PRE-OPERATIVE DIFFERENTIATION OF HIGH-GRADE GLIOMA FROM SOLITARY METASTASES OF BRAIN BY CLINICAL, RADIOLOGICAL AND HAEMATOLOGICAL PARAMETERS: AN OBSERVATIONAL STUDY

THESIS

Submitted to

All India Institute of Medical Sciences, Jodhpur

In partial fulfilment of the requirement for the degree of

MAGISTER CHIRURGIAE (M.Ch.)

NEUROSURGERY

JULY 2020 **DR VIKRANT SHARMA**

AIIMS, JODHPUR

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DECLARATION

I hereby declare that the thesis titled "**PRE-OPERATIVE DIFFERENTIATION OF HIGH-GRADE GLIOMA FROM SOLITARY METASTASES OF BRAIN BY CLINICAL, RADIOLOGICAL AND HAEMATOLOGICAL PARAMETERS: AN OBSERVATIONAL STUDY**" embodies the original work carried out by the undersigned in All India Institute of Medical Sciences, Jodhpur.

Dr Vikrant Sharma
Department of Neurosurgery
All India Institute of Medical Sciences, Jodhpur

All India Institute of Medical Sciences, Jodhpur

CERTIFICATE

This is to certify that the thesis titled "**PRE-OPERATIVE DIFFERENTIATION OF HIGH-GRADE GLIOMA FROM SOLITARY METASTASES OF BRAIN BY CLINICAL, RADIOLOGICAL AND HAEMATOLOGICAL PARAMETERS: AN OBSERVATIONAL STUDY**" is the bonafide work of **Dr Vikrant Sharma** carried out under our guidance and supervision, in the Department of Neurosurgery, All India Institute of Medical Sciences, Jodhpur.

Guide:

Dr Mayank Garg
Additional Professor
Department of Neurosurgery
All India Institute of Medical Sciences, Jodhpur.

Co-Guides:
Dr Poonam Elhence
Professor, Head
Department of Pathology
All India Institute of Medical Sciences, Jodhpur.

Dr Abhishek Purohit
Additional Professor
Department of Pathology
All India Institute of Medical Sciences, Jodhpur.

Dr Sarbesh Tiwari
Associate Professor
Department of Diagnostic and Interventional Radiology
All India Institute of Medical Sciences, Jodhpur.

Dr Jaskaran Singh Gosal,
Associate Professor
Department of Neurosurgery
All India Institute of Medical Sciences, Jodhpur.

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Dr Deepak Kumar Jha
Professor and Head
Department of Neurosurgery
AIIMS, Jodhpur.

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Dr Vikrant Sharma

LIST OF ABBREVIATIONS

1.	AUC	-	Area Under Curve
2.	Cho:Cr	-	Choline:Creatine ratio
3.	Cho:NAA	-	Choline:N-Acetyl Aspartate
4.	CT	-	Computed Tomography
5.	DLC	-	Differential Leucocyte Count
6.	EGFR	-	Epidermal Growth Factor Receptor
7.	HGG	-	High Grade Glioma
8.	Hb	-	Haemoglobin
9.	HPE	-	Histopathological Examination
10.	LGG	-	Low Grade Glioma
11.	MRS	-	Magnetic Resonance Spectroscopy
12.	MRI	-	Magnetic Resonance Imaging
13.	NLR	-	Neutrophil Lymphocyte Ratio
14.	PWI	-	Perfusion Weighted Imaging
15.	ROC	-	Receiver Operating Characteristic Curve
16.	rCBV	-	relative Cerebral Blood Volume
17.	SD	-	Standard Deviation
18.	SBM	-	Solitary Brain Metastasis
19.	TLC	-	Total Leucocyte Count

SUMMARY

Background

Solitary Brain Metastasis (SBM) and High-Grade Glioma (HGG) are similar looking entities on pre-operative radiological imaging. But the management is different for the two. HGG requires upfront surgery on one hand, SBM warrants further investigation of the primary. Problem arises when SBM is the initial presentation of unknown primary which occurs in almost 30% of patients. Hence, we utilized clinical, radiological, and hematological parameters to achieve pre-operative differentiation between the two.

Methods

prospective data of 45 patients operated for solitary brain lesion were collected from January 2021 to June 2022. Clinical, Hematological and Radiological parameters were noted. General, warning symptoms; exam findings were included in *clinical* group. Pre-operative Hb, TLC and NLR were included in *Hematology* group. Tumor characteristics in conventional MRI namely T1, T2, edema: mass ratio, contrast enhancement and pattern, and in special sequences namely rCBV (PWI), Cho:Cr and Cho:NAA ratios (MRS) were included in *Radiology* group. HPE reports were collected, and data hence obtained were subject to statistical analysis. Results were analyzed with *multivariate logistic regression analysis* and *p*-values were calculated for individual groups. ROC were plotted to know the AUC and cutoff values of significant variables to differentiate the two entities.

Results

There were 28 males (62.2%) and 17 females out of 45 patients. HGG was diagnosed in 24 patients (53.3%) and SBM in 7 (15.6%). Other 14 patients were diagnosed with

either LGG or lymphoma. The most common location of the tumour was frontal (23 patients, 51.11%). HGG was common in 40-60 years and SBM in 40-60 and 60-80 years age group. 7 out of 24 HGG patients (29.16%) and 2 out of 7 SBM patients (28.57%) had history of smoking. out of 7 SBM patients, 4 (57.14%) had history of unintentional significant weight loss. Headache was the most common symptom occurring in 62.2% of our patients. Hemiparesis was present in 62.2% patients, extensor plantars were present in 55.6%, lobar signs in 15.6%, pronator drift in 15.6%, decreased air entry in lungs in either of lobes were demonstrated in 11.1%. Although no definite correlation of NLR with either diagnosis was found, but it can be said that a value >cut off 2.67 was indicative of HGG and a value >cut off 4.57 was indicative of SBM. Edema: mass ratio showed the maximum AUC of 0.808, which shows the relevance of conventional MRI in differentiating. Our study showed that rCBV, Cho:Cr and Cho:NAA ratios are significantly associated with HGG. A value of rCBV, Cho:Cr, Cho:NAA above cutoff 3.95, 3.96, 7.35 respectively are indicative of HGG. The AUC for conventional MRI alone; and combined clinical exam findings, NLR, special MRI sequences were 0.7262 and 0.9702 respectively for HGG; 0.7262 and 0.9643 respectively for SBM.

Conclusion

Differentiating HGG from SBM is important pre-operatively. It is possible to differentiate the two entities with a multimodal approach combining clinical methods, hematological parameters and Radiological parameters including special MRI sequences. It involves a team effort.

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INTRODUCTION

Intracranial metastases and primary high-grade gliomas are two commonly found brain tumours in adults.[1] Management for the two entities are different and affects clinical outcome, hence pre-operative differentiation is important.[2] Clinical history, examination, and conventional imaging (CT, MRI) in cases of extracranial primary malignancy is often helpful. Diagnostic difficulty arises in cases of unknown primary owing to non-significant clinical findings and similar conventional imaging features. Solitary brain metastasis may be the first manifestation in up to 30% patients with systemic malignancy.[3]

Clinically, it has been shown that 40% of the cancer patients present with one or more warning signs of cancer weeks or months before the diagnosis of cancer is made. Although, mostly non-specific, but often contributory to the diagnosis in alliance with other modalities.[4]

Role of special imaging techniques have emerged as an aid to pre-operative differentiation between the two entities. Moreover, various haematological parameters have recently been found to correlate with outcome of malignancy.[5] Primary malignancy with intracranial metastasis is expected to trigger more inflammation, the haematological parameters would accordingly indicate. Hence, these parameters may indirectly point towards the existing pathology.

For long, neurosurgeons across the globe have been depending on conventional MRI features for the diagnosis of brain tumours. But the fact is often ignored that both entities have almost similar conventional imaging features (**figure A, B**). On standard MRI, enhancement and peritumoral oedema are common. FLAIR imaging can depict a large portion of the tumour, but they may be non-specific. Advanced MRI techniques, such as perfusion MRI, diffusion tensor imaging, and MR spectroscopy,

have improved the non-invasive grading of astrocytoma, and to distinguish the metastases from the astrocytoma.[6,7]

Relative cerebral blood volume (rCBV) maps derived from perfusion-weighted MR (PWI) in the peritumoral region, demonstrate elevated values in glioblastoma due to tumour infiltration in the normal brain parenchyma in comparison with brain metastases [8]. Spectroscopic MR (MRS) imaging allows differentiation of tumoral versus non-tumoral tissue, primarily through differences in choline metabolite, which reflects the cellular density and rate of cellular membrane turnover hence should be elevated in areas of tumoral infiltration, even in the absence of enhancement or T2 signal abnormality. Values such as Cho:Cr, Cho:NAA ratios have been found to be more significant [1](**figure C, D**).

Similarly, pre-operative Neutrophil Lymphocyte ratio (NLR) elevation is reportedly associated with poorer outcomes for patients with esophago-gastric cancer, colorectal cancer, hepato-cellular carcinoma, pancreatic cancer, renal cell carcinoma, lung cancer, breast cancer and many other malignancies.[5] To our knowledge, very little data is available on its association with brain tumours.

Despite various clinical, radiological, and haematological parameters being independently helpful in differentiation of the two entities, a composite study including these is still lacking. We seek to analyse the utility of these parameters and develop a system based on these parameters which would help conclude pre-operative diagnosis.

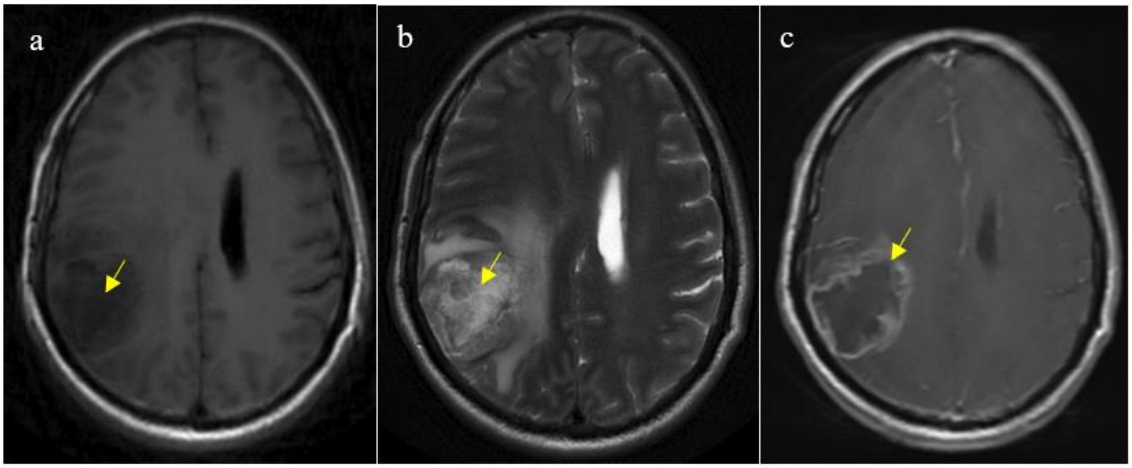


Figure A: conventional MRI sequences of a patient with HGG. (a)T1w image showing hypointense lesion. (b) T2w image showing same lesion as hyperintense. (c) contrast image showing peripheral rim enhancement.

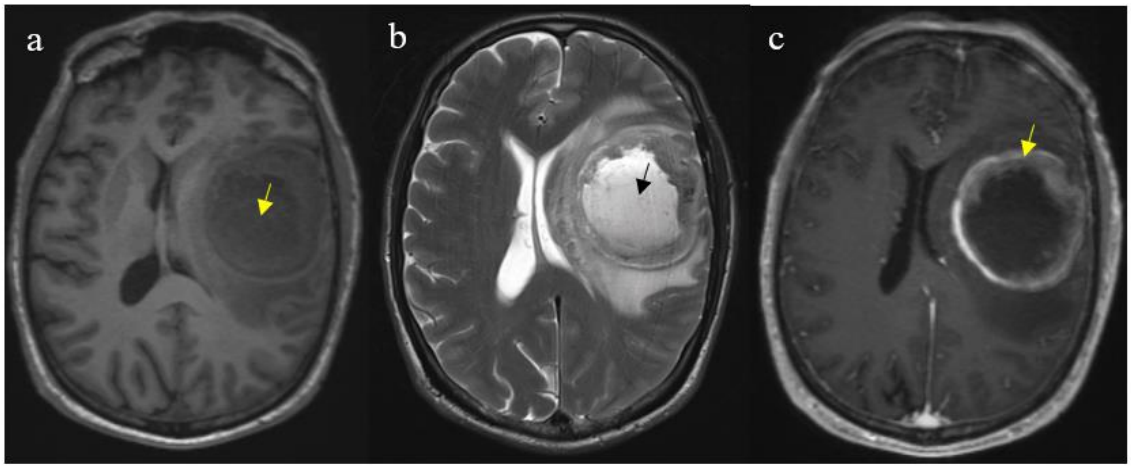


Figure B: conventional MRI sequences of a patient with SBM. (a) T1w image showing hypointense lesion. (b) T2w image showing same lesion as hyperintense. (c) contrast image showing peripheral rim enhancement.

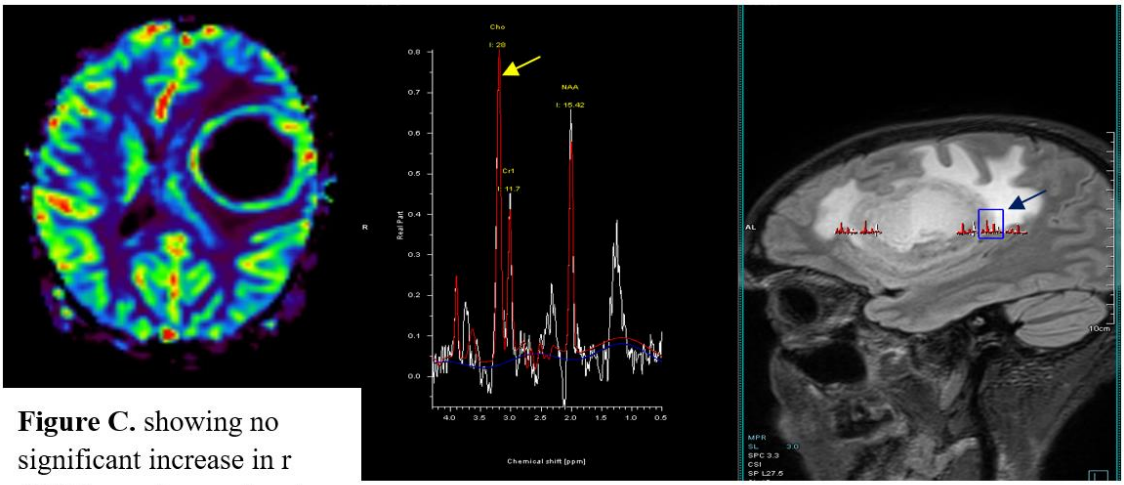


Figure C. showing no significant increase in r CBV in peritumoral region on PWI in above patient with SBM.

