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ROLE OF CONTRAST ENHANCED MRI IN THE DIAGNOSIS OF LOW GRADE AND HIGH GRADE GLIOMA AND REQUISITE FOR DIFFUSION STUDY

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ABSTRACT

Introduction:

Gliomas are tumors that develop when glial cells proliferate uncontrollably. Although they can develop in the spinal cord, gliomas often develop in the brain. About 27% of primary tumors of the central nervous system (CNS) and 80% of cancerous tumors are gliomas. Gliomas can be classified into 2 groups which are Low Grade and High Grade Glioma. For the detection and characterization of gliomas in the past, computed tomography (CT) scans and traditional magnetic resonance (MR) imaging techniques were employed. Contrast enhanced MRI is the gold standard diagnostic tool for diagnosis of Glioma.

Objective: The objective of the study is to evaluate the diagnostic role of MRI in patients with low-grade and high-grade gliomas and the Diffusion study in patients whom require it.

Materials and Method: It was a descriptive study. The duration of our study was 4 months from April 2023 – July 2023.Our study included all the patients that were referred by doctors for MRI scan. It included patients of both genders male and female presented with different symptoms of brain Glioma. The sample size was 25. On a 1.5T MRI system (GE Healthcare) with a head coil (GE Medical Systems), all 25 patients underwent multisequence imaging protocol.

Results: The majority of the patients in our study were female n = 14 (56%), while n = 11 (44%) were male. Out of 25 LGG were present in 15 while in 10 HGG glioma were present. In our study different age groups were present but mostly we found glioma in age group of 60-70. HGG glioma was mostly present in male and LGG was in females.

Conclusion: High sensitivity and specificity contrast enhanced MRI plays a crucial role in the initial diagnosis and grading of gliomas.

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Keywords: Magnetic Resonance Imaging (MRI), High Grade Glioma (HGG), Low Grade Glioma (LGG)

INTRODUCTION: -

All tumors deriving from glial cells are collectively referred to as gliomas, the most prevalent primary brain tumor. Gliomas are tumors that develop when glial cells proliferate uncontrollably. Normally, these cells help your central nervous system function by supporting nerves. Although they can develop in the spinal cord, gliomas often develop in the brain.[1] About 27% of primary tumors of the central nervous system (CNS) and 80% of cancerous tumors are gliomas.[2] They resemble normal glial cells histologically, and are typically given names that reflect these similarities. However, it is still unknown whether gliomas develop from healthy glial cells, glial or neural progenitors, stem cells, or other cell types.[3]

Histopathology has historically been used to determine the diagnosis and classification of gliomas. Astrocytic tumors, oligodendroglial tumors, oligoastrocytic tumors, ependymal tumors, neuronal tumors, and mixed neuronal-glial tumors (such as gangliogliomas) were the main glial tumor types according to the World Health Organization (WHO) classification of 2007.[4] These groups included more circumscribed grade I tumors such as pilocytic astrocytomas, pleomorphic xanthoastrocytomas, and subependymal giant cell astrocytomas, as well as the more common infiltrating gliomas, including grade II oligodendrogliomas and astrocytomas, and grade III anaplastic oligodendrogliomas, anaplastic astrocytomas, anaplastic oligoastrocytomas, anaplastic ependymomas, and grade IV glioblastomas (GBM).[5]

HGG exhibit significant heterogeneity, both between tumors of the same diagnostic and within the same tumor. This difference in the combinations of genetic and epigenetic alterations that have taken place throughout glioma formation is likely to a considerable measure to blame for this morphological, cellular, and molecular heterogeneity.[6] The genetic mutations of the tumor and the cell type from which it originated must be known in order to fully comprehend the complicated biology of gliomas. This knowledge could serve as the basis for developing novel, more effective, and more targeted treatment approaches.[6]

The diagnosis and treatment of gliomas both benefit from imaging. For the detection and characterization of gliomas in the past, computed tomography (CT) scans and traditional magnetic resonance (MR) imaging techniques were employed. Preoperative evaluation of gliomas has advanced due to recent developments in brain tumor imaging. The degree of the disease, grading, surgical planning, and prognosis are only a few of the first diagnosis-related factors that are evaluated by contemporary imaging modalities. Histopathology continues to be the gold standard for glioma diagnosis and grading. However, in daily practice, the therapeutic strategy for many people with CNS glioma is carried out primarily on the imaging findings because sampling is challenging and vulnerable to potential morbidities. The use of preoperative functional and anatomic imaging techniques has advanced therapeutic plans, leading to a safer surgical approach, higher survival, and a lower incidence of functional handicap following surgery.

The measurement of tumor vascularity can be done more precisely noninvasively using dynamic CT and MR perfusion imaging. You can perform MR perfusion with or without intravenous contrast. T2*-weighted dynamic susceptibility contrast-enhanced (DSC) and T1-weighted dynamic contrast-enhanced (DCE) are the two most popular methods of contrast-enhanced MR perfusion.[7, 8] This article discusses the diagnostic role of MRI in individuals with CNS gliomas.

REVIEW OF LITERATURE:

Eman A.SH. Geneidi *et al*, from Ain Shams University, Eman in 2016 studied 24 patients with HGG and LGG and evaluated that, about one-third of all adult intracranial tumors are gliomas, the most prevalent primary tumors of the central nervous system. The standard approach for assessing such malignancies both before and after therapy has always been magnetic resonance imaging (MRI). However, the applicability of MRI is restricted to morphological information when conventional MRI is used. The prognosis for glioma patients also depends on the histopathological grading, and it is still very bad for those with high-grade gliomas (HGGs) compared to those with low-grade gliomas (LGGs). Diffusion tensor imaging (DTI), an enhanced magnetic resonance imaging (MRI) technology, offers insight into the mobility of

water molecules. The most often employed primary DTI parameter, fractional anisotropy (FA), measures the directionality of molecule motion.[9]

Sarah Jost Fouke *et al*, from Swedish Neuroscience Institute, Sarah in 2015 studied Adults with a freshly discovered lesion that has been histopathological determined to be an LGG and evaluated that, Anatomic sequences for patients with suspected brain tumors should comprise T1 and T2 weighted, fluid attenuation inversion recovery (FLAIR) MR Sequences, and T1 weighted imaging following gadolinium-based contrast delivery. These anatomical sequences at the very least can aid in the identification of a lesion, as well as its location and possibilities for surgical intervention. For the evaluation of suspected LGGs, diffusion and perfusion weighted non-anatomic MR imaging is also employed. Serial imaging should be undertaken on patients with diagnoses of LGGs in addition to anatomic sequences to find new regions of contrast enhancement or substantial changes in tumor size, which may indicate transition to a higher grade.[10]

