Role of Diffusion Weighted Magnetic Resonance Imaging in Predicting Grade of Intracranial Gliomas in Adult Age Group

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Abstract:
Background: *Gliomas, the most prevalent primary brain tumors, are classified by the World Health Organization (WHO) into low-grade (grades 1 and 2) and high-grade (grades 3 and 4) categories. Low-grade gliomas typically affect younger individuals and have a more favorable prognosis, while high-grade gliomas are more common in adults and are associated with poorer outcomes. Accurate early grading of gliomas is crucial for determining appropriate management strategies and prognoses. Advanced magnetic resonance imaging (MRI) techniques, particularly diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) mapping, offer non-invasive alternatives that can detect pathological changes in gliomas by assessing alterations in cellularity and extracellular spaces.* ***Objective:*** *The aim of this study is to evaluate the role of Diffusion Weighted Imaging in predicting grade of gliomas in adult age group.* ***Material & Method:*** *This cross-sectional study, conducted at Dhaka Medical College & Hospital from March 2022 to February 2024, evaluated the efficacy of DWI in predicting glioma grades. The study included patients diagnosed with gliomas who underwent imaging investigations.* ***Result:*** *The study analyzed 50 glioma patients, comprising 32 males (64%) and 18 females (36%), with a mean age of 55.6 ± 13.05 years. Data analysis revealed that high-grade gliomas exhibited significantly lower ADC values compared to low-grade gliomas (p< 0.001). Receiver operating characteristic (ROC) curve analysis demonstrated high accuracy in glioma grading based on ADC values, with an area under the curve (AUC) of 0.945 and an optimal cut-off value of 816.5. MRI findings showed excellent sensitivity (92.31%) and specificity (81.82%) in detecting high-grade gliomas.* ***Conclusion:*** *Diffusion-weighted MRI, combined with ADC mapping, serves as a valuable non-invasive tool for preoperative glioma grading, aiding in clinical decision-making and potentially reducing the need for invasive procedures.*

Keywords: *Grading of Glioma, Diffusion Weighted Imaging (DWI), Apparent Diffusion Coefficient (ADC)*

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Introduction

Gliomas, which originate from glial cells in the central nervous system (CNS), are the most common and aggressive form of primary brain tumors, accounting for approximately 26% of all brain tumors and 81% of malignant brain tumors.[1,2] Glial cells, 5 to 10 times more abundant than neurons, play a significant role in tumor development due to their potential for abnormal growth.[3,4] While the exact etiology of gliomas remains unclear, hereditary factors (e.g., Li-Fraumeni syndrome, neurofibromatosis) and environmental exposures, such as ionizing radiation and certain chemicals, are recognized as risk factors.[1,2] The molecular pathogenesis of

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Received: 10 April 2025 **Revised:** 30 April 2025 **Accepted:** 1 June 2025 **Published:** 1 September 2025

gliomas involves various genetic mutations, including those in tumor suppressor genes (e.g., p53), epidermal growth factor receptor (EGFR), isocitrate dehydrogenase (IDH), and telomerase (TERT), which contribute to their malignant behavior.[7]

The World Health Organization (WHO) classification system for CNS tumors categorizes gliomas into grades 1 to 4, with grade 1 being benign and grade 4 representing the most aggressive, such as glioblastoma. Grading is primarily based on histological features such as cellular pleomorphism, mitotic activity, microvascular proliferation, and necrosis, which are essential for determining prognosis and guiding treatment strategies.[6,8] High-grade gliomas are characterized by their infiltrative nature, which complicates complete surgical resection and contributes to a high rate of recurrence.[9,10]

Currently, histological assessment via stereotactic brain biopsy is the gold standard for glioma grading; however, this method is invasive. Magnetic Resonance Imaging (MRI) has become the most important imaging modalities for evaluation of gliomas due to its superior soft tissue contrast.[11] MRI helps distinguish low- from high-grade gliomas: low-grade tumors are regular, uniform, well-defined, and show minimal edema, while high-grade tumors are irregular, heterogeneous, with indistinct borders, necrosis, cystic changes, or hemorrhage. DWI shows high signals in solid tumor areas, lower signals in cystic or necrotic regions, and post-contrast images often display ring-like enhancement.[4]

Diffusion-Weighted Imaging (DWI), an advanced MRI technique, provides valuable insights into tumor cellularity and extracellular space. DWI, in combination with the apparent diffusion coefficient (ADC) map, offers a non-invasive means to assess tumor density and differentiate between low-grade and high-grade gliomas.[12] Higher tumor density restricts water diffusion, lowering ADC values, while lower density allows greater diffusion, increasing ADC values.[13] Despite its promise, the diagnostic accuracy of conventional MRI remains limited, especially in distinguishing between tumor types and grades.[11]

This study aims to evaluate the clinical and quantitative application of DWI and its correlation with histopathological grading according to the WHO classification system to improve the diagnostic precision and management of gliomas.