MRS shows raised Cho: Cr ratio in the peritumoral region of the same Patient.

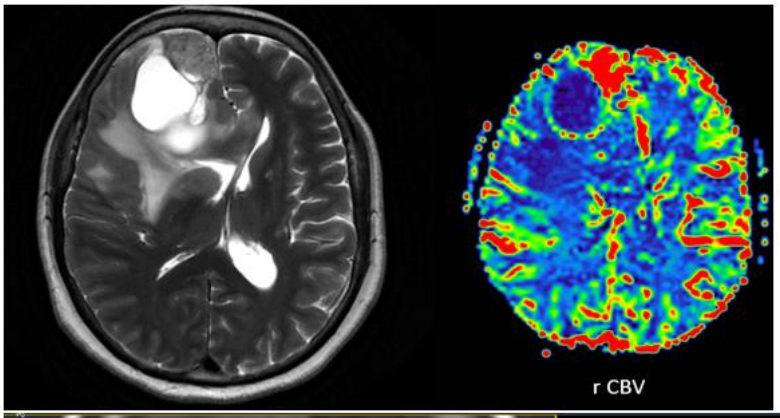
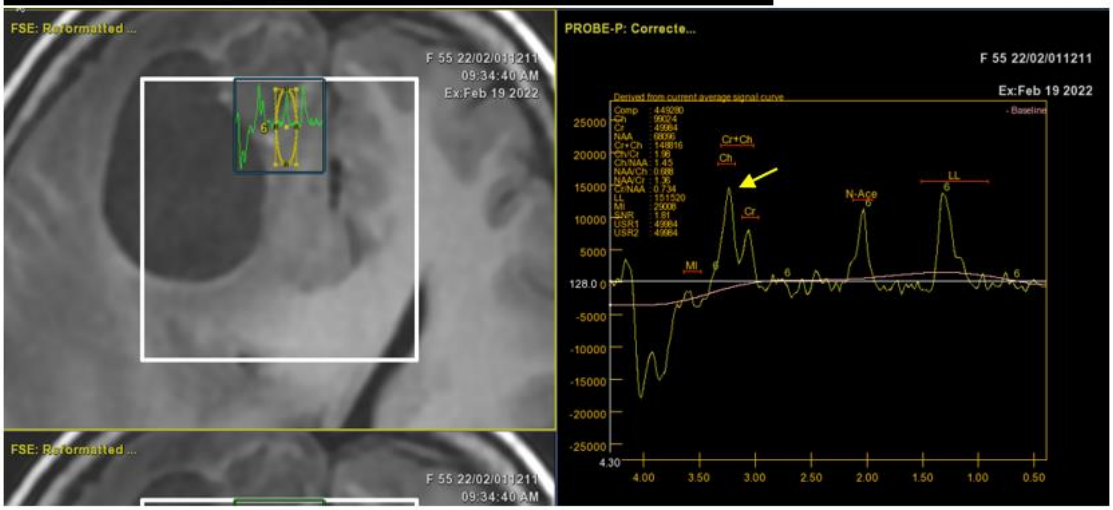


Figure D. showing significant increase in r CBV in peritumoral region on PWI in a patient with HGG. The MRS shows raised Cho: Cr ratio in the peritumoral region.



AIM AND OBJECTIVES

Aim

To determine role of clinical, haematological, and conventional radiological methods in pre-operative diagnosis of patients presenting with solitary brain lesion.

Objectives

- Clinical and haematological evaluation of patients with solitary brain lesion pre-operatively.
- Role of conventional radiological findings in pre-operative differentiation between high grade glioma and solitary metastasis of brain.
- Role of special radiological methods for conclusive diagnosis.

REVIEW OF LITERATURE

HGG and SBM may look similar on presentation and imaging, but their management is different. Conventional MRI is most used by clinicians to diagnose HGG, ignoring the fact that SBM may have similar features. Hence, its pre-operative differentiation is imperative to initiate correct management on time. Conventional MRI features may be non-contributory, hence role of other methods become important to reach the correct diagnosis. Differentiation of the two entities starts when the patient first becomes symptomatic. It is the role of patient's near and dear ones to identify the problem and report it to the clinician. Once the cranial pathology is confirmed, a neurosurgeon may request appropriate MRI sequences. Knowing each sequence's individual capability to differentiate between the entities is important, meanwhile keeping in mind the clinical and haematological findings.

Scheel and Holtedahl[4] conducted a Retrospective cohort study with prospective registration of cancer in general practice. 157 Norwegian general practitioners (GPs) reported 261 cancer patients. During 10 consecutive days, GPs registered all patient consultations and recorded any presence of seven focal symptoms and three general symptoms, commonly considered as *warning signs of cancer (WSC)*. Follow-up was done 6 to 11 months later. For each patient with new or recurrent cancer, the GP completed a questionnaire with medical record-based information concerning the diagnostic procedure. In 78% of cancer cases, symptoms, signs, or tests helped diagnose cancer. In 90 cases, there were 131 consultations recorded WSC that seemed related to the cancer. Further symptoms were reported for another 74 cases. Different clinical signs were noted in 41 patients, 16 of whom had no previous recording of symptoms. Supplementary tests added information in 59 cases; in 25 of these there were no recordings of symptoms or signs. Sensitivity of any cancer-relevant symptom

or clinical finding ranged from 100% for patients with uterine body cancer to 57% for patients with renal cancer. It concluded that *WSC had a major role as initiator of a cancer diagnostic procedure*. Low-risk and not-no-risk symptoms also played an important role, and in 7% of patients they were the only symptoms. Clinical findings and/or supplementary procedures were sometimes decisive for rapid referral.

Urabe *et al*[9] analysed the utility of NLRatio in prognosticating the malignancy. They performed a retrospective analysis of 1335 patients with gastric cancer, designed to determine the relationship between long-term outcomes and preoperative NLR. The second quartile group showed significantly longer relapse-free survival rather than the first quartile group when multivariate Cox regression analysis was applied to NLR in combination with other influential prognostic factors (hazard ratio: 0.69; 95% CI: 0.48–0.99; p = 0.048). This J-shaped relationship between the hazard ratios of relapse-free survival among the quartiles was supported by contrast testing (results like those were obtained in the analysis using the quintiles of NLR). This was the first study showing the association between the preoperative NLR values and long-term outcomes of gastric cancer patients to be nonlinear to a statistically significant degree.

Li *et al* [10] conducted a meta-analysis to assess the association of cigarette smoking with adult glioma. From PubMed and EMBASE, 7 cohort and 17 case-control studies were selected involving more than 2.3 million individuals. There was *no association between cigarette smoking and adult glioma except for small but statistically significant association in female past smokers*.

Ahn *et al* [11] analysed the association between cigarette smoking and the risk of developing malignant glioma by conducting a nationwide population-based cohort study. They used Korean National Health Insurance System cohort for collecting data

of 9,811,768 people over 20 years old without any cancer history in 2009 and followed up till 2017 end. 6100 malignant glioma cases were documented during the median follow-up of 7.31 years. Current smokers had a higher risk of developing malignant glioma as compared to non-smokers. This association was more in patients smoking > 20 cigarettes/day. The association was dose-dependent for those having pack years 30 or more. These results suggested a *possible association of smoking with glioma*.

Larieda *et al* [12] studied the association of abnormal body mass index and weight change with outcome in patients with brain metastasis. It was a retrospective observational study. 703 patients treated at University Hospital Zurich were assessed. A median relative weight loss of 5% within the first 6 months of diagnosis of brain metastasis (95% CI 3.3-6.5), and reduction exceeding the median was associated with an unfavourable outcome. Hence, *high body mass index is associated with better and underweight with worse outcome in patients with brain metastasis*.

Li *et al* [13] conducted a retrospective cohort study to analyse 133 patients with brain metastases from lung adenocarcinoma with EGFR mutations. NLR was assessed by AUC. An NLR value equal to or less than 2.99 was associated with prolonged survival. Hence, it concluded that *NLR is a useful prognostic biomarker for patients with brain metastasis*.

Ashwath *et al* [14] evaluated the utility of NLR in predicting the histopathological grade of brain tumors. 116 patients grouped into low- and high-grade brain tumors and their mean pre-operative NLRs were analysed. The mean NLR of low-grade tumors was 1.68±0.53 and that of high-grade tumors was 3.12±0.74. NLR>2.4 can be used to identify high grade brain tumors with a sensitivity of 80%, specificity of 92%,

excellent impact with likelihood ratio (+) of 10.1, and an odds ratio of 54.1. The mean NLR of extra-axial tumors was 1.68±0.62 and that of intra-axial tumors was 2.64±0.91. Hence, it concluded that *mean NLR is higher in high-grade tumors and intra-axial tumors* with a cutoff value of NLR>2.4 and >2.0, respectively.

Hu *et al* [15] conducted a retrospective observational study of patients with non-small cell lung cancer (NSCLC) diagnosed from January 2016 to December 2020. NLR were positively correlated with NSCLC brain metastasis. Hence, the study showed that *increased NLR levels were independently associated with increased risk of developing brain metastasis in patients with NSCLC*.

Law *et al* [1] analysed 51 patients with a solitary brain tumour (33 gliomas, 18 metastases). Of the 33 patients with gliomas, 22 underwent perfusion weighted MR imaging; nine, spectroscopic MR imaging; and two underwent both. Of the 18 patients with metastases, 12 underwent perfusion-weighted MR imaging, and six, spectroscopic MR imaging. The peritumoral region was defined as the area in the white matter immediately adjacent to the enhancing (hyperintense on T2-weighted images, but not enhancing on post-contrast T1-weighted images) portion of the tumor. Relative cerebral blood volumes in these regions were calculated from perfusion-weighted MR data. Spectra from the enhancing tumor, the peritumoral region, and normal brain were obtained from the two-dimensional spectroscopic MR acquisition. The measured relative cerebral blood volumes in the peritumoral region in high-grade gliomas and metastases were 1.31±0.97 (mean SD) and 0.39±0.19, respectively. Spectroscopic imaging demonstrated elevated choline levels (choline-to-creatine ratio was 2.28±1.24) in the peritumoral region of gliomas but not in metastases (choline-to-creatine ratio was 0.76 0.23). Although conventional MR imaging characteristics of solitary metastases and primary high-grade gliomas may sometimes be similar,

perfusion weighted, and spectroscopic MR imaging enable distinction between the two.

Hakyemez *et al* [8] 48 patients (22 high grade gliomas and 26 solitary brain metastasis) were analysed using perfusion weighted imaging and conventional MRI. rCBV ratio of intratumoral and peritumoral area was calculated. Morphometric analysis of area of peritumoral edema to mass area was done. Mean rCBV values of intratumoral areas were higher for high grade gliomas as compared to solitary brain metastasis. Morphometric analysis of peritumoral edema was also statistically significant between the two tumors types. It concluded that measuring *mass:edema and rCBV values pre-operatively is useful in differentiating the two entities*.

Fordham *et al* [16] provided an update on all radiological evidence regarding identification and differentiation of HGG and SBM. They made use of dynamic susceptibility contrast optimized for detecting relative cerebral blood flow and rCBV, DTI used to detect changes in mean diffusivity and Neurite orientation dispersion and density imaging used to detect changes in intra-cellular volume fraction, isotropic volume fraction, and extracellular volume fraction. MRS was used to detect Cho:NAA, Cho:Cr and NAA:Cr ratios. Radiomics and machine learning algorithms devised to assist improving diagnostic accuracy.

Maurer *et al* [17] evaluated MRI of patients with histologically proven GBM and SBM to know the MR signal characteristics of the mass and peritumoral area to distinguish solitary supratentorial metastasis from GBM. The logistic regression analysis revealed that diameter of peritumoral Edema: diameter of enhancing mass ratio is the only useful criterion to distinguish SBM from GBM with lower ratio favouring GBM (accuracy 68%, sensitivity 84% and specificity 45%).

Despite aforementioned studies depicting various clinical, radiological and haematological parameters being independently helpful in differentiation of the two entities, a combined study including above three and a system for better predictability is still lacking. Our study seeks to analyse the utility of these parameters, especially in context of brain tumors and develop a system which would help conclude pre-operative diagnosis. The study is an attempt for highlighting above useful pearls of diagnosis in Indian scenario.

MATERIAL AND METHODS

Study Period: January 2021 to June 2022.

14 months (January 2021 to March 2022) for data collection.

3 months (April 2022 to June 2022) statistical analysis.

Study Setting: All India Institute of Medical Sciences, Jodhpur is the tertiary care centre present in western Rajasthan. The patients undergoing surgery for intracranial space occupying lesions were enrolled for study.

Study Design: Prospective, Observational.

Study participants: All patients undergoing elective cranial surgeries during the study period.

Inclusion Criteria: Patients undergoing surgery for solitary brain lesion.

Exclusion Criteria: Recurrent high-grade glioma or brain metastasis, Diagnosed extra-cranial primary malignancy.

Data Collection:

Data collection was started after approval from the ethical committee.

The subjects fulfilling the inclusion and exclusion criteria during the study period were included in study by consecutive sampling and a total of 45 patients were enrolled for the study.

Data was collected using a predesigned, semi structured proforma (ANNEXURE 5).

CLINICAL: history and examination, general and warning signs of cancer.

HAEMATOLOGICAL: Hb, TLC, DLC, NLRatio.

RADIOLOGICAL: **Conventional MRI findings**- number of lesions, Location of lesion, Contrast enhancement and its pattern and peritumoral edema size, edema: mass ratio.

Special imaging findings- PWI findings (rCBV in peritumoral region); MRS (Cho:Cr, Cho:NAA ratios).