B. Hakyemez *et al,* from Department of Radiology, BURTOM. Hakyemez in 2005 in his study included 33 patients and concluded that, (MRI) method for determining the tumor's grade. Relative cerebral blood flow (rCBF) has received less research; the ratio of rCBF to rCBV can be used in MR perfusion analysis for assessment together with the rCBF ratio.33 patients (11 low-grade instances and 22 high-grade cases of glioma) participated in this study. All tumors underwent MRI using a standard MRI sequence, followed by a first-passage gadopentetate dimeglumine T2*-weighted gradient-echo single-shot echo-planar sequence. Through the deconvolution of an artery input function, the rCBV and rCBF were determined. The mean GSD values for the rCBV and rCBF ratios in high-grade gliomas were 6.50G4.29 and 3.32G1.87, respectively. The rCBV and rCBF ratios in low-grade gliomas were 1.69G0.51 and 1.16G0.38, respectively. Perfusion MRI is helpful in determining the histological grade of gliomas prior to surgery. Relative cerebral blood volume (rCBV) is a perfusion magnetic resonance imaging parameter that is often employed. High-grade gliomas had statistically different rCBV and rCBF ratios from low-grade gliomas (p! 0.001). Conventional MRI methods are effective in partially defining gliomas, however they are ineffective in detecting the grade of the gliomas prior to surgery. The normal or damaged blood-brain barrier may not fully represent the grade of malignancy, and the pathological contrast enhancement in conventional pictures may not

disclose the malignancy of tumor regions. Contrast enhancement on perfusion MRI is often independent of the compromised blood-brain barrier, in contrast to the contrast enhancement of gliomas on conventional MRI. Areas of contrast enhancement define the micro vascularity or neo vascularity (neovascularization) of tumor lesions. [11]

Eman A.SH. Geneidi *et al*, from Ain Shams University, Eman in 2016 included 30 patients in his study and evaluated that, the use of MR DTI played an important role in grading brain gliomas and was accurate in 24 cases. There was a significant correlation between histopathological grade and FA values measured in tumor and necrotic areas. No positive correlation was established in the perifocal region. Our results show that there is a significant difference between HGG and LGG, with mean rCBV ratios of 2.62 and 0.79, the best cutoff value (1.2). The combined use of MR-DTI and MR-perfusion improved the accuracy of glioma grading. [12]

Nisreen Haydar *et al*, from Department of Radiology, Tishreen University Hospital, Lattakia, Syria, Nisreen in 2022 did a cross- sectional studied of 39 patients and concluded that for predicting a prognosis and directing therapy, a precise histological diagnosis of gliomas is crucial. The observations of nuclear atypia, proliferative activity, microvascular proliferation, and necrosis are used to grade a tissue's histology. Although histopathological diagnosis is still the gold standard for glioma diagnosis, tumor heterogeneity, overlapping morphologic characteristics, and tumor sampling can make diagnosis challenging. In particular, magnetic resonance imaging (MRI) has become the imaging technique most commonly employed to assess gliomas, and it continues to play an increasingly diverse role in the identification, characterization, and treatment of gliomas. For all brain tumors, MRI is the medical imaging technique with the highest sensitivity. HGG have a variable level of enhancement and appear as irregular, unmarked masses with angioedema and a necrotic core. LGG often show as tiny lesions without contrast enhancement. According to the study's findings, high-grade glioma MRI scans had an overall sensitivity and specificity of 100% and 91%, respectively. Both the positive predictive value (PPV) and the negative predictive value (NPV) were 66.6% and 100%, respectively. Overall precision was 94.9%. The correlation between MRI and histological results was 72%. [13]

M. Watanabe *et al*, from Niigata University, Watanabe in 1992 26 individuals with untreated brain gliomas, the relationship between magnetic resonance imaging (MRI) and histological

results was examined. T2-weighted images showed highly homogenous, high-intensity lesions affecting both the grey and white matter in LGG. T2-weighted images showed substantial heterogeneity in signal intensity in HGGs, particularly grade IV, consisting of a hyper intense "core," a less hyper intense or normal intensity "rim," and surrounding finger-like patches of high intensity. With the exception of one instance, all of these HGGs analyzed with gadolinium-DTPA showed substantial and erratic contrast enhancement. Histological examination revealed that in both high-grade and low-grade gliomas, tumor cells extended to the borders of hyper intense areas shown on T2-weighted images, Tumor cells had spread in 5 of 8 LGGs and 4 of 18 HGGs. Isolated voting cells spread beyond the hyper intense region shown on T2-weighted images. The sensitivity of magnetic resonance imaging (MRI) in screening for intracranial tumors is widely debated. The purpose of this study was to determine whether there is a relationship between MRI and histopathological findings, whether MRI can accurately determine brain glioma grade, and whether MRI can accurately determine the grade of brain glioma, and whether tumors in untreated brain glioma can be evaluated. The aim was to investigate whether the histological boundaries of cell invasion could be defined.[14]

Qiang Tian MD *et al*, from Department of Radiology Tangdu Hospital, Qiang in 2018 in his study had 153 patients including 42, 33, and 78 patients with Grades II, III, and IV gliomas, respectively. This study concluded that, Texture functions were more effective in evaluating non-invasive gliomas than using histogram statistics, and multi parametric MRI combined showed higher evaluation efficiency. The proposed radiological strategy incorporating 3D texture features from multi parametric MRI was highly effective for noninvasive glioma staging. This may facilitate clinical decision making in patients with gliomas of various grades. [15]

Knopp, Edmond A *et al*, from the department of Radiology, New York University, Knopp in 1999 included 29 patients in his study, MRI imaging was performed on 29 patients using a first-pass dimeglumine gadopentetate T2*-weighted echo-planar perfusion sequence followed by conventional imaging. Perfusion data were processed to obtain a color map of relative regional CBV. The maximum relative CBV in high-grade astrocytomas (n = 26) varied between 1.73 and 13.7, with a mean of 5.07 ± 2.79 (± SD) and 0.92 to 0.92 in the low-grade cohort (n = 3). It fluctuated between 2.19. The mean was 1.44 ± 0.68. This difference in relative CBV was statistically significant (P<0.001; Student's t-test). Echo-planar perfusion imaging is useful for

preoperative assessment of tumor aggressiveness and provides diagnostic information not available with conventional MR imaging. Areas of circulatory impairment are invaluable for precise targeting of stereotactic biopsies. [16]

OBJECTIVE:

The objective of the study is to evaluate the diagnostic role of MRI in patients with LLG and HGG and the Diffusion study in patients whom require it.