Materials and Methods

A cross-sectional observational study was conducted in the Department of Radiology and Imaging, Dhaka Medical College Hospital, from March 2022 to February 2024 after approval from the Ethical Review Committee (ERC). Fifty adult patients suspected of gliomas and admitted for imaging investigations were included, using purposive non-random sampling.

Inclusion and Exclusion Criteria

- **Inclusion**: Adult patients are diagnosed with gliomas and admitted for treatment.
- **Exclusion**: Infratentorial gliomas, brainstem gliomas, mixed-cell gliomas, MRI contra-indications, previous brain surgery or radiation, uncooperative patients, and those with other malignancies.

MR Imaging and evaluation:

MRI was performed using a 1.5 Tesla Hitachi system with a head coil for optimal resolution. Standard sequences (T1WI, T2WI, FLAIR, and post-contrast T1WI) were used to exclude cystic, necrotic, or hemorrhagic areas. Diffusion-weighted imaging (DWI) was obtained with b=1000 s/mm^2, and ADC maps were automatically generated. The region of interest (ROI) showing the lowest ADC value (0.16 cm^2) was analyzed using inbuilt MRI software to determine minimum and mean ADC values. Two experienced radiologists independently interpreted ADC results, classifying tumors as high-grade (<800×10{ v mm^2/s) or low-grade (>800×10{ v mm^2/s).[5] Tissue samples from surgical resections were fixed, processed, and graded histopathologically according to WHO criteria by an expert pathologist who is blinded to the MRI findings. Finally, the correlation between DWI grading and histopathological grading was assessed

Statistical analysis

Data were gathered through structured data sheets, including clinical histories, MRI findings, and available investigations and were analyzed using SPSS software. Quantitative data were expressed as mean ± SD, while qualitative data were presented as frequency and percentage. Statistical tests included Chi-square and t-tests, with a p-value of <0.05 considered significant.