Sampling and Sample Size:

All patients fulfilling the inclusion and exclusion criteria were serially included for the study, by consecutive sampling, from January 2021 to March 2022. Statistical analysis was done from April 2022 to June 2022.

Statistical analysis:

Statistical Analysis was performed with help of Epi Info (TM) 7.2.2.2, which is a trademark of the Centers for Disease Control and Prevention (CDC). Descriptive statistical analysis was performed to calculate the means with corresponding standard deviations (s.d.). Test of proportion was used to find the Standard Normal Deviate (Z) to compare the difference proportions and Chi-square (χ^2) test was performed to find the associations. ROC (receiver operating characteristic curve) was used to find the area under curve (AUC) followed by Youden Method was used cut-off value of different parameters for outcomes. $p<0.05$ was taken to be statistically significant.

Methodology

Fig.1 shows the flowchart of methodology. Prospective data of 45 patients admitted from January 2021 to June 2022 with Solitary Brain Lesion (suspected either HGG or SBM) on MRI scan were collected. After those patients underwent surgery, the HPE diagnosis of either HGG, SBM or others such as Lymphoma/Meningioma etc. was established. Clinical, Hematological and Radiological data were collected for each.

Apart from demographic data such as name, age, sex, site and laterality of the tumor, *Clinical* data included *history* (smoking, weight-loss, behavioral changes, memory loss, limb weakness), *warning* symptoms (such as headache, seizures, limb weakness, loss of memory, speech alteration, vomiting, vision loss, bleeding PV or bleeding

PR); *exam* findings (such as decreased air entry on chest auscultation, abdominal lump on palpation, facial nerve palsy, hemiparesis, hemisensory loss, plantar response, lobar signs, pronator drift, impaired speech, cerebellar signs). *Hematological* data included pre-operative Hb, TLC, DLC and NLR. *Radiological* data included tumor characteristics in conventional MRI (T1, T2, edema size, contrast enhancement and pattern, edema/mass ratio), and tumor characteristic in PWI (i.e., rCBV), and in MRS (i.e., Cho:Cr ratio and Cho:NAA ratio) were included.

Each variable was analysed for its corelation with the final diagnosis of either HGG or SBM (univariate analysis). Their significance of association was found with the help of *chi square* or *Fischer extract* test (when frequency in one or more cells was 5 or less).

Multivariate Logistic regression analysis was done for different groups of methods (clinical/haematological/radiological) to know the association with the final diagnosis of HGG or SBM. This showed the individual capability of different methods to diagnose correctly. The ROC was used to know the area under curve (AUC) and cut off values for different quantitative variables to differentiate between HGG and SBM. The maximum AUC represented the most significant variable. The ROC curve shows us the values of sensitivity vs. 1-specificity as the value of the cut-off point moves from 0 to 1. The AUC (area under curve) gives us an idea of how well the model can distinguish between positive and negative outcomes. The AUC can range from 0 to 1. The value of AUC for a variable approaching 1, was significant. The curve was plotted for conventional MRI methods favouring the diagnosis of HGG and another curve was plotted having combined clinical (history and exam), pre-operative NLR and special MRI sequences to diagnose HGG. Both the curves hence plotted were

indicative of capability of conventional MRI alone versus combined clinical, haematological, and special MRI sequences to diagnose HGG and SBM.

Apart from knowing the significance of individual variables in differentiating HGG or SBM, the combined capability of each group, the overall combined capability of different methods to differentiate between the two entities, we tried to find the long debated corelation of smoking with glioma, and the less well-known association of pre-operative NLR with HGG or SBM.

NLR has recently been identified as having prognostic value in various cancers. Theoretically, they seem to have an association with the underlying pathology. Hence, in case of SBM with unknown/known systemic primary, the NLR should be high, and its levels must correlate with the occurrence of a systemic malignancy. This hypothesis was tested in our study. Results of the study were thus achieved.

Ethical considerations

There were no potential risks for the patients participating in the study.

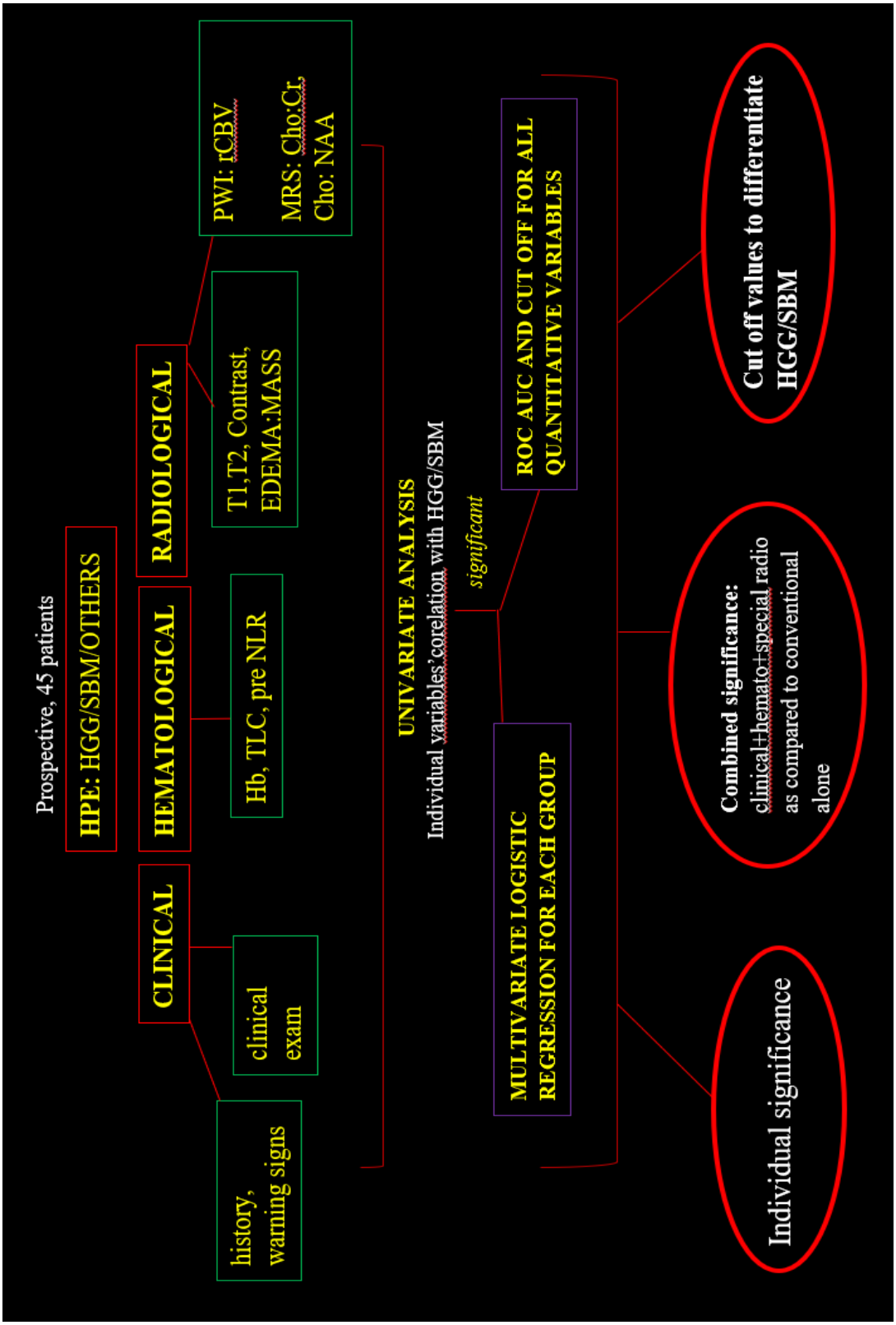


Fig.1. showing the flowchart of methodology of the study.

RESULTS

Out of 45 patients, there were 28 males (62.2%) and 17 females. HGG was diagnosed in 24 patients (53.3%), SBM was diagnosed in 7 (15.6%) and other diagnosis such as meningioma or lymphoma or LGG was present in 14 patients. Amongst others, 11 were LGG (78.6%), 2 were Meningioma (14.3%). Amongst HGG patients, 10 were females (41.66%) and 14 were males. Amongst SBM patients, 2 were females (28.57%) and 5 were males. The most common location of the tumour was frontal (23 patients, 51.11%) followed by temporal lobe (8 patients, 17.77%). There were none in the occipital lobe and 2 patients (4.44%) each for corpus callosum, thalamus, and insula. The solitary lesion was on the right side in 22 patients (48.9%). **Fig.2** shows the above results.

Age-wise distribution is given in **Fig.3**. HGG was most common in age group 40-60 years, with 14 patients out of 24 (58.3%) falling in this age group. the age-group common for SBM was 40-60 years and 60-80 years (3 patients (42.85%) in each group).

Summary of clinical findings is given in **Fig.4**. history of *smoking* was in 11 patients, out of which 7 patients had HGG and 2 patients had SBM, 1 patient had LGG. Hence, 7 out of 24 HGG patients (29.16%) had history of smoking. Similarly, 2 out of 7 SBM patients (28.57%) had history of smoking.

Unintentional weight loss was defined as loss of at least 10% of a person's body weight in six months or 5% in the last month.[18] *Significant weight loss* was defined as loss of >5% of usual body weight over 6-12 months.[19] It was present in 7 patients

including 5 of SBM, 2 of others (Lymphoma). So, out of 7 SBM patients, 4 (57.14%) had history of unintentional significant weight loss.

Amongst warning symptoms, *headache* was present in 28 patients (62.2%), making it the most common presenting symptom. *Vomiting* was present in 14 patients (31.1%). *Seizures* were the presenting complaint in 15 patients (33.3%). *Speech alteration* was present in 9 patients (20%). *Memory loss* was present in 6 patients (13.3%). Either of the *limb weakness* was the presenting complaint in 17 patients (37.8%). *Vision loss* was present in 6 patients (13.3%). *Hearing loss* in 2 patients (4.4%). *Bleeding per vaginum* or *per rectum* was present in 2 patients (4.4%). These symptoms may not be specific to a particular diagnosis but serve the purpose in identifying patients at risk. It is not only useful for the primary treating clinician, but also for the people akin to patients, who can identify these warning symptoms early and help initiate the management at earliest.

Exam findings are summarized in **Fig.5**. *Facial palsy* was present in 18 patients (40%). *Altered sensorium* was the presenting feature in 3 patients (6.7%). *Decreased air entry* in either lung lobes were present in 5 (11.1%). *Abdominal lump* on examination was present in none of the patients. *Hemiparesis* was present in 28 (62.2%) patients (left 15, right 13). *Extensor plantars* were present in 25 patients (55.6%). *Lobar signs* were elicited in 7 patients (15.6%). *Pronator drift* was present in 7 patients (15.6%). *Cerebellar signs* were present in 3 patients (6.7%). *Hemisensory loss* was there in 2 patients (4.4%). These findings assessed by the clinician help diagnose the cranial location of the lesion. It is a step above the suspicion of history and warning symptoms. Decreased air entry (may be present in

case of lung primary) and abdominal lump (in case of intra-abdominal primary) was to confirm any missed primary malignancy.

Haematological parameters are summarized in **Table 1**. pre-operative *Haemoglobin* (Hb) ranged from 8-16.6 g/dl with mean Hb 13.0±1.85. 7 patients (15.6%) were below 8 g/dl and 4 patients were above 16.6 g/dl (8.9%). The mean *Total Leucocyte Count* was 9.51±3.80 x 10^3 ranging from 3.79 - 20.66 x 10^3. 1 patient had count<3.79 (2.2%), 17 patients had counts>20.66 (37.8%). *Preoperative NLR* ranged from 1.264 - 41.227 with mean NLR being 6.18±8.63.

Amongst conventional MRI features, *T1* hypointense lesions were 31 (68.9%), isointense were 8 (17.8%), hyperintense were 5 (11.1%). *T2* hypointense lesions were 6 (13.3%), hyperintense were 29 (64.4%), isointense was 1 (2.2%). *Peritumoral oedema* was defined as mild (0-1 cm), moderate (1-2 cm), severe (>2cm). mild oedema was present in 9 patients (20.5%), moderate in 15 patients (34.1%), severe in 17 (38.6%). *Oedema: mass ratio* ranged from 1.00 - 17.65 with mean ratio of 9.53±5.05. *Contrast enhancement* was heterogenous in 37 patients (82.2%) and homogenous in 4 patients (8.88%). No enhancement was present in 4 patients. The *pattern of enhancement* was peripheral rim enhancing in 24 (58.5%) and central solid enhancing in 17 (41.5%). **Figure 6** Summarizes above parameters.

Special sequence MRI features are summarized in **Table 2**. The *rCBV* ranged from 1.0 - 7.8 with mean value of 3.29±1.84. 8 patients had value<1 (17.8%) and 4 had value>7.8 (8.9%). *Cho:Cr* ratio ranged from 0.70 - 6.80, with mean value of 2.94±1.45. 8 patients had value<0.70 (17.8%) and 1 patient had value>6.80 (2.2%). *Cho: NAA* ratio ranged from 0.40 - 22.67, with mean value of 5.16±4.46. 1 patient had value<0.40 (2.2%) and 18 patients had value>22.67 (40%).

After *chi square test or Fischer extract* test, each variables' association with either HGG or SBM was found (*p*-value). The significant variables were having $p<0.05$.

Unintentional significant weight loss was significantly associated with both HGG (p=0.017) and SBM (p=0.001). Similarly, decreased air entry was associated with both HGG (p=0.017) and SBM (p=0.001). History of smoking had no significant association with either HGG (p=1.0) or SBM(p=0.18). Although, the level of significance was higher for SBM. Hence, we could not find any definite causal relationship between smoking and development of solitary brain lesion. The level of significance was more with SBM denoting that these two findings on initial clinical assessment may raise a suspicion of SBM more than HGG. Exam findings were all non-significant for their association with either of the entities. This signifies that solitary brain lesion may lead to similar neurologic exam findings irrespective of their histopathological diagnosis. Behavioral changes and 7^{th} nerve palsy were significantly associated with HGG (p=0.036 and 0.019 respectively).

