



EVALUATION OF ISOCITRATE DEHYDROGENASE 1 MUTATIONS IN CNS TUMORS

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**ABSTRACT**

**Introduction:**

The annual global age-standardized incidence of primary malignant brain tumors is ~3.7 per 100,000 for males and 2.6 per 100,000 for females [1, 2] Central nervous tumors are the tumors which constitute about 1%–2% of all the neoplasm.[3]

**Aims and Objectives:**

- To study the association of IDH mutation with the WHO grading system of CNS tumors.

**Materials & Methods:**

- This study was conducted in the Department of Pathology, Mahatma Gandhi Memorial Medical College and M.Y. Hospital, Indore Madhya Pradesh, India. IDH1 mutation was analyzed by IHC in 100 patients of CNS tumors.

**Results** - Out of 100 CNS tumors 42 cases were gliomas and IDH1 mutation were absent in grade I Glioma (out of 02 cases), in grade II gliomas IDH1 mutations were observed in 12/14 cases, in grade gliomas all cases are showing IDH1 mutation (p4 cases) in grade IV glioma. 08/22 cases show IDH mutation, Increased glioma grades are associated with increased age and Ki67 index Other 58 tumors include meningioma, medulloblastoma, metastatic and others **Conclusion** - IDH1 mutations are associated with the progression of grade of gliomas and the presence or absence of IDH mutations can help to predict the prognosis.

**KEYWORDS :** IDH (isocitrate dehydrogenase), CNS tumors.

**INTRODUCTION**

- The annual global age-standardized incidence of primary malignant brain tumors is ~3.7 per 100,000 for males and 2.6 per 100,000 for females [1, 2] Central nervous tumors are the tumors which constitute about 1%–2% of all the neoplasm.[3]
- As central nervous system (CNS) tumors have variable histology, divergent morphological, and differentiation features, therefore, they pose major diagnostic challenges.[4]
- Nowadays, for the diagnosis of brain tumors, advances in immunohistochemistry (IHC), molecular pathology, and biomarkers play important role.[5].
- Molecular parameters are included in the classification of CNS tumors in the recent update 2021 CNS WHO which has broken the century-old rule of diagnosis dependent only on microscopy. [6]

**Isocitrate Dehydrogenase**

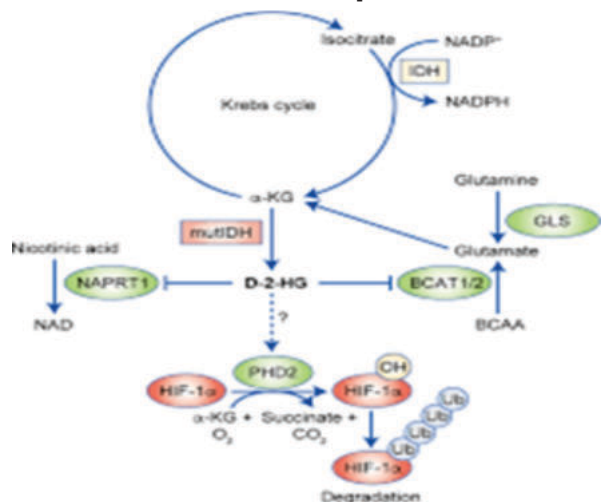
- IDH is a small molecule protein that is mainly distributed in the liver, heart muscle and skeletal muscle [13].
- IDH is involved in several cellular processes, including mitochondrial oxidative phosphorylation, glutamine metabolism, lipogenesis, glucose sensing, and regulation of cellular redox status [14,15].
- IDH catalyzes the oxidative decarboxylation of isocitrate to alpha-ketoglutarate (α-KG) and plays an important role in the reduction of NADP+ to reduced nicotinamide adenine dinucleotide phosphate NADPH.

**MATERIALS & METHODS**

This study was conducted in the Department of Pathology, Mahatma Gandhi Memorial Medical College and M.Y.

Hospital, Indore Madhya Pradesh, India.

- Place of Study:** Department of Pathology, M.G.M medical college and M.Y. Hospital, Indore. & MDRU lab of MGM Medical College.
- Sample Size:** 100 cases.
- Inclusion Criteria:** Histo-pathologically and clinically diagnosed cases of CNS tumors of all age groups.
- Exclusion Criteria:** Inflammatory lesions of CNS.