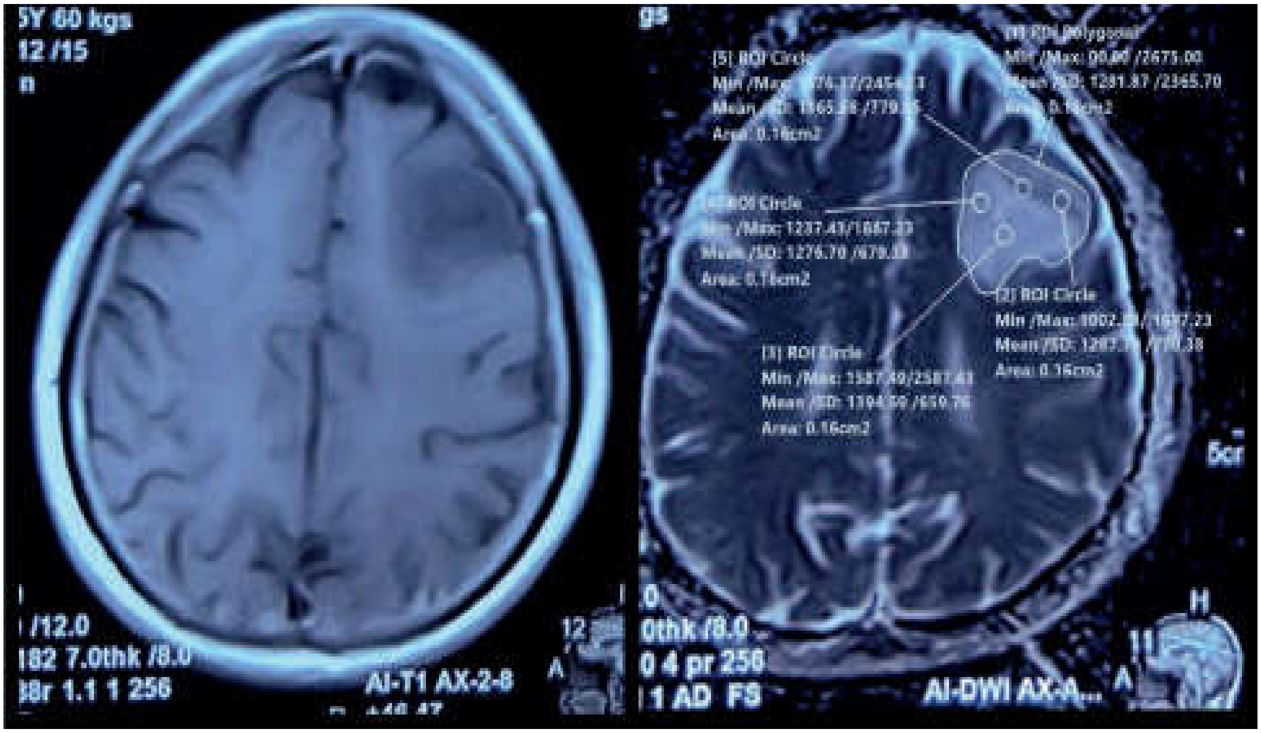

Fig.-1: *Non enhancing DWI non restricted lesion at left frontal region; on ADC the darkest area within the tumor had lowest mean ADC value 1165.58 (>800) represents Low Grade Glioma. Histopathological diagnosis was Astrocytoma, WHO grade 2.*

Results:

The study analyzed 50 glioma patients, comprising 32 males (64%) and 18 females (36%), with a mean age of 55.6 ± 13.05 years. 3 patients were not taken due to unavailability and one patient due to unfavorable (metastasis) histopathology report.

Figure 2 shows the distribution of study patients by MRI diagnosis. Among the patients 24% of the participants were diagnosed with Low Grade Glioma (ADC >800), while a substantial majority of 76% were diagnosed with High Grade Glioma (ADC <800).

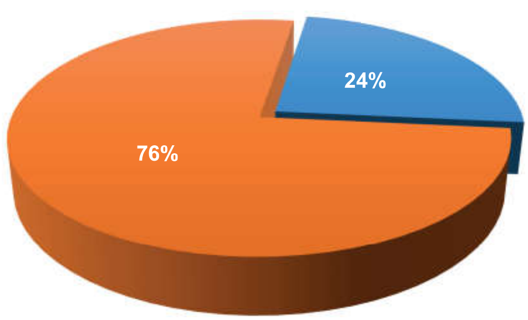

Figure 2: *Pie diagram showing the MRI findings of the study subject*

Table I

Presents the baseline demographic characteristics of the study participants

Variables	Number of patients	Percentage (%)
Age group (years)		
22-40	8	16.0
41-60	23	46.0
61-84	19	38.0
Mean±SD	55.6±13.05	
Range (min-max)	(22-84) years	
Gender		
Male	32	64.0
Female	18	36.0
Male: Female ratio	1.8:1	