Pre-operative Haemoglobin had no significant association with HGG (OR 1.10, p=0.59) or SBM (OR 1.03, p=0.91). Similarly, TLC association was insignificant with HGG (OR 0.95, p=0.56) or SBM (OR 1.27, p=0.08). pre-operative NLR was not significantly associated with HGG (OR 1.02, p=0.67) or SBM (OR 0.85, p=0.31). hence, we could not find any definite role of pre-operative NLR in diagnosis or differentiation of HGG or SBM.

Oedema: mass ratio was significant for diagnosis of SBM (p=0.047) but not for HGG (p=0.534). hence, denoting the fact that oedema is more in proportion to mass in case of SBM. The ratio can differentiate HGG and SBM. It can be helpful in settings where special MRI sequence is not available. Contrast enhancement was significant

for diagnosis of HGG (p=0.039) but not for SBM (p=0.479). Similarly, rCBV had significant association with HGG (p=0.004) but not for SBM (p=0.219). Cho: Cr ratio was significant for HGG (p=0.001) but non-significant for SBM (p=0.054). Cho: NAA ratio was significant for HGG (p=0.003) but non-significant for SBM (p=0.484).

Logistic regression results are given in **Table 3**. for both groups HGG and SBM and significant variables are highlighted therein. Clinical history of behavioral changes and facial asymmetry was significant for diagnosing HGG. History of weight loss was significant for diagnosing SBM. Oedema: mass ratio was almost significant for diagnosing SBM when only conventional MRI was considered. Cho:Cr ratio was significant for diagnosing HGG when special MRI sequences were considered.

Fig.7, table 4 and **Fig.8, table 5** show the ROC and AUC for different variables to diagnose HGG and SBM respectively. There individual cut off values are shown in tables 1 and 2. Cho:Cr ratio has the maximum AUC of 0.929 for HGG with cut off 3.96. This denotes that a value above this cut off will be able to differentiate between SBM and HGG. Oedema: mass ratio has the maximum AUC for SBM with cut off 14.45. Above findings signify that both conventional MRI and special sequence MRI have a role in differentiating the two entities.

Fig.9, 10 show the comparison ROC and AUC for conventional MRI alone versus clinical, pre-operative NLR and special sequence MRI combined to diagnose HGG or SBM. There was increase in the AUC for combined methods, making it clear that it is wiser to consider other methods apart from conventional MRI alone for pre-operative differentiation.

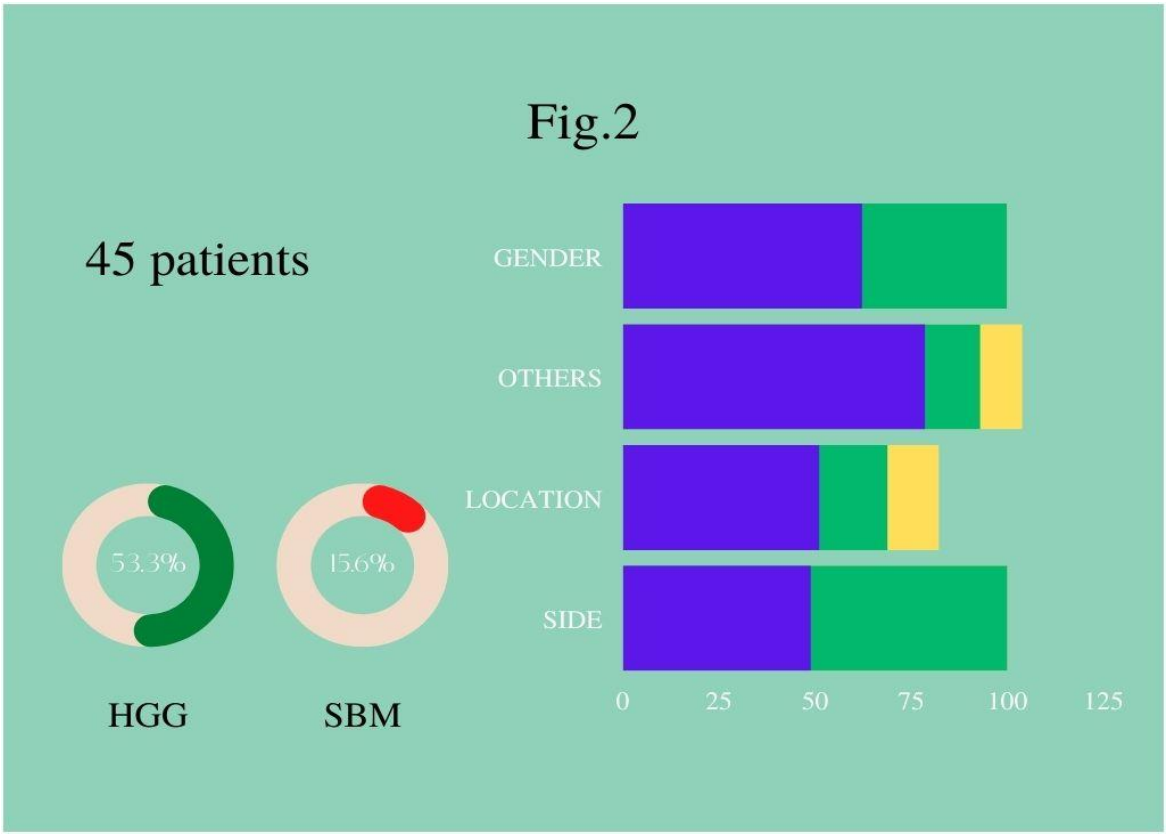


Fig.2
45 patients
GENDER
OTHERS
LOCATION
SIDE
0
25
50
75
100
125
53.3%
15.6%
HGG
SBM


FIG 3
AGE DISTRIBUTION
HGG
VS
SBM
0-20 yrs
20-40 yrs
40-60 yrs
60-80 yrs
>80 yrs

FIG.4
CLINICAL FINDINGS

24.44%
SMOKING

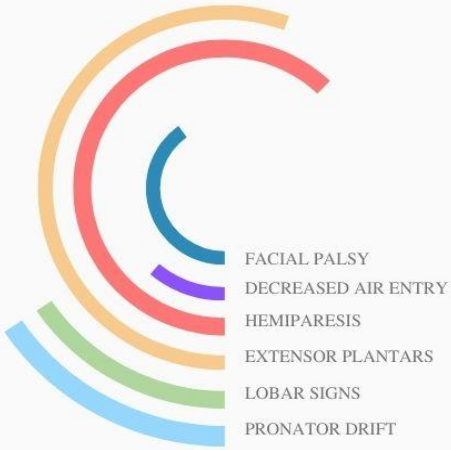
15.55%
WEIGHT LOSS

68.2%
HEADACHE

31.1%
VOMITING

33.3%
SEIZURES

FIG.5. EXAM FINDINGS



40%
FACIAL PALSY

11.1%
DECREASED AIR ENTRY

62.2%
HEMIPARESIS

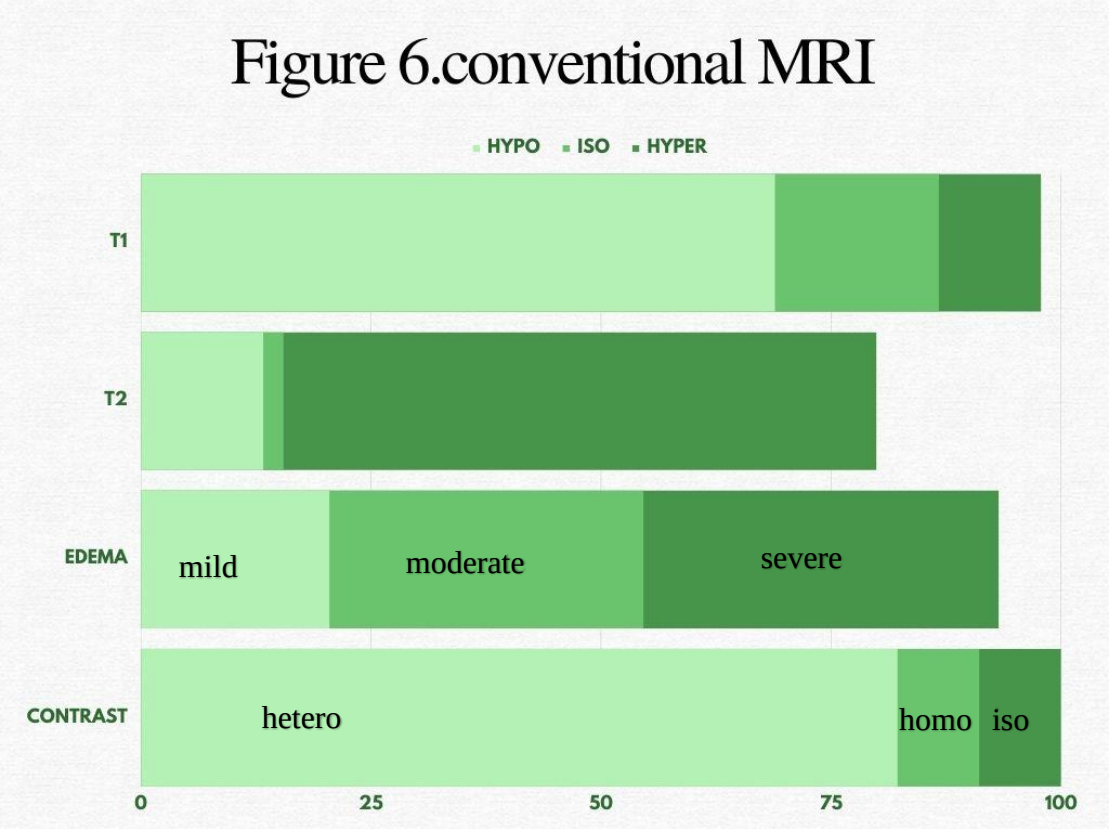
55.6%
EXTENSOR PLANTARS

15.6%
LOBAR SIGNS

15.6%
PRONATOR DRIFT

	PREOP_HB	Preop-TLC	Preop NLR
Mean ± SD	13.00±1.85	9.51±3.80	6.18±8.63
Median	13.4	9	2.966
Range	8.0 - 16.6	3.79 - 20.66	1.264 - 41.227

Table 1: the haematological parameters



	r CBV	Cho: Cr	Cho: NAA
Mean ± SD	3.29±1.84	2.94±1.45	5.16±4.46
Median	3	2.5	3.2
Range	1.0 - 7.8	0.70 - 6.80	0.40 - 22.67

Table 2: the special MRI parameters

Logistic regression of HGG with clinical history						
HGG	**Odds Ratio**	**Std. Err.**	**z**	**P>z**	**[95% Conf.**	**Interval]**
history_smoker	0.6	0.528	-0.530	0.595	0.13	3.20
warning_headache	4.3	3.643	1.720	0.086	0.81	22.65
gen_signs_behaviouralchanges	13.6	16.986	2.090	0.036	1.18	157.04
warning_memoryloss	2.9	3.559	0.890	0.374	0.27	31.59
warning_speechdifficulty	0.6	0.584	-0.520	0.601	0.09	4.02
warning_facialasymmetry	8.2	7.304	2.340	0.019	1.41	47.21
warning_alteredsensorium	0.3	0.515	-0.710	0.476	0.02	6.52
warning_difficultywalking	1.0	1.218	0.030	0.973	0.11	10.31
Logistic regression of SBM with clinical history						
SBM	**Odds Ratio**	**Std. Err.**	**z**	**P>z**	**[95% Conf.**	**Interval]**
generalsigns_sigweightloss	48.03	90.39	2.06	0.04	1.20	1920.13
relevant_signs_decreasedairen	47.64	108.82	1.69	0.09	0.54	4191.67
history_smoker	0.55	0.94	-0.35	0.73	0.02	15.35
warning_headache	4.42	7.59	0.86	0.39	0.15	128.23
warning_speechdifficulty	2.06	3.08	0.48	0.63	0.11	38.70
warning_facialasymmetry	0.89	1.24	-0.09	0.93	0.06	13.72

Table 3: summary of clinical findings.

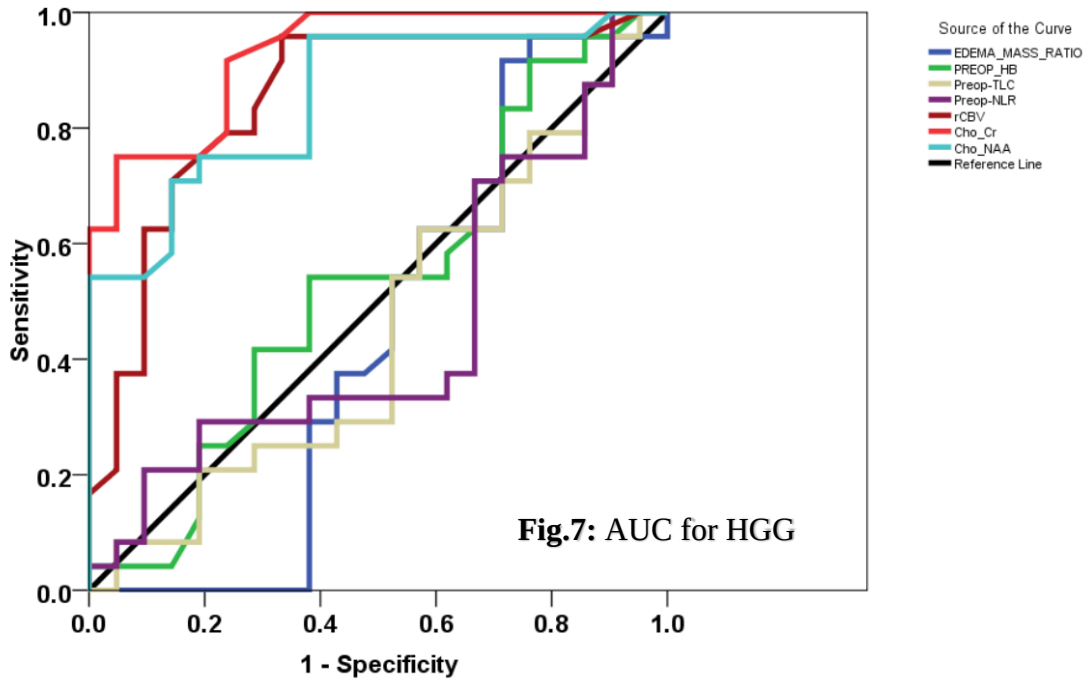


Fig.7: AUC for HGG

Variables	Area Under the Curve (AUC)	Cut-off value
CHO:CR	0.929	3.96
CHO: NAA	0.853	7.35
rCBV	0.850	3.95
PREOP HB	0.533	13.50
Preop NLR	0.456	2.67
Preop TLC	0.454	8.63
EDEMA: MASS RATIO	0.438	11.24