MATERIALS AND METHODS: -

4.1 Study Design:

It was a descriptive study

4.2 Study Duration:

The duration of our study was 4 months from April 2023 – July 2023.

4.3 Study Population:

Our study included all the patients that were referred by doctors for MRI scan. It included patients of both genders male and female presented with different symptoms of brain Glioma.

4.4 Sample Size:

The sample size was 25.

4.5 Sampling Technique:

The sampling technique was simple random sampling. We selected all random patients of Glioma of all age group from 10 to 70 years. The purpose of our study was to determine the type of Glioma either low grade or high grade Glioma in different age group patients.

4.6 Inclusion Criteria:

All the patients were selected suffering from signs and symptoms of Glioma. We included all patients who complained for unconsciousness, fever, vertigo, and hypertension.

4.7 Exclusion Criteria:

The patients who were not requested by a physician for MRI scan were excluded. Patients with other diseases were not selected. Pregnant females were also excluded. Patients with severe allergic reactions to contrast material were also excluded from this study. Patients with metallic implants were also excluded.

4.8 Modality / Machine:

On a 1.5T MRI system (GE Healthcare) with a head coil (GE Medical Systems), all 25 patients underwent multisequence imaging protocol.

4.9 Patient Preparations:

The patients were informed of the MRI process and its indications. Additionally, we searched the patient's body for any metal, including inner ear implants, artificial joints, a pacemaker or defibrillator, specific kinds of heart valves, vascular stents, and brain aneurysm clips. In order to get the sharpest photos, we also told the patients to remain still. We also checked patients RFTs for creatinine level. We provided earplugs to help you avoid being distracted by the MRI machine's noises. In order to better understand how the magnetic field of an MRI can harm developing children, we questioned female patients if they were expecting a child. We position the patient on the MRI table in supine position. Then we placed the arms of the patient along the sides of the body. We also placed head coil over the patient head and in some cases we tied the head.

4.10 Data Collection:

Data was collected from the patients of Glioma at Radiology Department of Allied Hospital Faisalabad. We asked permission from Medical superintendent of Allied Hospital Faisalabad. On a typical MR study, the axial plane was employed for fluid-attenuated inversion recovery (FLAIR) sequences (TR/TE/TI 8000/80/2100), T1-weighted spin-echo (SE) sequences (TR/TE 100/10) and T2-weighted fast spin-echo (FSE) sequences (TR/TE 4195/105).

4.11 DATA ANALYSIS PROCEDURE:

- Statistical Software for Social Sciences (SPSS version 24.0) and Microsoft Excel 2010 were used to evaluate and analyses the data.

RESULTS: -

25 patients, ranging in age from 10 to 70. The majority of the patient's n = 14 (56%) were female, while n = 11 (44%) were male. Out of 25 Ten of the patients' gliomas were HGGs, and fifteen were LGGs.

Table 1: Descriptive analysis of the Gender, Glioma and Age in patients

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Statistics				
		Gender	Glioma	AGE
N	Valid	25	25	25
	Missing	0	0	0
Mean		1.5600	3.4000	4.1600
Median		2.0000	3.0000	5.0000
Mode		2.00	3.00	5.00[a]
Std. Deviation		.50662	.50000	1.77200
Variance		.257	.250	3.140
Range		1.00	1.00	5.00
Sum		39.00	85.00	104.00

In our study we found Glioma (SD= .5000) in 25 patients in different ages groups in both male and female gender with Range of 1.00. In descriptive analysis of data, we concluded the variance of Gender in our study is 0.257, variance of Glioma is 0.250 and of Age is 3. 140.In our study there is no missing value present. The mean we get is as Gender mean= 1.5600, Glioma mean= 3.4000 and Age mean= 4.1600.

Table 2: Frequency Table showing percent between Male and Female

Gender					
		Frequency	**Percent**	**Valid Percent**	**Cumulative Percent**
Valid	Male	11	44.0	44.0	44.0

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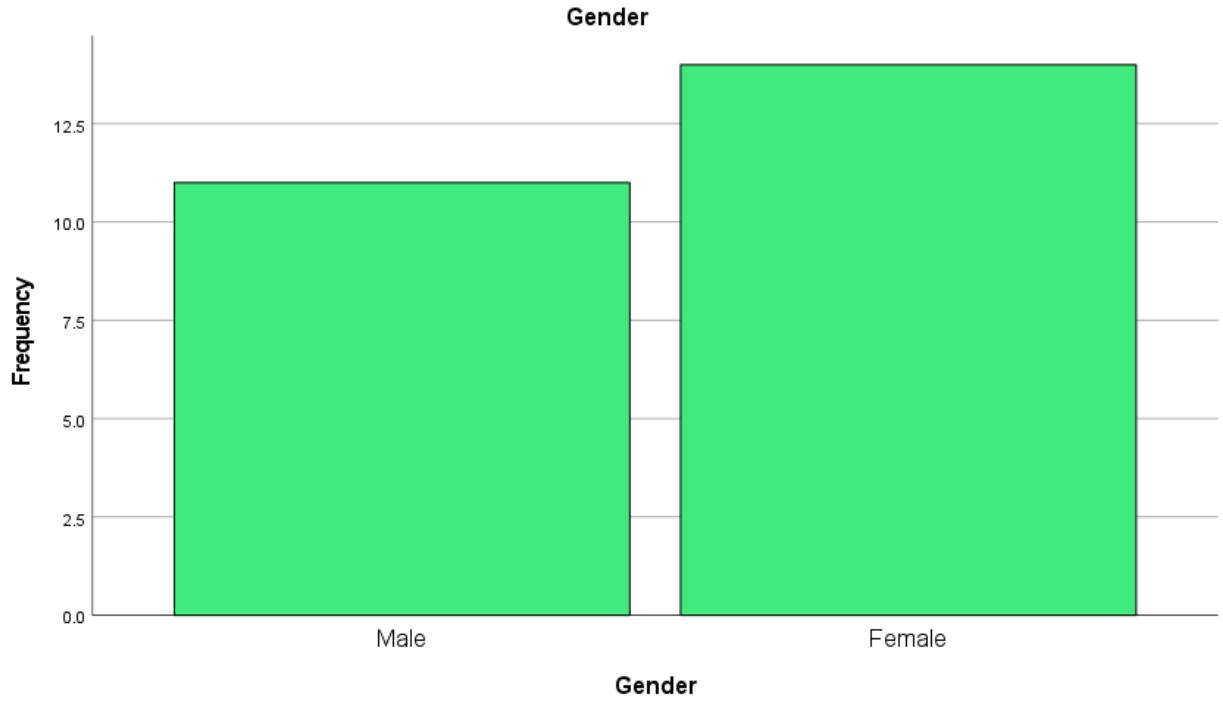
	Female	14	56.0	56.0	100.0
	Total	25	100.0	100.0	