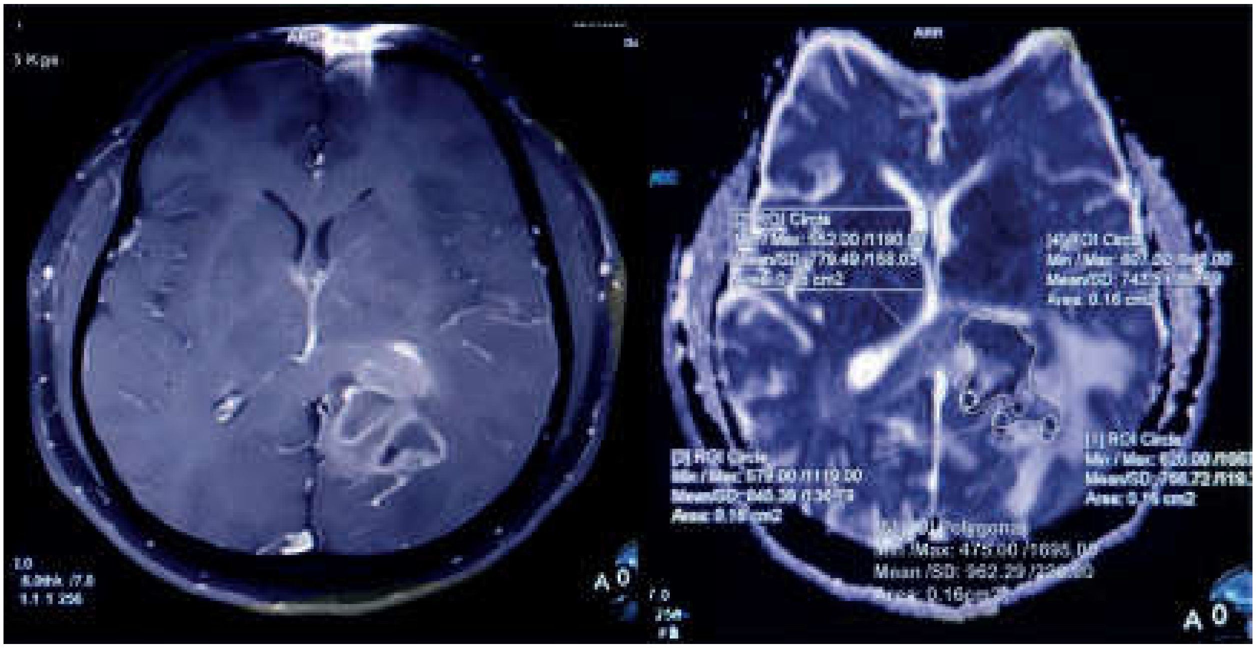

Figure 3: Rim enhancing DWI restricted lesion at left occipital region; on ADC the darkest area within the tumor had lowest mean ADC value 743.51 (<800) represents High Grade Glioma. Histopathological diagnosis was Astrocytoma, WHO grade 3.

Table II indicates a predominance of high-grade gliomas, with glioblastoma comprising 50% of cases, while lower grade astrocytomas and oligodendrogliomas were relatively uncommon.

Table III highlights that MRI features such as extensive edema, strong enhancement, and diffusion restriction were more frequent in high-grade gliomas, whereas low-grade gliomas mostly exhibited mild edema and minimal enhancement.

Table-II

Distribution of the study patients by tumor type (histopathological findings) (n=50)

Tumor type	Number of patients	Percentage (%)
Astrocytoma Grade 2	10	20.0
Astrocytoma Grade 3	11	22.0
Oligodendroglioma Grade 2	1	2.0
Oligodendroglioma Grade 3	3	6.0
Glioblastoma	25	50.0
Total	50	100.0

Table III

Association of MRI findings with histopathological findings (n=50)

	Histopathological findings		
	High grade (n=39)	Low grade (n=11)	p-value
Peritumoral oedema			
Mild	4(10.3%)	9(81.8%)	<0.001
Moderate	14(35.9%)	2(18.1%)	
Extensive	21(53.8%)	0(0.0%)	
Strength of enhancement			
Minimal	7(17.9%)	8(72.7%)	<0.001
Moderate to strong	32(82.0%)	3(27.3%)	
Restriction in DWI	31(79.5%)	1(9.1%)	<0.001

p-value obtained by Chi-square test, $p<0.05$ was considered as a level of significant

Table-IV

Comparison of ADC values among histopathological findings (n=50)

	Histopathological findings		
	Low grade (n=11)	High grade (n=39)	p-value
The minimum ADC throughout the tumour	945.5±96.8	250.6±226.4	<0.001
The lowest mean ADC within the ROI	1045.0±194.3	585.3±188.2	<0.001

p-value obtained by Unpaired t- test, p<0.05 considered as a level of significant

Table IV demonstrates a clear distinction in ADC values between low- and high-grade gliomas, with low-grade tumors showing higher ADC due to lower cellularity and less dense tissue, allowing greater water diffusion, while high-grade gliomas exhibit lower ADC because increased cellularity restricts diffusion.

The ROC curve analysis was conducted to determine the best cut-off value for the lowest mean ADC within the ROI in adult intracranial glioma patients. The Area Under the Curve (AUC) was calculated to be 0.945, indicating a high level of accuracy in predicting the cut-off value. The optimal cut-off value identified was 816.5, with a sensitivity of 92.3% and specificity of 81.8%.