Table 4: cut off values for HGG

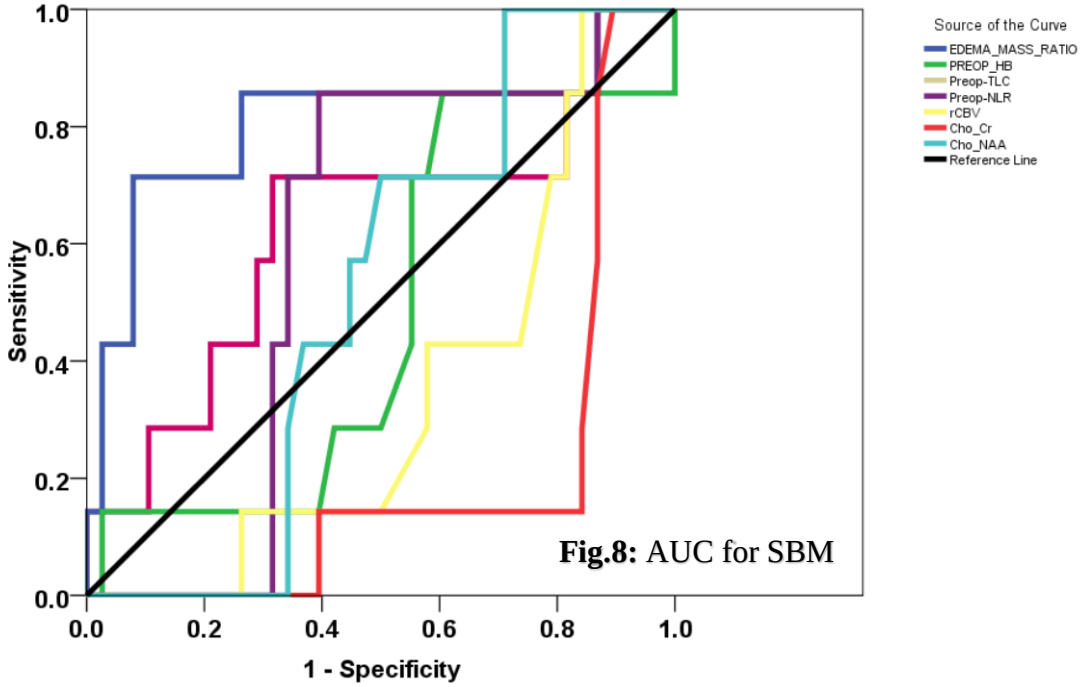


Fig.8: AUC for SBM

Variables	Area Under the Curve (AUC)	Cut-off value
EDEMA:MASS RATIO	0.808	14.45
Preop-TLC	0.628	11.27
Preop-NLR	0.586	4.57
CHO:NAA	0.515	3.80
PREOP_HB	0.477	13.30
rCBV	0.348	2.06
CHO:CR	0.205	1.80

Table 5: cut off values for SBM

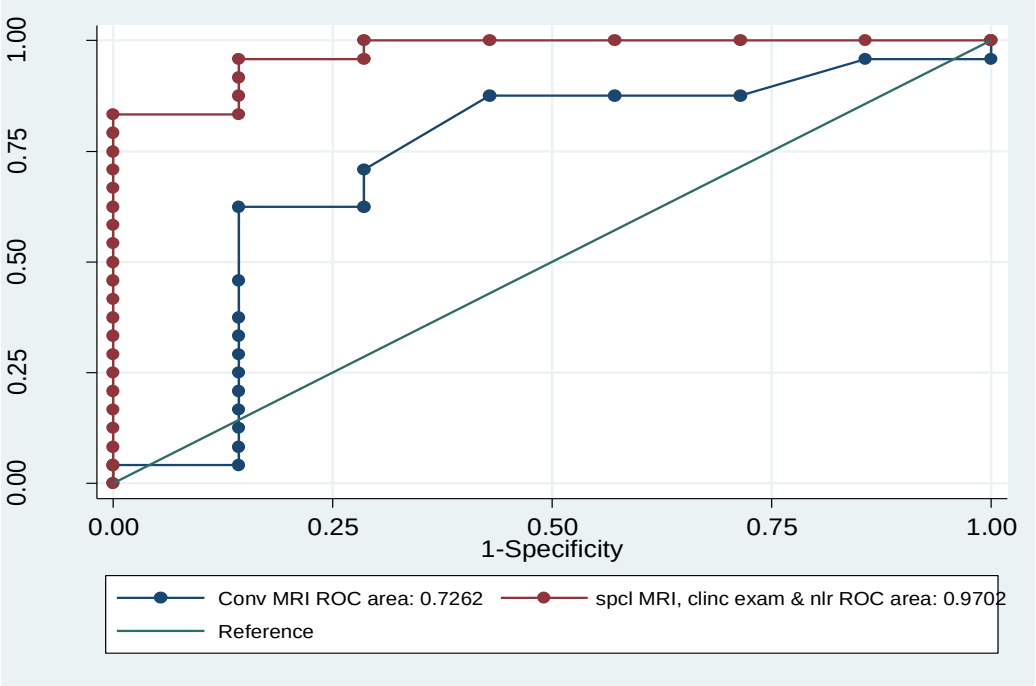


Figure 9: AUC for comparison of conventional MRI alone versus combined special MRI sequences, NLR, clinical exam for the diagnosis of HGG.

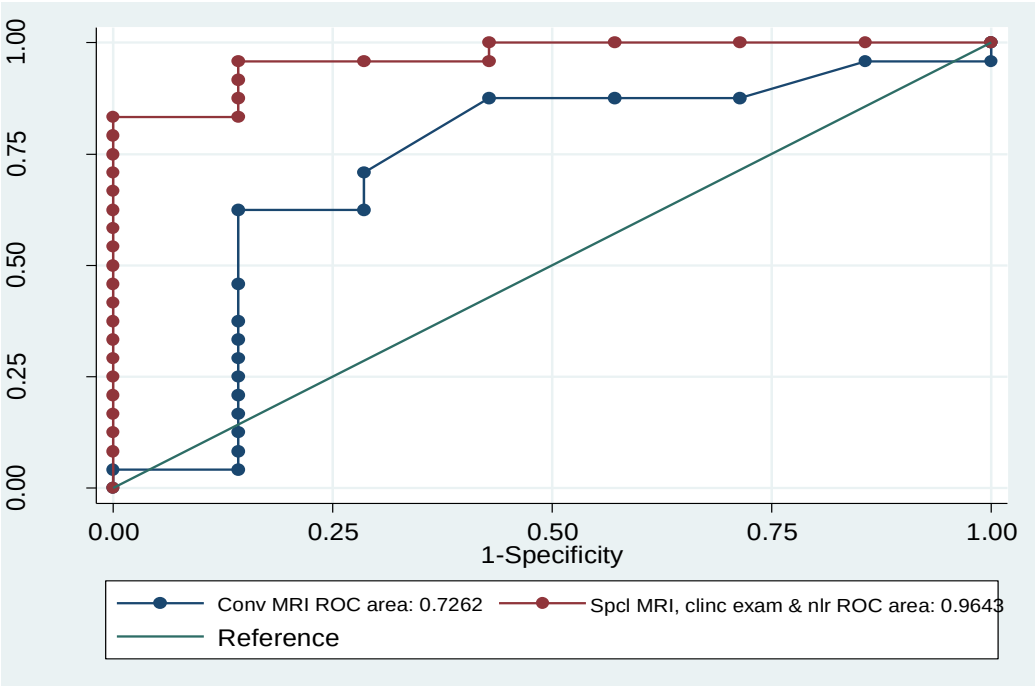


Figure 10: AUC for comparison of conventional MRI alone versus combined special MRI sequences, NLR, clinical exam for the diagnosis of SBM.

DISCUSSION

The most common location is frontal lobe in our study. This was in accordance with neurosurgery literature.[20] HGG is more common in men. Similar finding was in our study. The most common age group was 40-60 years for HGG in our study. The similar finding has been described in study by Wang et al, 2022.[21] It has been known that the incidence of glioblastoma increases with age as described by *Chen et al in 2021*.[22] SBM was more commonly described in older age group, although our study showed its prevalence in even younger age groups. It can hence be said that it can occur in age group 40-80 years. As the incidence of many other malignancies are increasing in younger age groups due to multiple factors such as dietary, smoking, environmental,[23] alcohol consumption, the same trend is followed by the secondaries. Although, the sample size was not adequate to comment on such fact, needs a large sample multicenter study.

Smoking is a long-debated topic when it comes to its relationship with glioma occurrence. *Li et al in 2016* [10] had stated in their meta-analysis that cigarette smoking has no association with glioma. On the contrary, its definite association has been established with occurrence of malignant glioma in the article by *Ahn et al in 2020*.[11] The pathophysiology explained behind above fact is that it affects BBB. Our study shows 29.16% patients having history of smoking turned out to be having HGG, whereas 28.57% with smoking history were having SBM. Above association might be incidental, but it is not too low to be ignored. A larger sample size might be helpful with this respect.

Association of weight loss with brain metastases have been described in paper by *Larieda et al in 2019*.[12] As with other systemic malignancies, weight loss has not been described in relation to glioma. It is often ignored by the clinicians while taking

history keeping glioma in mind. They tend to forget the fact that SBM may have similar presentation. In that case, not only neurologic exam but other systems detailed exam becomes important to know the possible location of primary. In our study, 57.14% patients of SBM had history of unintentional significant weight loss.

Warning symptoms of importance have been described for different malignancies by *Scheel and Holtedahl in 2015*.[4] Also, their importance for a general practitioner identifying their major role in initiation of cancer diagnosis. Although their article fails to define the warning symptoms of a brain malignancy. We identified few symptoms after review of literature of neurosurgery as possible warning symptoms for a brain tumor. Tested its validity in diagnosis. Headache was the most common symptom occurring in 62.2% of our patients. It is possibly the most common presenting symptom in a neurology OPD. For a general practitioner or patient's akin or himself, it should be a warning symptom. Other warning symptoms were limb weakness (37.8%), seizures (33.3%), vomiting (31,1%), speech alteration (20%), memory loss and vision loss (13.3% each). Their role is also important, when a patient comes with primary complaint of headache which is associated with them. Of special mention, complaints of bleeding PV or Bleeding PR may help locate the primary in case of SBM. We hence deduce that it is education about identification of above symptoms, which might help initiate the management at earliest.

Once the above symptoms have been identified, a precise general and systemic exam will be next step to confirm the diagnosis and know the possible location of primary. Hemiparesis was present in 62.2% patients, extensor plantars were present in 55.6%, lobar signs in 15.6%, pronator drift in 15.6%, decreased air entry in lungs in either of lobes were demonstrated in 11.1%. These may not be specific but are quite sensitive

in diagnosing a cranial pathology, as mentioned in many standard neurologic exam textbooks.

There is very little scope for a solitary brain lesion to bleed internally and cause changes in Hemoglobin before causing changes in intracranial pressure. Only 15.6% patients had Hb<8 g/dl in our study. Except for hemangioblastoma, very rarely does a brain lesion causes high Hb. It was excluded owing to its benign nature and almost no similarity with HGG. For a neuro-radiologist, it is not a diagnostic difficulty. Systemic malignancies secreting Erythropoietin are extremely rare to metastasize to brain. Hb>16.6 was present in only 8.9%.

Cancer triggers secondary systemic inflammatory process causing increase in neutrophils and eventual fall in lymphocytes.[15] This is the core reason why pathologists worldwide are considering the NLR to be more sensitive marker of malignancy. A rise in total leucocyte count may occur in many infective and inflammatory conditions. They cannot contribute to narrowing down the diagnosis of solitary brain lesion. Conversely, a DLC can not only be indicative of the pathology behind but may predict survival also. This has been concluded in several studies. *Ashwath et al in 2019* [14] have demonstrated a high pre-operative NLR in HGG and intra-axial tumors. *Li et al in 2020* [13] have laid down its prognostic significance for brain metastasis. Recently, *Hu et al (2022)* [15] have correlated elevated NLR with increased risk of developing brain metastasis. However, in current study no definite correlation of either diagnosis was found. Only this much can be said that a value above the cut off 2.67 was indicative of HGG and a value above the cut off 4.57 was indicative of SBM. Hence, a higher value of pre-operative NLR may indicate the diagnosis of SBM.

Fordham et al in 2021 [16] have said that conventional MRI shows similar features in HGG and SBM. However, *Hakyemez et al in 2010* [8] have already mentioned about the role of simple conventional MRI features such as oedema: mass ratio in differentiation of HGG and SBM. We now have special MRI sequences to be more specific to the diagnosis. But, in settings where special MRI sequences cannot be used owing to unavailability or contrast allergy etc., these simpler methods may be used. In our study, the ROC for SBM showed the maximum AUC of 0.808 which means that it can't be ignored when suspicious of SBM after history and clinical exam.

Even if the peritumoral edema is more in proportion to the mass in case of SBM as compared to HGG, there might be some cases when it is non-conclusive or equal or even less than expected. It is the peritumoral edema inherent characteristic which is most significant in differentiating between the pathologies causing that edema. This has been explained in paper by *Guo et al in 2012*.[24] Tumor cells in case of HGG breach the surrounding pia and infiltrate the surrounding parenchyma and cause changes in local circulation which may be demonstrated in special MRI sequences such as PWI (rCBV) and MRS (Cho:Cr and Cho:NAA). The rCBV denotes peritumoral circulation as per the article by *Aydin et al (2020)* [25] which helps in differentiating HGG from SBM. Our study not only showed that rCBV, Cho:Cr and Cho:NAA ratios are significantly associated with HGG, but it also proposes the cut offs for these parameters. A value of rCBV above 3.95, Cho:Cr ratio above 3.96, Cho:NAA ratio above 7.35 are indicative of HGG.

Neurosurgeons across the world mostly rely completely on conventional MRI features to diagnose various brain lesions namely HGG, LGG, Lymphoma, Meningioma etc. in case the HPE diagnosis comes out to be SBM, it is already late for working up of

the primary. Post-operative recovery, delay of wound healing, complications then become the considerations before initiating adjuvant Radiotherapy or chemotherapy.