**Figure 01 - Mechanism of IDH**

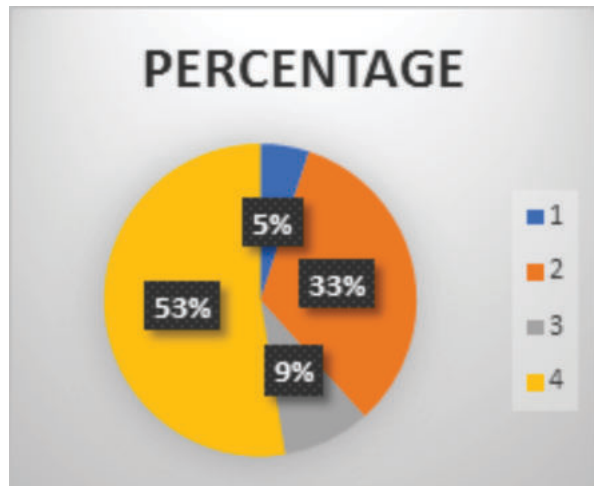
**RESULTS**

Out of 100 CNS tumors 42 cases were gliomas and IDH1 mutation were absent in grade I Glioma (out of 02 cases), in grade II gliomas IDH1 mutations were observed in 12/14 cases, in grade gliomas all cases are showing IDH1 mutation

(p4 cases) in grade IV glioma. 08/22 cases show IDH mutation, Increased glioma grades are associated with increased age and Ki67 index. Other 58 tumors include meningioma, medulloblastoma, metastatic and others

**Table 01 - Histological Grade Of Different CNS Tumors**

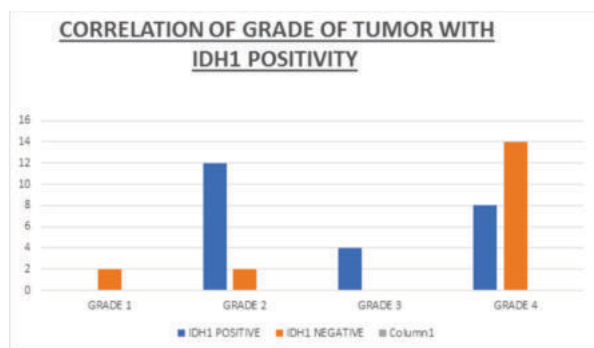
GRADE	FREQUENCY	PERCENTAGE %
GRADE I	02	5
GRADE II	14	33
GRADE III	04	09
GRADE IV	22	53
Total	42	100



**Graph 01 - Pie Chart Showing Histological Grade Of Different CNS Tumors**

**Table 02- Correlation Of Grade Of Tumor With IDH1 Positivity**

Grade of tumor	No. of cases	IDH Positivity
I	02	Negative
II	12	Positive
	02	Negative
III	04	Positive
IV	08	Positive
	14	Negative



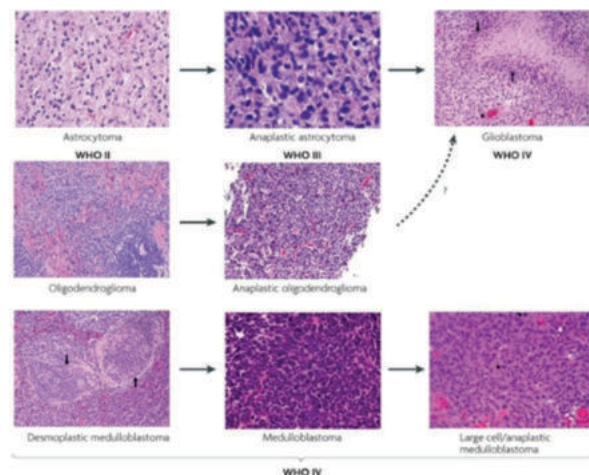
**Graph 02- - Correlation Of Grade Of Tumor With IDH1 Positivity**

**DISCUSSION**

Distribution of Gliomas according to the WHO grade An analysis was done to assess the distribution of gliomas as per the WHO grade. This was compared to the study Jaiswal et al (2016) and Ghangoria S et al (2014). While Grade I accounted for the most common glioma, Grade III had a

decreased frequency of occurrence in the studies.

STUDY	TOTAL CASES	GRADE I	GRADE II	GRADE III	GRADE IV
Shaista M. Hamdani et al (2019)	117	81%	06%	03%	10%
Jaiswal et al (2016)	1468	6.1 %	1.5 %	7.6 %	38 %
Ghangoria S et al (2014)	16	6.2 %	0 %	68.7 %	25 %
Our study	50	48 %	16 %	02 %	34 %



**Figure 02- Grades Of Tumors**

**CONCLUSION**

To sum up, according to our results, IDH1 immunohistochemical expression is more detected in WHO Grade III gliomas, including anaplastic astrocytoma and anaplastic oligodendroglioma than in the WHO Grade IV glioblastoma which support its relative involvement in early glioma genesis. Moreover, IDH1 expression is associated with better response to radiotherapy and adjuvant chemotherapy treatment.

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