Table V and Figure 5 shows that MRI demonstrated excellent diagnostic accuracy for glioma grading, with 92.31% sensitivity, 81.82% specificity, 94.74% positive predictive value, and 75.00% negative predictive value. The overall diagnostic accuracy was 90.00%, confirming MRI's strong reliability in differentiating glioma grades

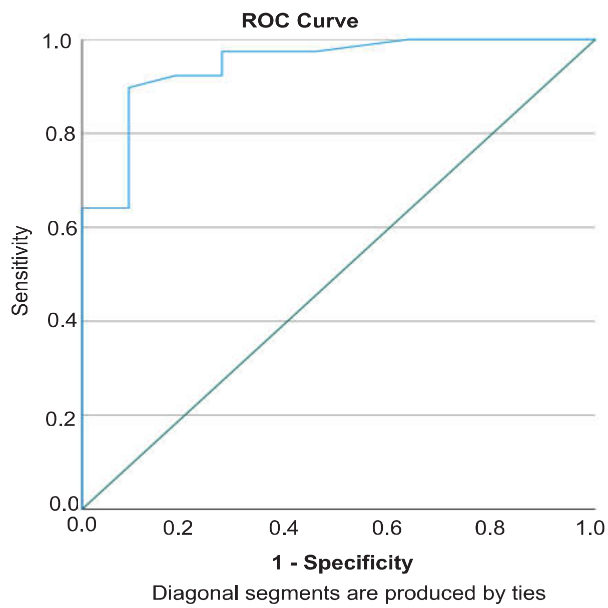

Figure 4: ROC curve analysis performed to predict the best cut off value the lowest *mean ADC within the ROI of intracranial gliomas patients in adult age group.

Area Under the Curve							
Test Result Variable(s):		The lowest mean ADC					
AUC	SE	Cut off value	Sensitivity	Specificity	p-value	95% CI	
						Lower	Upper
.945	.036	816.5	92.3%	81.8%	<0.001	.875	1.000

Table V

Diagnostic performance test of MRI findings of intracranial gliomas in adult patients with histopathological findings

MRI findings	Histopathological findings		Total	p-value
	High grade	Low grade		
ADC (<816)	36(TP)	2(FP)	38	<0.001
ADC (>816)	3(FN)	9(TN)	12	
Total	39	11	50	

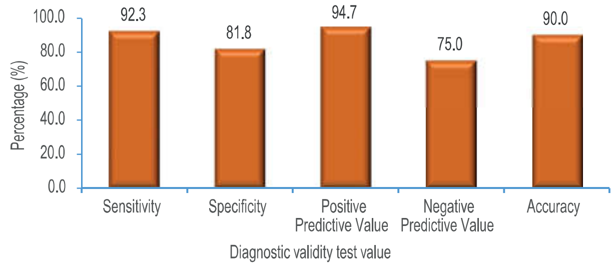

Figure 5: Diagnostic performance test of MRI findings of intracranial gliomas in adult patients with histopathological findings

Discussion:

The cross-sectional observational study was conducted at the Department of Radiology & Imaging, Dhaka Medical College Hospital, in collaboration with the Department of Neurosurgery. Fifty patients diagnosed with glioma were targeted, aiming to evaluate the role of Diffusion Weighted Imaging (DWI) in predicting glioma grades in adults.

In this study, 46% of patients were aged 41–60 years, 38% were above 60 years, and 16% were between 20–40 years, with a mean age of 55.6 ± 13.05 years. Males accounted for 64% of cases, giving a male-to-female ratio of 1.8:1, consistent with findings by Khan et al. (2023) and Shoaib et al. where male are predominant.[2,9]

Headache (94%) was the most common clinical symptom, followed by vomiting (82%) and seizures (70%). Other frequent symptoms included visual disturbance (38%), hemiparesis (28%), and dementia (44%). Symptom distribution varied slightly from other studies, such as Iqbal et al. highlighting differences in clinical presentation across populations.[13]

MRI findings showed that high-grade gliomas commonly had irregular or indistinct margins (87.1%), inhomogeneous signal intensity (92.3%), extensive perilesional edema (53.8%), internal necrosis (51.3%), and mass effect (94.9%). In contrast, low-grade gliomas exhibited regular margins (90.9%), homogeneous signals (63.6%), mild edema (81.8%), and minimal contrast enhancement (72.7%).[6] In this study, seven high-grade gliomas showed minimal enhancement and three low-grade gliomas showed moderate enhancement, aligning with Hakyemez et al.[14] Similarly, Zhang et al. reported that about 20% of low-grade gliomas show partial enhancement, while one-third of non-enhancing gliomas are high-grade.[15]

Based on MRI, 76% of patients had high-grade gliomas (ADC <800) and 24% had low-grade gliomas (ADC >800), comparable to the distribution reported by Darbar et al.[5] Histopathology confirmed 22% Grade 2, 28% Grade 3, and 50% Grade 4 gliomas, with glioblastoma being the most common type, consistent with findings by Shoaib et al. and Al-Agha et al.[9,16]