Frequency Chart between Male and Female



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Pie-Chart showing frequency distribution between two different Sex in patients

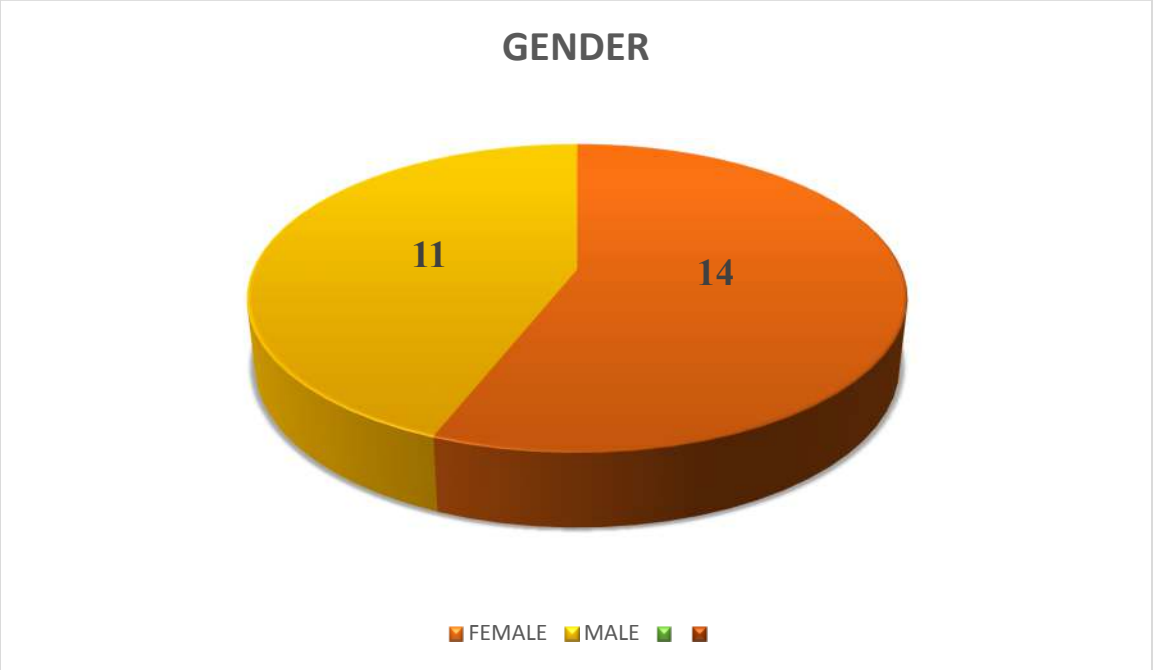

Table 3: Frequency distribution between Grades of Glioma

Glioma					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Low Grade Glioma	15	60.0	60.0	60.0
	High Grade Glioma	10	40.0	40.0	100.0
	Total	25	100.0	100.0	

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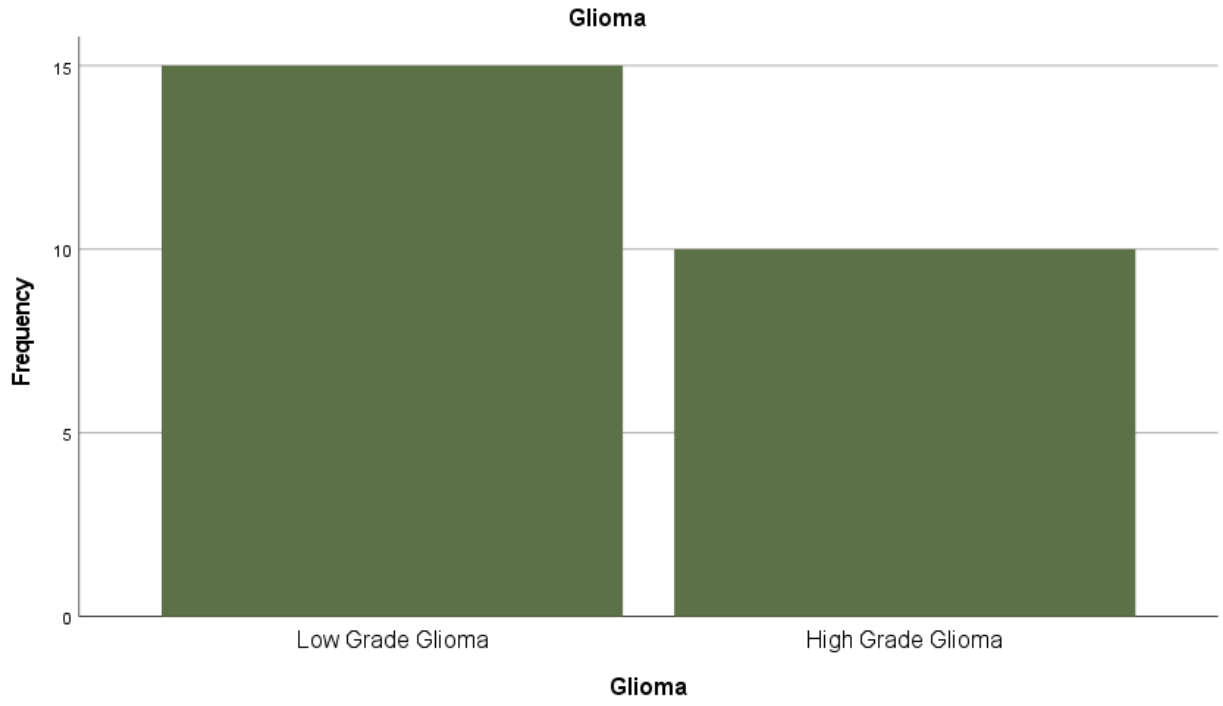
Frequency Chart between Low Grade and High Grade Glioma