CONCLUSION

Differentiating HGG and SBM pre-operatively is necessary. Combining clinical methods, haematological parameters, and MRI features can better differentiate between HGG and SBM than conventional MRI alone, hence a multimodal approach is better. Although insufficient alone, every method has its own role to play in pre-operative diagnosis. A team effort in the form of registering proper history, identification of warning symptoms by patient's acquaintances and general physicians; confirmation of the cranial pathology by the specialist neurosurgeon as well as ordering the correct MRI sequences; their timely interpretation by the neuroradiologist is the key to differentiating high grade glioma from solitary brain metastasis and initiating timely management.

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ANNEXURE-1

अखिल भारतीय आयुर्विज्ञान संस्थान, जोधपुर
All India Institute of Medical Sciences, Jodhpur
संस्थागत नैतिकता समिति
Institutional Ethics Committee

No. AIIMS/IEC/2022/5419 **Date: 22/12/22**

Duplicate Copy

ETHICAL CLEARANCE CERTIFICATE

Certificate Reference Number: **AIIMS/IEC/2021/3400**

Project title: **"Pre-operative differentiation of high grade glioma from solitary metastases of brain by clinical, radiological and haematological parameters: an observational study"**

Nature of Project:	**Research Project Submitted for Expedited Review**
Submitted as:	**M.Ch. Dissertation**
Student Name:	**Dr. Vikrant Sharma**
Guide:	**Dr. Mayank Garg**
Co-Guide:	**Dr. Poonam Elhence, Dr. Abhishek Purohit, Dr. Sarbesh Tiwari & Dr. Jaskaran Singh Gosal**

Institutional Ethics Committee after thorough consideration accorded its approval on above project.
The investigator may therefore commence the research from the date of this certificate, using the reference number indicated above.

Please note that the AIIMS IEC must be informed immediately of:

- Any material change in the conditions or undertakings mentioned in the document.
- Any material breaches of ethical undertakings or events that impact upon the ethical conduct of the research.

The Principal Investigator must report to the AIIMS IEC in the prescribed format, where applicable, bi-annually, and at the end of the project, in respect of ethical compliance.

AIIMS IEC retains the right to withdraw or amend this if:

- Any unethical principle or practices are revealed or suspected
- Relevant information has been withheld or misrepresented

AIIMS IEC shall have an access to any information or data at any time during the course or after completion of the project.

Please Note that this approval will be rectified whenever it is possible to hold a meeting in person of the Institutional Ethics Committee. It is possible that the PI may be asked to give more clarifications or the Institutional Ethics Committee may withhold the project. The Institutional Ethics Committee is adopting this procedure due to COVID-19 (Corona Virus) situation.

If the Institutional Ethics Committee does not get back to you, this means your project has been cleared by the IEC.

On behalf of Ethics Committee, I wish you success in your research.

Dr. Praveen Sharma
Member secretary
Institutional Ethics Committee
AIIMS,Jodhpur

Enclose:
1. Annexue-1

Institutional Ethics Committee
All India Institute of Medical Sciences, Jodhpur

Annexue-1

Meeting of Institutional Ethics Committee held on **10-03-2021** at **11:00** AM.

Following members were participated in the meeting:-

S/No.	Name of Member	Qualification	Role/Designation in Ethics Committee
1.	Dr. F.S.K Barar	MBBS, MD (Pharmacology)	**Chairman**
2.	Justice N.N Mathur	LLB	Legal Expert
3.	Dr. Varsha Sharma	M.A (Sociology)	Social Scientist
4.	Mr. B.S.Yadav	B.Sc, M.Sc (Physics), B.Ed	Lay Person
5.	Dr. K.R.Haldiya	MD (General Medicine)	Clinician
6.	Dr. Arvind Mathur	MBBS, MS (General Medicine)	Clinician
7.	Dr. Surajit Ghatak	MBBS, MS (Anatomy)	Basic Medical Scientist
8.	Dr. Sneha Ambwani	MBBS, MD (Pharmacology)	Basic Medical Scientist
9.	Dr. Kuldeep Singh	MBBS, MD (Pediatrics), DM (General Medicine)	Clinician
10.	Dr. Pradeep Kumar Bhatia	MBBS, MD (Anaesthesiology)	Clinician
11.	Dr. Abhinav Dixit	MBBS, MD (Physiology), DNB (Physiology)	Basic Medical Scientist
12.	Dr. Pankaj Bhardwaj	MBBS, MD (CM&FM)	Clinician
13.	Dr. Tanuj Kanchan	MBBS, MD (Forensic Medicine)	Basic Medical Scientist
14.	Dr. Praveen Sharma	M.Sc, PhD (Biochemistry)	Member Secretary

Dr. Praveen Sharma
Member secretary
Institutional Ethics Committee
AIIMS,Jodhpur

ANNEXURE-2

All India Institute of Medical Sciences, Jodhpur, Rajasthan

Informed Consent Form

Title of Thesis/Dissertation: Pre-operative differentiation of high-grade glioma from solitary metastases of brain by clinical, radiological, and haematological parameters: an observational study

Name of Investigator: Dr Vikrant Sharma **Tel.No.** 9051105143

Patient/Volunteer Identification No.: _____

I,_____ S/o or D/o_____

R/o_____

_____give my full, free, voluntary consent to be a part of the study "Pre-operative differentiation of high grade glioma from solitary brain metastases by clinical, radiological and haematological parameters: an observational study", the procedure and nature of which has been explained to me in my own language to my full satisfaction. I confirm that I have had the opportunity to ask questions. I understand that my participation is voluntary and am aware of my right to opt out of the study at any time without giving any reason.

I understand that the information collected about me and any of my medical records may be looked at by responsible individuals from Department of Neurosurgery, AIIMS, Jodhpur or from regulatory authorities. I give permission to these individuals to have access to my records.

Date: _____ Place: _____

_____

Signature/Left thumb impression

This to certify that the above consent has been obtained in my presence.

Date: _____ Place: _____

_____ Signature of Student

1. Witness 1 2. Witness2

_____ _____

Signature: _____ Signature: _____

Name: _____ Name: _____

Address : _____ Address : _____

ANNEXURE-3

अ खल भारतीय आयु र्वज्ञान संस्थान, जोधपुर, राजस्थान

सू चत सहमति प्रपत्र

थी सस / शोध प्रबंध का शीर्षक: क्लिनिकल, रेडियोलॉजिकल और हेमेटोलॉजिकल मापदंडों द्वारा मस्तिष्क के एकान्त मेटास्टेसिस से उच्च ग्रेड ग्लियोमा के पूर्व-ऑपरेटिव भेदभाव: एक अवलोकन अध्ययन

अन्वेषक का नाम: डॉ। वक्रांत शर्मा Tel.No. 9051105143

रोगी / स्वयंसेवक पहचान संख्या: _____

मैं, _____ S / o या D / o _____

R / o

_____ अपने पूर्ण, मुक्त, स्वैच्छिक सहमति को अध्ययन का हिस्सा बनने के लए नैदानिक क्लिनिकल, रेडियोलॉजिकल और हेमेटोलॉजिकल मापदंडों द्वारा मस्तिष्क के एकान्त मेटास्टेसिस से उच्च ग्रेड ग्लियोमा के पूर्व-ऑपरेटिव भेदभाव: एक अवलोकन अध्ययन", जिस प्र क्रया और प्रकृति से मुझे अपनी भाषा में अपनी पूर्ण संतुष्टि के लए समझाया गया है। मैं पुष्टि करता हूं क मुझे सवाल पूछने का अवसर मला है। मैं समझता हूं क मेरी भागीदारी स्वैच्छिक है और बिना कसी कारण के कसी भी समय अध्ययन से बाहर निकलने के मेरे अ धकार से अवगत हूं।

मैं समझता हूं क मेरे और मेरे कसी भी मे डकल रिकॉर्ड के बारे में एकत्रित जानकारी को न्यूरोसर्जरी वभाग, एम्स, जोधपुर के जिम्मेदार व्यक्तियों या नियामक अ धकारियों से देखा जा सकता है। मैं इन व्यक्तियों को अपने रिकॉर्ड तक पहुंच की अनुमति देता हूं।

दिनांक: _____ स्थान: _____

_____ हस्ताक्षर / बाएं अंगूठे का निशान

यह प्रमा णत करने के लए क मेरी उपस्थिति में उपरोक्त सहमति प्राप्त हुई है।

दिनांक: _____ स्थान: _____

_____ छात्र का हस्ताक्षर

1. साक्षी 1 2. गवाह 2

हस्ताक्षर: _____ हस्ताक्षर: _____

नाम नाम: _____

पता पता : _____

ANNEXURE-4

All India Institute of Medical Sciences, Jodhpur, Rajasthan

Patient Information Sheet

Name of the patient: Patient ID:

Title of the study: pre-operative differentiation of high-grade glioma from solitary metastases of brain by clinical, radiological, and haematological parameters: an observational study.

Aim of the study: This study is being carried out to determine role of clinical and conventional radiological methods in pre-operative diagnosis in patients presenting with solitary brain lesion.

Study setting: This study shall be carried out in the Department of Neurosurgery at AIIMS, Jodhpur.

Study procedure: Demographic and operative and Radiological and laboratory investigation details of all patients undergoing elective craniotomy for tumour excision, will be noted. Postoperatively, patients' HPE reports will be collected. The diagnosis thus obtained will be compared with the provisional diagnosis made based on clinical, radiological, and haematological parameters, preoperatively. The data will be subject to statistical analysis and results will hence be obtained.

Expected duration of participation: First 24 hours before the surgery.

Benefits from the study: This study will help us analyse the utility of clinical, haematological, and radiological parameters, especially in context of brain tumours and develop a system which would help conclude pre-operative diagnosis. The study is an attempt for highlighting above useful pearls of diagnosis in Indian scenario.

Risks expected from the study: Enrolment in this study poses no substantial risk to the participants. An MRI scan does not give ionising radiation exposure to the patient. Routine laboratory investigations will be performed as is done for any pre-operative case. Routine and special sequence MRI scans will be done as per current management practices. The participants will not be exposed to any additional scans for the sole purpose of the study. Patients will be carefully monitored, as routinely done.

Confidentiality of records: All data collected from the participants and his/her medical records will be kept strictly confidential. The confidentiality will be maintained during data collection, analysis, and publication. The records will be preserved for a minimum duration of 3 years.

Compensation for participation: No compensation will be provided to the participants for enrolment in this study.

Freedom to withdraw from the study: All participants are free to withdraw from the study at any point, without assigning any reason, and without the otherwise medical care being affected.

Contact details of the Principal Investigator:

Dr Vikrant Sharma,
Senior Resident,
Department of Neurosurgery, AIIMS, Jodhpur
Phone: 9051105143
Email: vikrant_snmc@yahoo.co.in

Signature of the Principal Investigator

ANNEXURE-5

अखिल भारतीय आयुर्विज्ञान संस्थान, जोधपुर, राजस्थान

रोगी सूचना पत्रक

रोगी का नाम: रोगी आईडी:

अध्ययन का शीर्षक: क्लिनिकल, रेडियोलॉजिकल और हेमेटोलॉजिकल मापदंडों द्वारा मस्तिष्क के एकान्त मेटास्टेस से उच्च-श्रेणी के ग्लियोमा का प्री-ऑपरेटिव भेदभाव: एक अवलोकन अध्ययन।

अध्ययन का उद्देश्य: यह अध्ययन एकान्त मस्तिष्क घाव वाले रोगियों में पूर्व-संचालन निदान में नैदानिक और पारंपरिक रेडियोलॉजिकल तरीकों की भूमिका निर्धारित करने के लिए किया जा रहा है।

अध्ययन सेटिंग: यह अध्ययन एम्स, जोधपुर के न्यूरोसर्जरी विभाग में किया जाएगा।

अध्ययन प्रक्रिया: ट्यूमर छांटने के लिए वैकल्पिक क्रैनियोटॉमी से गुजरने वाले सभी रोगियों की जनसांख्यिकीय और ऑपरेटिव और रेडियोलॉजिकल और प्रयोगशाला जांच विवरण नोट किया जाएगा। ऑपरेशन के बाद, मरीजों की एचपीई रिपोर्ट एकत्र की जाएगी। इस प्रकार प्राप्त निदान की तुलना क्लिनिकल, रेडियोलॉजिकल और हेमेटोलॉजिकल मापदंडों के आधार पर किए गए अनंतिम निदान के साथ की जाएगी। डेटा सांख्यिकीय विश्लेषण के अधीन होगा और इसलिए परिणाम प्राप्त किए जाएंगे।

भागीदारी की अपेक्षित अवधि: सर्जरी से पहले 24 घंटे पहले।

अध्ययन से लाभ: यह अध्ययन हमें क्लिनिकल, हेमेटोलॉजिकल और रेडियोलॉजिकल पैरामीटर्स की उपयोगिता का विश्लेषण करने में मदद करेगा, विशेष रूप से ब्रेन ट्यूमर के संदर्भ में और एक ऐसी प्रणाली विकसित करेगा जो प्री-ऑपरेटिव डायग्नोसिस को समाप्त करने में मदद करेगी। यह अध्ययन भारतीय परिदृश्य में निदान के उपयोगी मोतियों को उजागर करने का एक प्रयास है।

अध्ययन से अपेक्षित जोखिम: इस अध्ययन में नामांकन से प्रतिभागियों को कोई बड़ा जोखिम नहीं है। एक एमआरआई स्कैन रोगी को आयनकारी विकिरण जोखिम नहीं देता है। किसी भी प्री-ऑपरेटिव केस की तरह नियमित प्रयोगशाला जांच की जाएगी। नियमित और विशेष अनुक्रम एमआरआई स्कैन मौजूदा प्रबंधन प्रथाओं के अनुसार किया जाएगा। अध्ययन के एकमात्र उद्देश्य के लिए प्रतिभागियों को किसी भी अतिरिक्त स्कैन से अवगत नहीं कराया जाएगा। मरीजों की सावधानीपूर्वक निगरानी की जाएगी, जैसा कि नियमित रूप से किया जाता है।

अभिलेखों की गोपनीयता: प्रतिभागियों से एकत्र किए गए सभी डेटा और उनके चिकित्सा अभिलेखों को कड़ाई से गोपनीय रखा जाएगा। डेटा संग्रह, विश्लेषण और प्रकाशन के दौरान गोपनीयता बनाए रखी जाएगी। अभिलेखों को न्यूनतम 3 वर्ष की अवधि के लिए संरक्षित किया जाएगा।

भागीदारी के लिए मुआवजा: इस अध्ययन में नामांकन के लिए प्रतिभागियों को कोई मुआवजा नहीं दिया जाएगा।

अध्ययन से हटने की स्वतंत्रता: सभी प्रतिभागी किसी भी समय, बिना कोई कारण बताए, और अन्यथा चिकित्सा देखभाल प्रभावित हुए बिना अध्ययन से हटने के लिए स्वतंत्र हैं।

प्रधान अन्वेषक का संपर्क विवरण:

डॉ विक्रांत शर्मा,
वरिष्ठ निवासी,
न्यूरोसर्जरी विभाग, एम्स, जोधपुर
फोन: 9051105143
ईमेल: vikrant_snmc@yahoo.co.in

प्रधान अन्वेषक के हस्ताक्षर

ANNEXURE-6

All India Institute of Medical Sciences, Jodhpur, Rajasthan

Declaration by the Student

I hereby declare that:

1. The study will be done as per ICMR/GCP guidelines.

2. The study has not been initiated and shall be initiated only after ethical clearance.

3. Voluntary written consent of the volunteers/patients will be obtained.

4. In case of children or mentally handicapped volunteers/patients, voluntary written informed consent of the parents/guardians will be obtained.