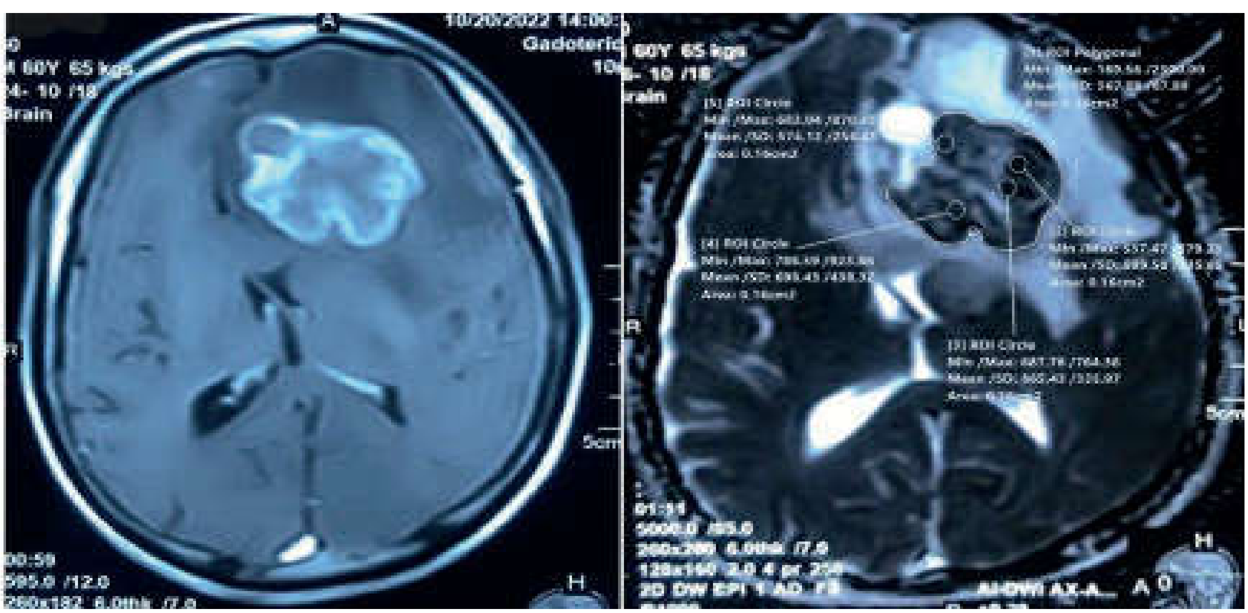

Figure 6: Heterogeneously enhancing DWI partially restricted lesion at left frontal region; on ADC the darkest area within the tumor had lowest mean ADC value 567.08 (<800) represents High Grade Glioma. Histopathological diagnosis was Glioblastoma, WHO grade 4.

ADC values showed a progressive decline with increasing tumor grade, reinforcing their usefulness as a noninvasive marker for glioma classification. ROC analysis demonstrated excellent diagnostic performance (AUC = 0.945) with an optimal ADC cut-off of 816.5, providing 92.3% sensitivity and 81.8% specificity. Similarly, Hitawala et al. reported significantly higher mean ADC values in low-grade compared to high-grade gliomas, supporting the diagnostic value of ADC in glioma grading.[17]

Overall, DWI demonstrated strong diagnostic performance, with 92.31% sensitivity, 81.82% specificity, and 90% overall accuracy in differentiating glioma grades. These findings align with previous studies Khan et al. and Haydar et al. that reinforce the clinical utility of DWI and ADC measurements as reliable tools for non-invasive glioma grading.[2,18]

Limitations:

1. All the samples were collected from a single tertiary care centre, therefore may not reflect the regional variation of the country.
2. 3.0 T MRI could have more diagnostic accuracy.

Conclusion and recommendation:

This study demonstrates that Diffusion-Weighted Magnetic Resonance Imaging (DWI) is a robust, non-invasive modality for detecting and grading intracranial gliomas in adults, showing a strong correlation with histopathological outcomes. Future large-scale, multi-center prospective studies are recommended to validate these findings and enhance their generalizability. Integrating DWI with advanced imaging techniques, such as perfusion-weighted imaging, magnetic resonance spectroscopy, and radiomic analysis, may further refine diagnostic precision, enable comprehensive tumor characterization, and support personalized treatment planning.

Acknowledgement

The authors express sincere gratitude to the Department of Radiology and Imaging and the Department of Neurosurgery, Dhaka Medical College Hospital, for their support and collaboration.

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