Pie-Chart showing Percentage Distribution between Low Grade and High Grade Glioma

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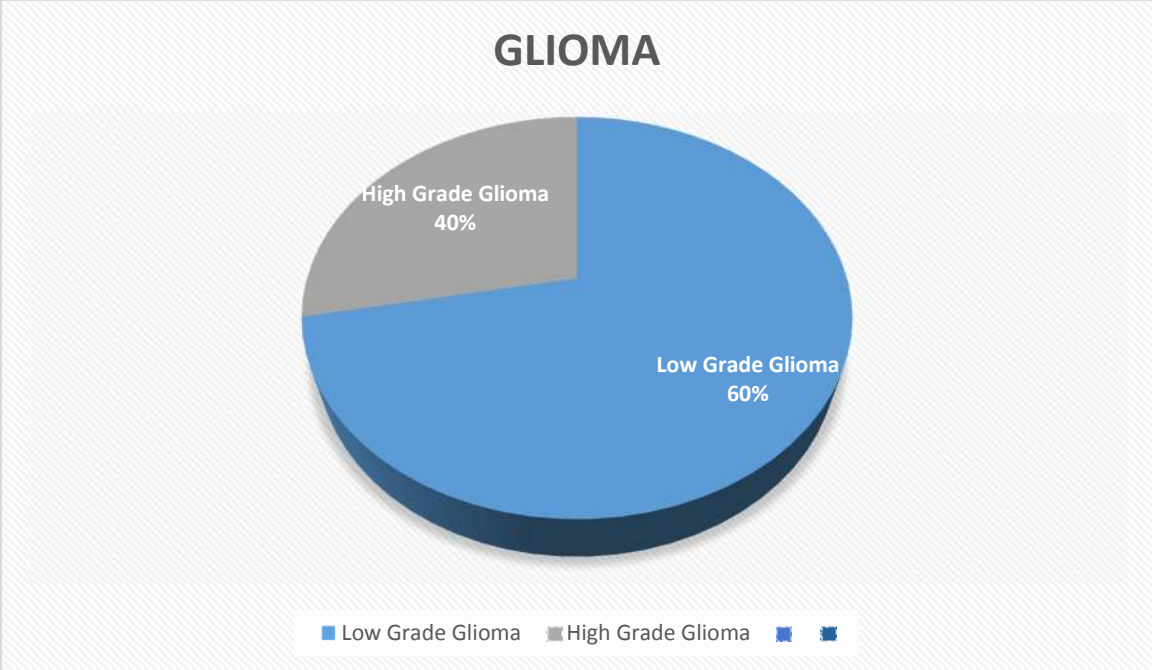

Table 4 Frequency table of different age groups

AGE					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	10-20	3	12.0	12.0	12.0
	20-30	3	12.0	12.0	24.0
	30-40	2	8.0	8.0	32.0
	40-50	3	12.0	12.0	44.0
	50-60	7	28.0	28.0	72.0
	60-70	7	28.0	28.0	100.0
	Total	25	100.0	100.0	

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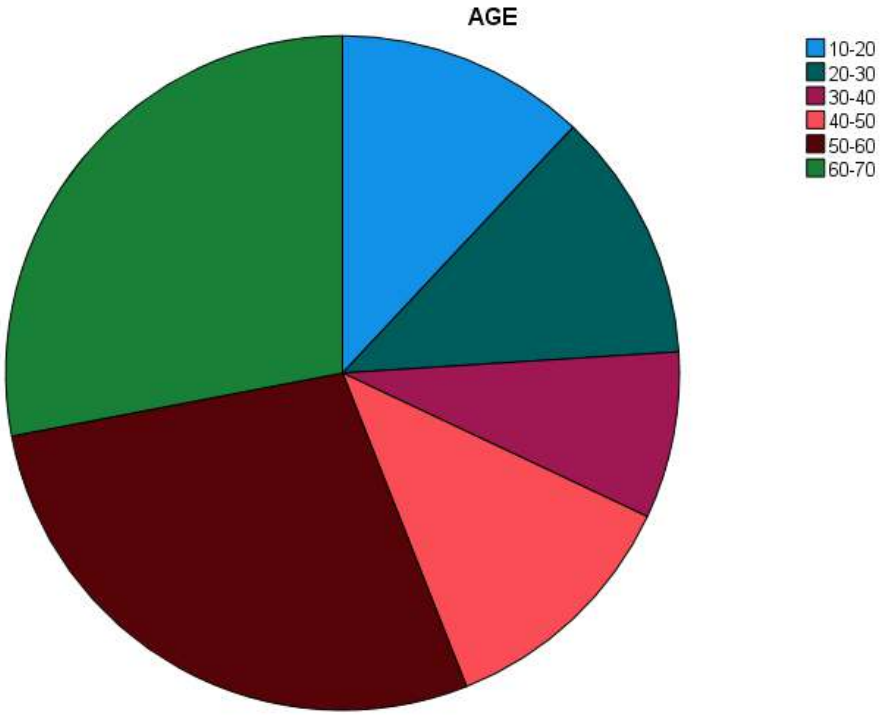
Pie-Chart of Different Age Group Glioma Patients