5. The probable risks involved in the study will be explained in full to the subjects/parents/guardians in their own language.

6. Volunteers/patients/parents/guardians will be at liberty to opt out of the study at any time without assigning reason.

7. I will terminate the study at any stage, if I have probable cause to believe, in the exercise of the good faith, skill and careful judgement required for me that continuation of the study/experiment is likely to result in injury/disability/death to the volunteers/subject.

Date: _____

Department _____ (Signature of Student)

Department _____ (Signature of Guide)

ANNEXURE-7

Data collection proforma

Serial number:

1. **Demographic details:**
   Name: Age/sex: Hospital number:

   Contact number: Diagnosis:

2. **Operation details**

   Date of surgery: Surgery performed:

3. **HPE report:**

4. **Pre-operative clinical:**

   General signs of cancer: present/absent details:

   Warning signs of cancer: present/absent details:

   Signs relevant of Brain tumour: present/absent details:

   Relevant Examination findings: present/absent details:

5. **Preoperative haematological:**

   Hb:
   TLC:
   DLC:
   NLR:

6. **Preoperative Radiological:**

   Conventional MRI findings: Location:
   T1 characteristics:
   T2 characteristics:
   Contrast enhancement:
   Peritumoral edema:
   Edema: mass ratio:

   Special imaging: PWI-
   rCBV in peritumoral region:

   MRS- Cho:Cr ratio:
   Cho:NAA ratio:

7. **Remarks:**
8. **Signature:**

MASTER CHART

S.NO.	NAME	AGE	SEX	HOSPITAL ID	DIAGNOSIS	DATE OF SX	HPE REPORT	CLINICAL					HEMATOLOGICAL			
								history	GENERAL Signs		WARNING SIGNS	EXAM FINDINGS	PREOP HB	TLC	DLC	preNLR
1	shiva ram	56	m	2020/11/000715	left TEMPORO-PARIETAL SOL	07-11-2020	glioblastoma (WHO grade 4) (HGG)	weight loss (aco TB), BIDI SMOKER	left upper lobe air entry reduced		headache, memory loss, slurring of speech, right sided weakness	right hemiparesis, motor dysphasia	13.8	9.05	N73.1L15.5M9.1E2.1B0.2	4.716
2	Khiwraj	54	m	2021/01/020914	left Frontal SOL	31-01-2021	angiomatous meningioma(OTHERS-MENINGIOMA)	generalised weakness	confusion(BEHAVIOURAL)		seizures	frontal lobe signs (apathy, abulia, personality changes)(lobar), plantars extensors	15.2	8.01	N79.9L12.4M7.5E0.1B0.1	6.443
3	Heena Malviya	22	f	2013/02/02323	right frontal glioma	20-06-2021	GLIOMA GRADE 2(OTHERS-LGG)				seizures, headache, vomiting	left UMN 7th nerve palsy, bilateral pronator drift	9.5	9.46	N74.7L13.4M11.4E0.2B0.3	5.574
4	Gopal K Lohra	71	m	2021/02/006321	corpus callosal SOL	05-03-2021	glioblastoma grade 4(HGG)	generalized weakness, low mood, disturbed sleep, giddiness	behavioural changes		headache	left monoparesis, left plantar extensor, lobar signs (depressed mood, reduced writing)	10.4	13	N93.4L3.9M2.6E0B0.1	23.948
5	Prameela Mathur	56	F	2020/12/002613	right frontal solid cystic SOL	14-12-2020	anaplastic astrocytoma (grade 3)(HGG)				headache, left focal seizure with secondary generalisation	left hemiparesis, bilateral plantars flexors	12.9	11.98	N83.6L13.8M1.5E0.5B0.6	6.057
6	Pemp Kanwar	55	F	2020/11/005099	Left frontal SOL	24-11-2020	metastasis of epithelial malignancy(SBC)	generalized weakness	non significant weight loss		headache, incontinence,vomiting, right sided weakness	right hemiparesis, left plantar extensor	16.1	12.48	N77.7L14.3M6.7E0.7B0.6	5.433
7	Kanav	14	m	2021/05/006666	left temporal SOL	21-05-2021	left temporal high grade glioma (possible anaplastic ependymoma, confirmed from NIMHANS)(HGG)				headache, seizures	right 7th UMN palsy, right pronator drift, bilateral plantars extensors	13.3	6.22	N53.3L32.3M10.1E3.7B0.6	1.65
8	Shoaib Ansari	49	m	2021/05/006722	right parietotemporal SOL	29-05-2021	high grade CNS lymphoma (DLBCL)(OTHERS-LYMPHOMA)	generalized weakness	significant weight loss		left sided weakness, irrelevant talk, imbalance	left UMN 7h nerve palsy, left hemiparesis, left plantar extensor	14.1	12.59	N87.5L2.3M4.2E0B0	38.043
9	Daku	53	f	2020/12/001549	right frontal SOL	05-07-2021	oligodendroglioma grade 2(OTHERS-LGG)			bleeding P/V (adenocarcinoma cervix)	headache, seizures, right sided weakness, speech difficulty	right UMN 7th nerve palsy, dysarthria, right hemiparesis, right plantar extensor	9	6.64	N50.7L40.1M7.5E1.5B0.2	1.264
10	sukdi	58	f	2021/06/001843	left thamalic HGG	01-07-2021	epitheloid glioblastoma(HGG)			HEMISENSORY LOSS	right sided weakness, speech difficulty, urinary incontinence	left ptosis, right UMN 7th palsy, dysarthria, right hemiparesis, right plantar extensor, pain and temp impaired over right side of body	14.7	9	N64.6L23.9M10.9E0.8B0.3	2.7
11	gulab nath	50	m	2020/10/002187	right thalamic SOL	01-09-2021	high grade B cell Hodgkin lymphoma(OTHERS-LGG)			HEMISENSORY LOSS	left sided weakness, slurring of speech	left hemiparesis, left plantar extensor	13.6	7.62	N61.5L28.7M7.1E2.2B0.5	2.142
12	bheekha ram dudi	61	m	2021/07/017130	right temporal glioma	10-09-2021	glioblastoma grade 4(HGG)	bidi smoker	diminished vision		headache	left temporal field cut, bilateral plantars flexors	16.6	6.16	N78.2L13.9M7.1E0.6B0.2	5.625
13	lata devi	30	f	2021/09/002855	left frontal SOL	07-09-2021	pilocytic xanthoastrocytoma (grade 2)(OTHERS-LGG)				headache, seizures	right UMN 7th nerve palsy, right hemiparesis, right plantar extensor	10.8	13.32	N91.4L4.6M3.9E0B0.1	19.869
14	bilkish bano	60	f	2015/05/010903	right frontal SOL	10-09-2021	glioblastoma grade 4(HGG)				memory loss, left sided weakness	left hemiparesis, left pronator drift	12.3	9.33	N54L39.8M5.0E0.9B0.3	1.356
15	chuna ram	51	m	2021/07/006453	left Frontal SOL	12-09-2021	oligodendroglioma grade 3(HGG)	cigarette smoker	behavioural changes		seizures, headache, dysphasia	bilateral plantars flexros, speech fluency and comprehension reduced	14.6	6.72	N63.7L27.5M6.3E1.6B0.9	2.316
16	hema ram	50	m	2021/09/009140	right temporoparietal SOL	17-09-2021	gliobastoma IDH-1 mutant(HGG)				headache, vomting, left sided weakness	right UMN 7th palsy, left hemiparesis, left grade 1 spasticity, left plantars extensors	13.8	4.11	N67.6L31M8.5E2.5B0.4	2.18
17	deva ram	50	m	2021/09/012198	left temporal SOL	27-09-2021	anaplastic astrocytoma (grade 3)(HGG)	bidi smoker			right sided weakness, right focal seizures	right hemiparesis	12.3	7.65	N56.2L29.2M11.5E2.2B0.9	1.924
18	honey bhawnani	48	f	2021/09/016420	right medial temporal SOL	22-02-2021	gemistocytic astrocytoma grade 2(OTHERS-LGG)				left focal seizures	bilateral plantars flexors	13.4	11.42	N71.5L24.1M3.6E0.4B0.4	2.966
19	magan devi	48	f	2021/08/003718	right insular glioma	29-11-2021	diffuse astrocytoma grade 2(OTHERS-LGG)				seizures, headache	left UMN 7th nerve palsy, left hemiparesis, left plantar extensor	10.9	4.27	N61.1L27.9M9.6E0.9B0.4	2.189
20	sugno	54	f	2021/12/001464	right temporal SOL	09-12-2021	epitheloid glioblastoma with sarcomatoid transformation(HGG)				reduced speech output, seizures, headache, vomiting	left UMN 7th palsy, left pronator drift	11.1	9.25	N52.8L35.8M9.0E1.5B0.8	1.474
21	savita	26	f	2021/12/004767	left middle frontal SOL	27-12-2021	gliosarcoma grade 4 IDH wild(HGG)		left eye deviation, behavioural changes		headache, vomiting, memory loss, left facial deviation	right UMN 7th palsy, bilateral plantars extensors	14.3	17.3	N90.3L6.0M3.7E0B0	15.05
22	mahendra meghwal	17	m	2021/11/012541	left cerebellar SOL	02-02-2022	pilocytic astrocytoma grade 1(OTHERS-LGG)				altered sensorium, intermittent left side swaying(imbalance), headache, vomiting	grade 1 papilledema, cerebellar signs	12.6	3.79	N74.9L19.6M4.3E0.6B0.6	3.821
23	sharvan choudhary	48	m	2022/02/002277	right temporal glioma	28-02-2022	glioblastoma grade 4 IDH mutant(HGG)				focal sensory seizure, left tingling/numbness	bilateral plantars flexors	14.7	7.3	N49.8L34.6M9.0E6.1B0.5	1.439
24	sata ram	63	m	2022/01/025667	left parital glioma (postcentral)	28-02-2022	metastatic cancer(SBC)	chronic smoker, opioid addict	significant weight loss	bilateral air entry reduced, wheeze	Right Upper Limb numbness and weakness	bilateral plantars mute, right 7th UMN paresis, right handgrip weak(monoparesis), right hand sensation reduced by 50%(paresthesia)	12.9	10.29	N77.4L15.5M6.5E0.1B0.5	4.993
25	babu lal	58	m	2022/02/008507	cerebellar vermian SOL	07-04-2022	metastatic cancer (lung)(SBC)	chronic smoker	non significant weight loss	reduced air entry in left hilar region	dysarthria, difficulty walking	pendular knee jerk, tandem gait	13.3	13.02	N72.7L15.9M4.1E6.6B0.7	4.572
26	ladu ram	65	m	2022/04/005541	right temporal SOL	2/5/22, 4/5/22	metastatic cancer (large cell neuroendocrine carcinoma lung)(SBC)	pulmonary TB, generalised weakess	significant weight loss, left chest decreased air entry	left chest air entry reduced	slurring of speech	right UMN 7th palsy, left plantar extensor, broca's aphasia	13.4	11.27	N76.9L15.5M6.9E0.5B0.2	4.961
27	sultan alam	68	m	2017/02/008897	left temporal SOL	31-05-2022	B cell NHL(OTHERS-LGG)	smoker	non significant weight loss		memory loss, reduced naming(speech alteration),confusion	frontal lobe signs present(lobar)	12.1	7.61	N57L26.9M10.2E5.4B0.5	2.118
28	goutam bhakal	37	m	2022/07/000670	left Frontal SOL	03-07-2022	glioblastoma grade 4(HGG)		reduced vision left eye, BEHAVIOURAL CHANGES		seizures, vomiting, headache, difficulty walking	right pronator drift, bilateral plantars flexros	12.7	11.13	N69.1L22.9M7.4E0.4B0.2	3.017
29	paru devi	51	f	2022/03/007850	left frontal	14-03-2022	metastatic cancer (adenocarcinoma colon)(SBC)	smoker	significant weight loss	bleeding P/R, abdominal pain, constipation	right sided weakness, headache	right hemiparesis, right plantar extensor, right UMN 7th palsy, abdominal mass palpable	8	20.66	N76.4L17.2M6.2E0.2B0	4.441
30	lal singh	63	m	2021/06/011656	RIGHT FRONTAL	27-06-2021	metastatic cancer (lung)(SBC)	smoker	significant weight loss	decreased air entry bilateral	headache	left hemiparesis, left plantar extensor	13.6	5.55	N44.4L13.5M16.6E7.6B0.9	3.288
31	ram nivas	36	m	2021/05/008290, 2021/08/005192	LEFT FRONTAL	06-10-2021	glioblastoma grade 4(HGG)		confusion(BEHAVIOURAL)		seizure, right sided weakness	right hemiparesis	14.3	7.15	N69.3L28.1M8.5E3.9B0.2	2.466
32	Sohni Devi	73	f	2021/12/011207	right frontal SOL	18-02-2022	angiomatous meningioma(OTHERS-MENINGIOMA)	chronic bidi smoker		left chest air entry reduced	headache, left upper limb weakness	left UMN 7th palsy, left pronator drift, bilateral plantars extensor	13.4	7.33	N72.5L18.2M8.5E0.4B1.2	3.983
33	Bhagirath	60	m	2022/02/007009	right frontotemporal glioma	18-02-2022	anaplastic oligodendroglioma(HGG)	cigarette smoker			headache, vomiting, reduced sensorium, left sided weakness	left UMN 7th palsy, left hemiparesis	12.7	8.26	N80.7L11.3M7.9E0B0.1	7.141
34	Kalawati	55	f	2022/02/011211	right frontal glioma	20-02-2022	glioblastoma grade 4(HGG)		behavioural changes		headache, vomiting	left UMN 7th palsy, plantars bilateral extensors	11.6	5.83	N65.7L24.8M7.9E1.4B0.2	2.649
35	Bagda Ram	40	m	2022/03/013631	left frontal glioma	27-03-2022	glioblastoma grade 4(HGG)	cigarette smoker			right upper limb weakness, difficulty walking	right lower limb spastic weakness, right UMN 7th palsy, right hemiparesis, plantars bilateral extensors	13.7	7.87	N68.9L24.4M6.2E0.4B0.1	2.823
36	durga ram	32	m	2021/09/008453	left fr MFG glioma	07-10-2021	diffuse astrocytoma with oligodendroglioma (grade 2)(OTHERS-LGG)				seizures	frontal lobe signs(lobar), decreased fluency, altered behavior	14.7	7.21	N61.4L28.8M6.5B0.2E3.1	2.131
37	BHOORI DEVI	32	M	2021/09/016075	corpus callosal SOL	08-10-2021	glioblastoma grade 4(HGG)				HEADACHE, LEFT SIDED WEAKNESS, URINE INCONTINENCE, DECREASED SPEECH	DECREASED FLUENCY, FRONTAL LOBE SIGNS(lobar), LEFT HEMIPARESIS, PLANTAR LEFT EXTENSOR	13	5.49	N59.6L29.5M8.6B0.5E1.8	2.02
38	JAWAN RAM	36	M	2021/07/011376	LEFT INSULAR GLIOMA	25-10-2021	GRADE 2 GLIOMA(OTHERS-LGG)	bidi smoker			HEADACHE, SEIZURES, ALTERED SENSORIUM	BILATERAL PLANTARS EXTENSOR	16	15.51	N76.8L12.1M11.1E0B0	6.347
39	KAVITA	11	F	2021/10/015587	RIGHT FRONTAL SOL	29-10-2021	pilocytic astrocytoma grade 1(OTHERS-LGG)		LISCH NODULES, MULTIPLE HYPERPIGMENTED SPOTS, NEUROFIBROMA, CAFÉ AU LAIT		HEADACHE,VOMITING, ALTERED SENSORIUM	BILATERAL TEMPORAL HEMIANOPIA, GR 4 PAPILLOEDEMA, PLANTARS LEFT EXTENSOR	13.9	11.92	N48.9L38.1M10.7E1.7B0.6	1.283
40	MUBAREEK HUSSAIN	37	M	2021/11/002606	LEFT FRONTAL GLIOMA	09-11-2021	glioblastoma grade 4(HGG)	GENERALISED WEAKNESS	DECREASED VISION		HEADACHE, VOMITING	RIGHT HEMIPARESIS, FRONTAL LOBE SIGNS(lobar), PLANTARS RIGHT UPGOING	12.5	9.31	N80.8L35.7M3E0.1B0.4	2.263
41	MAGHU KANWAR	34	F	2021/11/006851	RIGHT FRONTAL SOL	17-11-2021	diffuse astrocytoma with oligodendroglioma (grade 2)(OTHERS-LGG)				SEIZURES, LEFT SIDED WEAKNESS	LEFT HEMIPARESIS, PLANTARS BILATERAL FLEXOR	13.5	7.26	N68.5L25.5M5.9E0B0.1	2.686
42	AJAY KUMAR	46	M	2022/01/020061	RIGHT FRONTAL GLIOMA EXTENDING TO LEFT	05-01-2022	glioblastoma grade 4(HGG)		BLURRING OF VISION		HEADACHE, VOMITING, SEIZURES	PLANTAR LEFT extensor	9	12.9	N90.7L2.2M7.1E0B0	41.227
43	RAJU RAM	60	F	2022/05/019157	LEFT PRECENTRAL GYRUS	02-06-2022	glioblastoma grade 4(HGG)	bidi smoker	BEHAVIOURAL CHANGES		HEADACHE, VOMITING, DECREASED SPEECH	RIGHT PRONATOR DRIFT, RIGHT PLANTAR EXTENSOR	13.9	12.86	N71.5L27.9M5.6E0B0	2.562
44	RAJAK KHAN	27	M	2022/06/018310	RIGHT FRONTAL SOL	30-06-2022	anaplastic oligodendroglioma(HGG)		DOUBLE VISION		HEADACHE, VOMITING, FORGETFULNESS(memory loss)	LEFT PLANTAR EXTENSOR	13.5	4.67	N56.6L31.6M7.3E3.9B0.6	1.791
45	HARJI RAM	29	M	2022/05/003411	RIGHT CEREBELLAR	24-07-2022	glioblastoma grade 4(HGG)	generalized weakness	DECREASED HEARING		HEADACHE, VOMITING, IMBALANCE	RIGHT UMN 7TH PALSY, RIGHT HEMIPARESIS, CEREBELLAR SIGNS	13.5	18.07	N89.1L8.1M2.6E0.2B0	11

