancement on T1 FFE. It showed significant diffusion restriction with low ADC values. Few blooming on SWI seen.On MRSI, both the tumors showed increased choline peak, increasedlipid lactate peak, reduced NAA, and reduced creat peak. There was increasedcho/creat ratio of 4.5(±0.55), increased cho/NAA ratio of 2.5(±0.22) andreduced NAA/creat ratio of 0.9(±0.33). (Refer Table-11.6)We got diagnostic accuracy of 100% and significant association betweenMR Spectroscopy findings and Histopathological findings for Medulloblastoma with p=0.0017 ($p<0.05$ being significant). Our study is in agreement withstudy done by Koeller Ket al. (69)

METASTASIS

We had seven patients with histopathological diagnosis of metastasis. They were in 4th and 7th decade. Common primary malignancies to metatsases to brain are from lungs, breast, kidneys, thyroid, prostate. They can manifest in any forms but commonly as ring enhancing lesion near grey and white matter junction.On conventional MR, heterogeneous to hypointense on T1 andheterogenously hyperintense on T2, with perilesional edema. The lesions were well defined, and showed intense ring enhancement on post contrast T1 FFE. Three of the lesions showed blooming on gradient suggestive of haemorrhagic component. On MRSI, Strong Cho peak at long TE without elevation in surroundingperitumoral edema. Reduced NAA and creat. Increased lipid/lac peak in one ofthe tumors. There was increased cho/creat ratio of 2.5(±0.55), increased cho/NAA ratio of 2.3(±0.22) and reduced NAA/creat peak at 0.8(±0.33).cho/creat ratio was not elevated in peritumoral edema. (Refer Table-11.4)We got sensitivity of 42%, specificity of 95% and diagnostic accuracy of 88% and significant association betweenMR Spectroscopy findings and Histopathological findings for Metastasis with p=0.0148 ($p<0.05$). our study is in agreement with study done by Law M, ChaS, Knopp EA, et al.24.

International Journal Dental and Medical Sciences Research
Volume 4, Issue 4, July-Aug 2022 pp 275-290 www.ijdmsrjournal.com ISSN: 2582-6018

Abscess

Abscess are one of the common differentials for ICSOL especially in developing countries with more burden of infectious disease. Common etiologies are bacterial, fungal, tubercular in origin. We had three cases of abscess.

On conventional MR, they appear as isointense on T1 andhyperintense on T2. The lesion was well defined, having both solid and cysticcomponent. The lesion showed perilesional edema. No blooming was noted on SWI. Following contrast administration there was peripheral ring like enhancement was noted on post contrast T1 FFE.On MRSI, there was increased choline, increased lactate peak, reducedNAA and reduced creat peak. Increased cho/creat ratio of 2.03, increasedcho/NAA ratio of of 1.93 and reduced NAA/creat ratio of 0.8.We got sensitivity of 66%, specificity of 100%,diagnostic accuracy of 100% and significant association betweenMR Spectroscopy findings and Histopathological findings with p=0.0024(p<0.05). Our findings are in agreement with the study done by Sarkar Cet al.

Meningioma

We had two patients with histopathological diagnosis of invasive meningioma. Meningiomas are common extra-axial tumors commonly seen in females which shows uniform and homogenous postcontrast enhancement with characteristic dural tail sign.Patient were 40 – 50 years old male and female patient.On conventional MR**,** T1 isointense and T2/FLAIR hyperintense lesion was seen involving left frontoparietal convexity with invasion into brain parenchyma. On post contrast there was intense and homogenous enhancement. On MRSI elevated choline and lipid lactate peaks, reduced NAA andcreat peaks were observed. Increased cho/creat ratio of 2.0 and cho/NAA ratio of 1.9 and reduced NAA/creat ratio of 1.4. Our study shows similar resultobtained in the study by Koeller KK et al.71.We got diagnostic accuracy of 100% and significant associationbetween MR Spectroscopy findings and Histopathological findings for meningioma p=0.0008 (p<0.05 being significant).

Pineal Gland tumor

We had two patients with pineal gland tumors – one was pineal gland germinoma and another was misdiagnosed as pineal parenchymal tumor of intermediate differentiation which on HPR diagnosed as diffuse midline glioma. Patients are in 12 year old girl.Onconventional MRI, the lesion appears as ill defined heterogeous signal intensity lesion with seen in region of pineal gland. It appears predominantly isointense in T1WI and heterogeneously hyperintense on T2/FLAIR images with areas of diffusion restriction with low ADC values. It shows blooming on SWI images possibly due to calcification. The lesion had both solidand cystic component. On post contrast, lesion showed heterogenous postcontrast enhancement. On MRSI lesion showed increase choline and reduced NAA. IncreasedCholine/creatine ratio of 2.03 and increased choline/NAA ratio of 2 wasobserved in our study. It was confirmed on histopathology. Our findingswere similar to study done by Andrea Falini, Giovanna Calabrese, DanielaOriggi et al. We got diagnostic accuracy of 98% and significant association between MR Spectroscopy findings and Histopathological findings for pineal gland tumor p=0.0392 (p<0.05 being significant).

VII. CONCLUSIONS

1)Our study shows that MRS and DWI acts as an useful diagnostic tool adjunct with conventional MRI in diagnosing various brain tumors, its grade, response assessment, differentiating between radiation necrosis and recurrence. It has high sensitivity, specificity and diagnostic accuracy in diagnosing various brain tumors.

2) In this study it was observed that accuracy of MRI in diagnosing various ICSOL is high and for most of them it is > 90%.

3) In this study it was observed that sensitivity of MRI in diagnosing various brain tumors is high (>95%) except in few conditions like abscess, midline glioma. This may be because of small sample size.

4) In this study it was observed that specificity of MRI in diagnosing various brain tumors is high (>92%) Most common brain tumor seen in our study was gliomas. This may be in contrast to the fact that common brain tumor seen is metastases. This difference may be due to the fact that many patients with MR diagnosis of metastases do not undergo biopsy and histopathology examination instead will be evaluated for primary tumor and treated accordingly.

5) From our study we can conclude that in vivo MR spectroscopy can beused as a reliable method for glioma grading. It is useful indiscriminationbetween WHO grade II and grade III, IV astrocytomas as well as other intra cranial space occupying lesion such as metastases, medulloblastoma, meningioma, lymphoma, craniopharyngioma, midline gliomas and pineal gland tumor.

6) Our study also demonstrates that spectroscopic MRmeasurements in the peritumoral region can be used to demonstrate differencesin solitary metastases and high-grade gliomas and also peritumoral infiltrativenature of certain intraaxial brain tumor.
7) Other intracranial space occupying lesions namely abscess shows elevated lipidlactate peaks, diffuse midline glioma, medulloblastoma, metastases showed elevated Cho/Cr and Cho/NAA ratios as well as decreased NAA/Cr ratios of varying degrees within the areas of hyperintensity on T2-weighted images and in enhancing part of the tumor. Amino acids – glutamate, glutamine are seen in pyogenic abscess, lipids more in tubercular abscess, trehalose in fungal abscess.
8) Diffusion weighted Imaging is very useful adjunct tool in grading the lesion. It indicates cellularity of the lesion and cytotoxic edema. It can be used in response assessment as after successful treatment and decrease in tumor cellularity there is increase in ADC vaues. It helps to identify acute infarcts and DWI-FLAIR mismatch is used to identify patients in window period for thrombolysis. Abscess shows uniform diffusion restriction with very low ADC values. Metastases, demyelinating lesions, tumors shows restriction in periphery of the lesion.
9) MRS maps helps to identify high grade areas in the lesion and thus acta as a guide for the target area for biopsy