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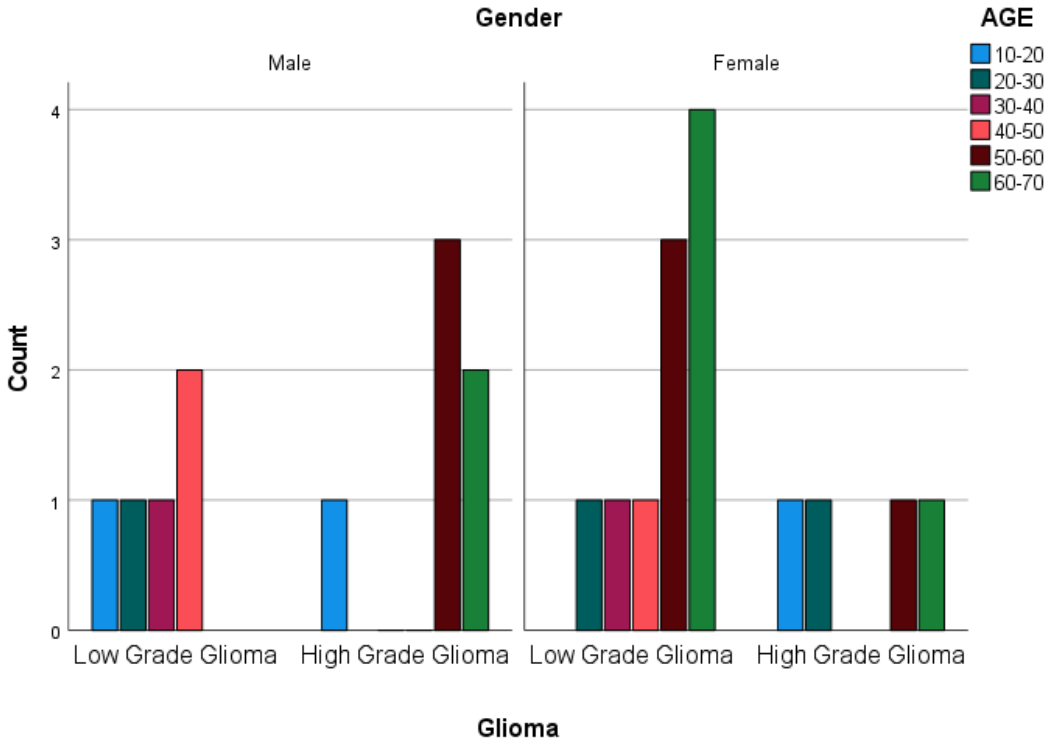
Clustered and simple Bar-Chart between Glioma and Gender in different Age Groups



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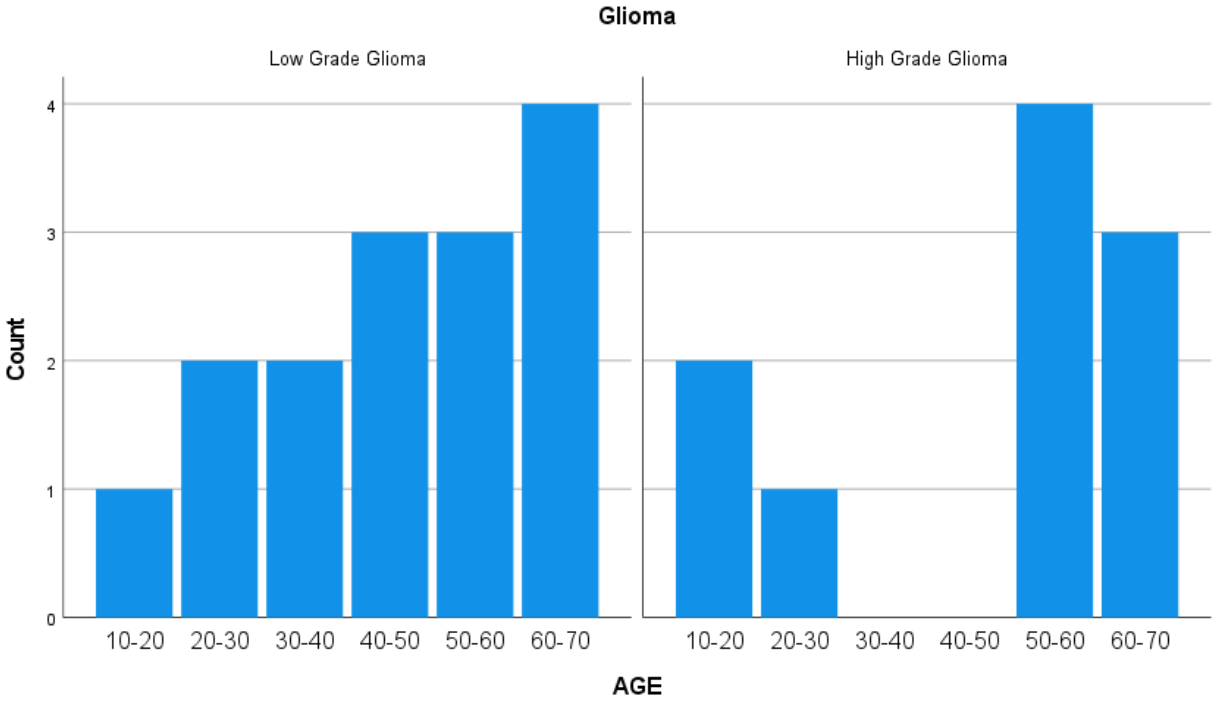