S.NO.	NAME	AGE	SEX	HOSPITAL ID	RADIOLOGICAL								
					CONVENTIONAL MRI						PWI	MRS	
					LOCATION	T1	T2	CONTRAST enhancement	PERITUMORAL EDEMA	EDEMA: MASS RATIO	rCBV	Cho:Cr	Cho:NAA
1	shiva ram	56	m	2020/11/000715	left temporal lobe								
2	Khiwraj	54	m	2021/01/020914	LEFT ANTERIOR FRONTAL	HYPER	HYPER	HETEROGENOUS ENHANCING	severe edema(>2cm)	11.21	6.7	1.2	0.4
3	Heena Malviya	22	f	2013/02/02323	right frontal, upto cingulate gyrus	hypo	hypre (hetero)	enhancement (peripheral)(HETEROGENOUS)	no (0cm)	1.34	2.4	1.8	3
4	Gopal K Lohra	71	m	2021/02/006321	right frontoparietal upto left parietal	hypo	hetero	peripheral	severe edema(>2cm)	12.44	6.9	4.02	22.67
5	Prameela Mathur	56	F	2020/12/002613	right frontal, upto cingulate gyrus	iso	hyper	homogenous (solid part)	severe edema(>2cm)	11	3.7	3.2	4.1
6	Pemp Kanwar	55	F	2020/11/005099	left frontoparietal	HYPO	HYPER	irregular peripheral(HETERO)	MODERATE(1-2cm)	12.31	2.8	1.8	2.2
7	Kanav	14	m	2021/05/006666	left parietotemporal	hypo	hyper	homogenous	MILD(<1cm)	16.67	4.8	3.5	3.8
8	Shoaib Ansari	49	m	2021/05/006722	right frontoparietal	hypo	hypo	HOMOGENOUS (SOLID)	severe edema(>2cm)	10.47	1.8	0.97	0.87
9	Daku	53	f	2020/12/001549	right frontal operculum and inferior frontal gyrus	hypo	hyper	none	severe edema(>2cm)	15.87	1.2	1.97	1.87
10	sukdi	58	f	2021/06/001843	left thalamus	hypo	hetero	peripheral(hetero)	severe edema(>2cm)	13.9	3.2	2.9	4.9
11	gulab nath	50	m	2020/10/002187	right thalamus	HYPO	HYPER	HOMOGENOUS ENHANCING	MODERATE(1-2cm)	6.78	1.6	1.1	1.2
12	bheekha ram dudi	61	m	2021/07/017130	right temporal	hyper	hyper	heterogeneous	MODERATE(1-2cm)	4.55	7.2	4.6	8.9
13	lata devi	30	f	2021/09/002855	left frontal	ISO	HYPO	NONE	MILD(<1cm)	1.8	1.4	2.3	1.8
14	bilkish bano	60	f	2015/05/010903	right frontal	hypo + hyper	hypo	peripheral with nodular internal(hetero)	severe edema(>2cm)	12.87	6.4	3.01	11.3
15	chuna ram	51	m	2021/07/006453	left frontal (superior and middle)	hypo	hetero hyper	heterogeneous	MODERATE(1-2cm)	5.67	3	2	2.7
16	hema ram	50	m	2021/09/009140	right temporo-parietal	ISO	HYPER	HETEROGENOUS ENHANCING	MILD(<1cm)	2.33	1.1	6.8	4.7
17	deva ram	50	m	2021/09/012198	left medial temporal lobe	hypo	hyper	peripheral ring enhancement(hetero)	severe edema(>2cm)	13.77	2.4	2.5	2.4
18	honey bhawnani	48	f	2021/09/016420	right anterior and medial temporal lobe with extension to right insula	iso	hyper	hetero	severe edema(>2cm)	16.2	2.2	2.6	1.99
19	magan devi	48	f	2021/08/003718	right frontal inferior gyrus, operculum. Insula	hypo	hyper	none	MODERATE(1-2cm)	8.99	3	2	1.9
20	sugno	54	f	2021/12/001464	right temporal	iso	hetero hyper	hetero	moderate edema(1-2cm)	5.43	5	2.3	3.3
21	savita	26	f	2021/12/004767	left frontal and insular	iso	iso	hetero	moderate edema(1-2cm)	4.53	4	6	4
22	mahendra meghwal	17	m	2021/11/012541	left cerbellar hemisphere	hypo	hyper	hetero	MILD(<1cm)	8.77	1.1	2.7	3.05
23	sharvan choudhary	48	m	2022/02/002277	right superior temporal and insular	hypo	hyper	peripheral(hetero)	MILD(<1cm)	3.44	2.4	2.4	2.8
24	sata ram	63	m	2022/01/025667	left postcentral gyrus	hypo	hypo hyper (solid)	HETEROGENOUS ENHANCING	mild edema(<1cm)	2.11	1.7	1.6	6.4
25	babu lal	58	m	2022/02/008507	cerebellar vermis	HYPO	HYPER	HETEROGENOUS ENHANCING	severe edema(>2cm)	14.14	1.9	1.2	2.2
26	ladu ram	65	m	2022/04/005541	left frontal operculum	hypo	hyper	irregular peripheral(HETERO)	severe edema(>2cm)	17.65	1.5	1.8	4.9
27	sultan alam	68	m	2017/02/008897	left temporal lobe	hypo	hyper	HETEROGENOUS ENHANCING	MILD(<1cm)	11.65	1.9	0.7	3.2
28	goutam bhakal	37	m	2022/07/000670	left frontal	hypo	hyper	hetero	severe edema(>2cm)	13.22	>10	5.2	8.8
29	paru devi	51	f	2022/03/007850	LEFT FRONTAL	ISO	HYPO	HETERO, PERIPHERAL, IRREGULAR	severe edema(>2cm)	16.46	2	1.9	3.2
30	lal singh	63	m	2021/06/011656	RIGHT FRONTAL	HYPO	HYPO	HETERO, PERIPHERAL, IRREGULAR	severe edema(>2cm)	14.45	3	1.5	5.8
31	ram nivas	36	m	2021/05/008290, 2021/08/005192	left frontal insular	hypo	hyper	hetero	MODERATE(1-2cm)	11.21	5	2.4	14.9
32	Sohni Devi	73	f	2021/12/011207	right frontal	hyper	hyper	hetero	severe edema(>2cm)	16.89	3.4	0.98	1.1
33	Bhagirath	60	m	2022/02/007009	right fronto-temporal	hypo	hetero hyper	irregular peripheral(HETERO)	severe edema(>2cm)	13.22	7.8	3.8	2.4
34	Kalawati	55	f	2022/02/011211	right frontal pole	hypo	hetero hyper	irregular peripheral(HETERO)	severe edema(>2cm)	11.13	6.7	4.01	11.1
35	Bagda Ram	40	m	2022/03/013631	left frontoparietal pre and post central gyrus	hyper	hyper	hetero	MODERATE(1-2cm)	9.88	3	4.9	12.3
36	durga ram	32	m	2021/09/008453	LEFT MIDDLE SFG	HYPO	HYPER	NO	MILD(<1cm)	1.44	1	2.5	2.3
37	BHOORI DEVI	32	M	2021/09/016075	RIGHT MIDDLE AND SFG	HYPO	HYPER	irregular peripheral	MODERATE(1-2cm)	12.21	2.5	3.9	9.7
38	JAWAN RAM	36	M	2021/07/011376	LEFT INSULAR	HYPO	HYPER	MINIMAL	MODERATE(1-2cm)	3.41	2	2.8	1.8
39	KAVITA	11	F	2021/10/015587	right frontal	HYPO	HYPER	MINIMAL	MILD(<1cm)	1.9	1.1	2.3	1.7
40	MUBAREEK HUSSAIN	37	M	2021/11/002606	LEFT FRONTAL	HYPO	HYPER	irregular peripheral(HETERO)	moderate edema(1-2cm)	12.88	5	5.67	9.9
41	MAGHU KANWAR	34	F	2021/11/006851	RIGHT SFG AND MFG(frontal)	HYPO	HYPER	MINIMAL	no (0cm)	1	2.3	3.8	1.1
42	AJAY KUMAR	46	M	2022/01/020061	CINGULATE GYRUS	HYPO	HYPER	irregular peripheral(HETERO)	moderate edema(1-2cm)	10.99	4	2.4	9
43	RAJU RAM	60	F	2022/05/019157	LEFT FRONTAL	HYPO	HYPER	irregular peripheral(HETERO)	moderate edema(1-2cm)	11.88	3.9	4.5	7.9
44	RAJAK KHAN	27	M	2022/06/018310	RIGHT PARAMEDIAN FRONTAL LOBE	ISO	HETERO HYPER	PARIETAL SOLID	no (0cm)	3.54	3.2	4.2	6.8
45	HARJI RAM	29	M	2022/05/003411	RIGHT CEREBELLAR	HYPO	HYPER	irregular peripheral(HETERO)	moderate edema(1-2cm)	6.76	3.5	4.5	9