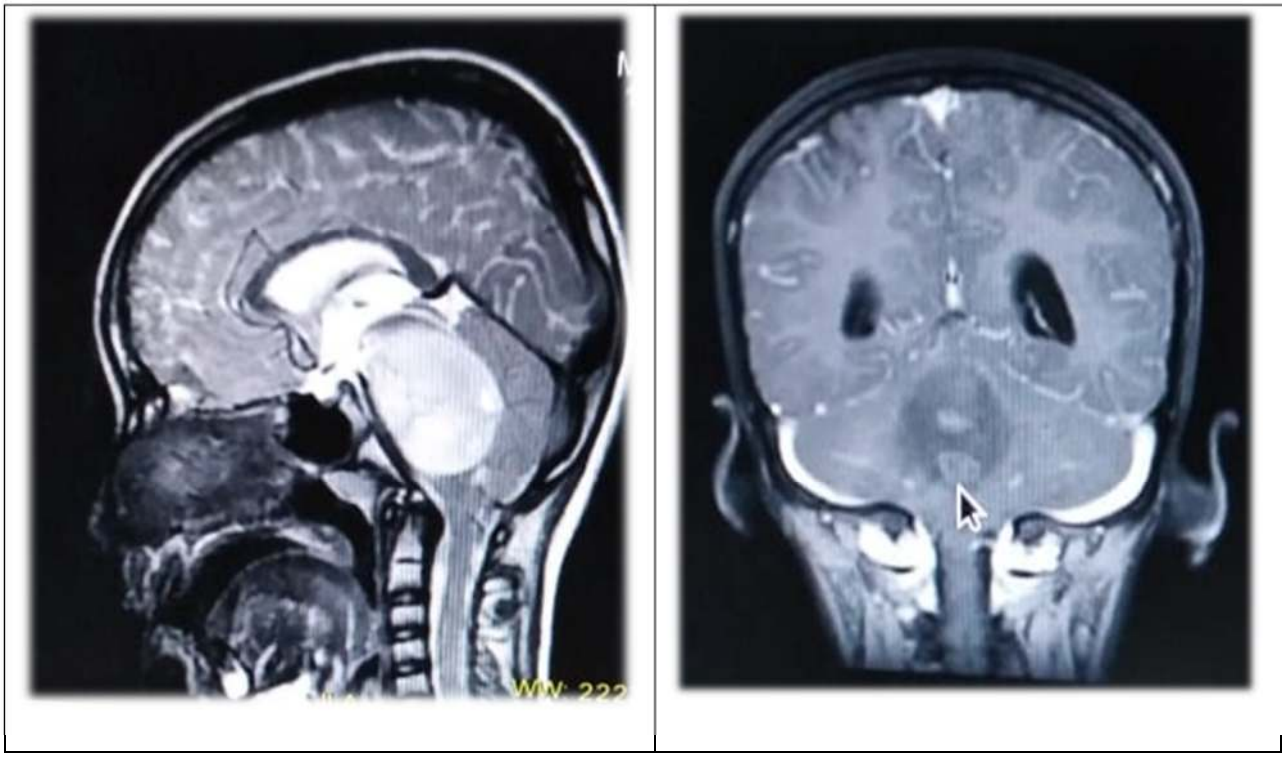

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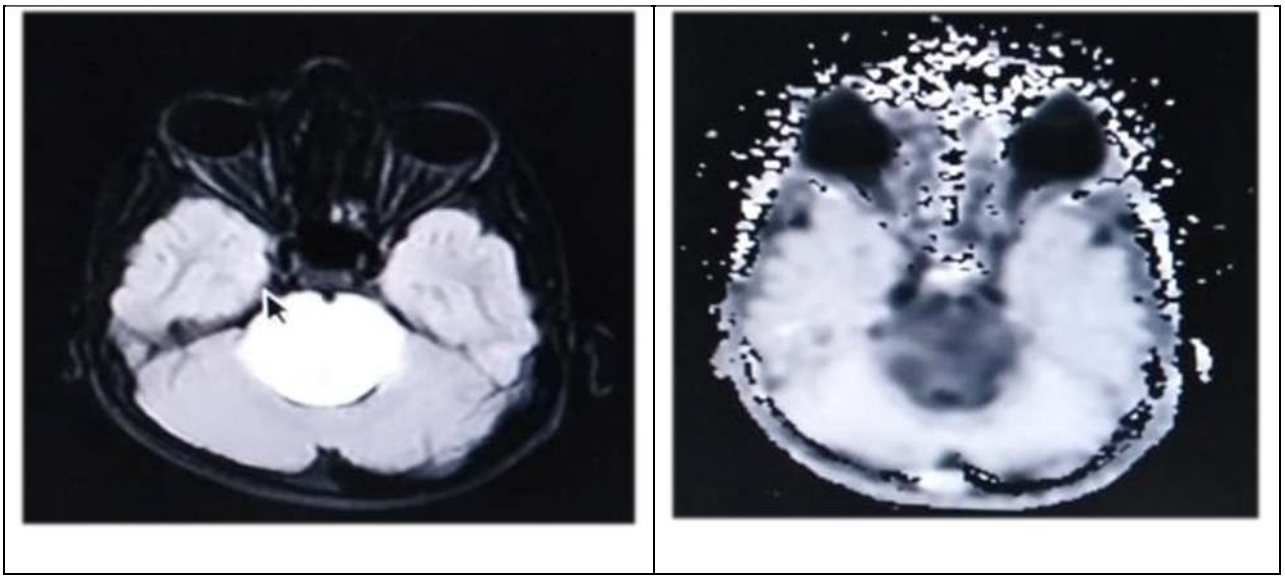
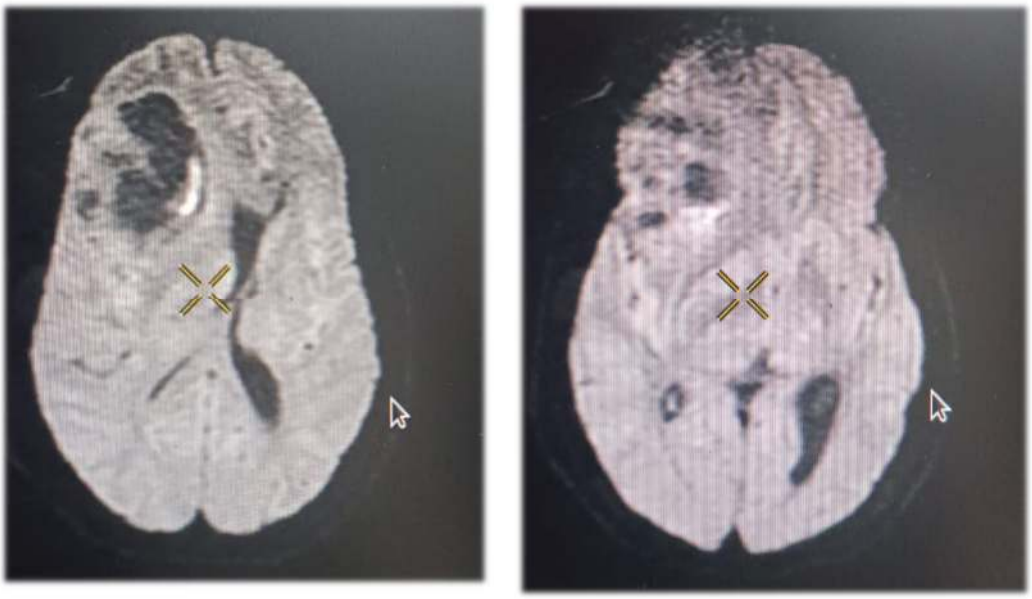


Figure 1; MRI Contrast enhanced images shows features of brain stem glioma. There is appreciated T1W, iso- intense T2W and FLAIR hyper intense well defined rounded lesion involving brain stem measuring 4×4cm with upwards extension to right half of mid brain and downwards extension up to medulla causing compression on 4th ventricle mild hydrocephalus. Lesion is showing subtle heterogeneous enhancement on post contrast scan.



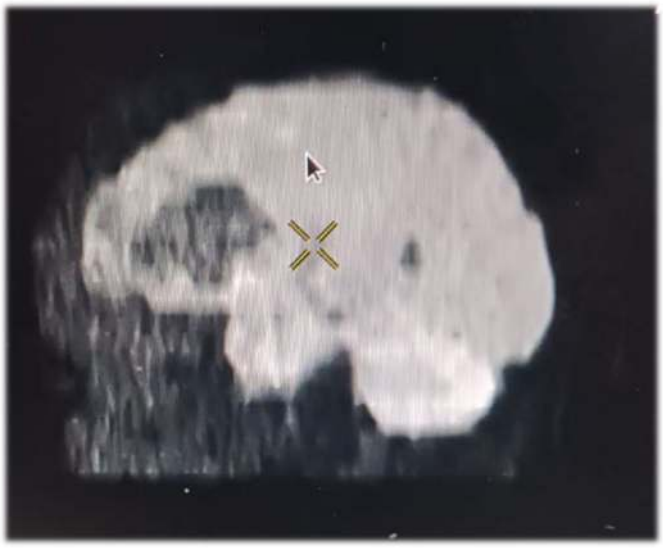


Figure 2 In this case there is intraaxial complex lesion measuring 5.5×5cm in right frontal lobe with enhancing septas and solid component with surrounding gross edema. Lesion is causing compression of ipsilateral lateral ventricle along with midline shift and subfalcine herniation. Features give the impression of right frontal lobe complex Glioma.

DISCUSSION: -

The most prevalent primary malignant brain tumors in adults are gliomas, which can be categorized and graded according to a range of histologic factors. Pilocytic astrocytoma, diffuse astrocytoma, anaplastic astrocytoma, and glioblastoma are the four different grades. The most common investigation to diagnose it and establish its grade are conventional magnetic resonance imaging with T1, T2, FLAIR, and contrast enhancement. All 25 patients in our study, 11 men and 14 women, had been given a brain glioma diagnosis. Ten patients had HGGs, while 15 had LGGs. In our investigation, which is comparable to the cross sectional study from Nisreen Haydar *et al* (2022), all gliomas were hyper intense in T2 and FLAIR, while 92% of them were hypo intense in T1.[13]

According to a research by Law *et al*. that involved 160 patients, conventional MR imaging had a 72.5% sensitivity for differentiating between low- and high-grade gliomas. [17]It can occasionally be challenging to characterize a case depending on contrast enhancement, perifocal

edema, hemorrhage, necrosis, and mass effect, especially in uncommon instances.[17-19] Ginsberg *et al*.'s investigation, which involved 50 patients, found that 20% of high-grade gliomas did not exhibit enhancement whereas 25% of low-grade gliomas did. In our study of 25 glioma patients with MRI diagnoses, 7 cases of HGGs (70%) displayed heterogeneous enhancement on post-contrast imaging, whereas 10 cases of LGGs (66%) did not. HGGs in our study displayed greater contrast enhancement on post contrast pictures than LGGs, which is similar to a study by EASH Geneidi *et al* (2015). [9]

The blood-brain barrier has broken down, which is easily demonstrated by conventional MR imaging and is frequently linked to higher tumor grade. However, as seen in our work, contrast enhancement alone is not always reliable in predicting cancer grade. Implementing the diagnosis of the CNS glioma and afterwards differentiating between different grades is one of the most difficult tasks encountered by radiologists. Conventional MRI and Diffusion Weighted MRI are essential in the diagnosis, and DWI is now regarded as a standard procedure in brain tumor protocols. However, we still want additional functional imaging to fully realize the potential of MRI as a tool for glioma grade differentiation.

This study also focused on the function of MRS in some patients in which further investigation required and Cho/Cr ratio was most significant in separating HGGs from LGGs, according to our analysis of MRS parameters, but Cho/NAA index, which has been mentioned by other researchers like Caulo *et al* and McKnight *et al*, appeared to be more accurate. These researchers found that a Cho/NAA index (CNI) of 2.5 had 90% sensitivity and 86% specificity in separating tumor tissue from non-tumor tissue.[19, 20]

Chakrabarti *et al* state that the afflicted anatomic subsides are more prevalent overall, with the exception of the posterior fossa in males and the posterior fossa in women (which have an equal male: female ratio).[21] According to Bilello *et al*, the affected lobes in men are the left temporal lobe and the periventricular frontal region, while in women it is the right temporal lobe and the periventricular frontal region. [22]According to Li et al., it depends on the position of the tumor; in men, the temporal lobe is more common than the frontal lobe (proximal to the ventricle), and the reverse is true in women.[23] Our investigation, which involved 25 individuals, discovered that tumors affected the lobes and varied depending on the location, much like Bilello and Li's study, but we did not discover any tumors in the fossae, as Chakrabarti claimed. These patients

included 8 female patients who had glioma in the left and right frontal lobe or front parietal lobe, and 6 male patients in whom glioma was suspected in the right and left temporoparietal lobe. We also diagnose 2 male's patients and 6 female patients with brain stem glioma.

In our study Clustered bar chart between gender, glioma and different age group shows that HGG is more common in male and LLG in female. From this chart we also concluded that glioma affect all age group but its prevalence is more common in 60-70 age group. In our study we also evaluated that in our study sample glioma is more common in females.So we concluded that there is big role of MRI in the diagnosis of Glioma and in differentiating the grade of glioma.

CONCLUSION:-

High sensitivity and specificity contrast enhanced MRI plays a crucial role in the initial diagnosis and grading of gliomas. MRI can be used to grade gliomas prior to surgery and can offer important supplementary data on tumour hemodynamics that are not available with traditional imaging methods.According to our study the conclusion is that the gold standard for glioma diagnosis is MRI.

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