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Research article

STUDY OF CLINICAL PROFILE, TOXICITY AND QUALITY OF LIFE IN HIGH GRADE GLIOMAS RECEIVING CHEMORADIATION

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ABSTRACT

Aim: Study of Clinical profile, Toxicity and Quality of life in high-grade Gliomas receiving Chemoradiation. **Methodology:** After obtaining institutional ethical committee approval and informed consent, a total no. of 20 patients were planned. It is hospital based observational prospective study was carried out in department of radiotherapy, Govt. General Hospital, Vijayawada for a period of 10 months Feb 2023 to Dec 2023. All the patients were staged with clinical examination, Chest X ray, and abdomen pelvis ultrasound. After initial staging all patients underwent a computed tomography (CT) scan and MRI Brain. External beam radiation therapy was delivered using linear accelerator with 6 MVphotons. A dose of 60 Gy was delivered in 30 fractions, using a four shrinking field technique and was treated 5days/week. Concurrent chemotherapy was administered using Cap.Temozolamide 75mg/m2. Followed by monthly TMZ at a dose of 150- 200mg/m2 on 5 out of every 28days for 6 cycles**.** Weekly assessment was carried out and toxicity was graded according to the common criteriaversion3.0 Hemogram. RFT, LFT were repeated every week prior to clinical examination. Assessment of tumor response was done using clinical assessment and response evaluation criteria in solid tumors (RECIST) criteria. **Statistical analysis:** Data was analyzed by obtaining rates and proportions. Chi- square test and T test was used to find the significance. This whole analysis was done using SPSS software version 26. **Results:** Out of the 20 patients recruited for study, 19 patients came for first follow up after completion of chemo radiation and advised adjuvant chemotherapy. Only 18 patients completed adjuvant chemotherapy. Out of 20 patients, two persons did not go for adjuvant chemotherapy. The median follow up duration was 10 Months (Range 6-16 months). After 6 months MRI was done for all 20 patients, out of 20 Patients in 11 members has complete response of tumor (27 %), Partial response in 7 (18%), and 2 patients has Progressive disease (5%). Toxicities like Grade 1 headache (40%) during chemo radiation. Grade 1 vomiting's (25%), Grade 2 toxicity in 2 patients (10%) during chemo radiation, Grade 1 nausea (20%), 1 patient had Grade 2 Nausea (5%). Both upper and lower Limb weakness had improved in 10% of the patients. They were no other toxicities like Blurring of vision, Double vision, decreasing of Hearing, Hematological toxicities, Dyselectrolytemia and Tinnitus. **Conclusion:** The present study demonstrated a moderately clinically relevant improvement to HRQOL although there were patients with toxicities like headache, nausea and Vomiting during the course of chemo radiation, but overall Quality of life not Deteriorated. About 50% of the patients had very good tumor response with concurrent Chemo radiation where the quality of life is good in this group.

INTRODUCTION

Among CNS neoplasms, Gliomas are the most common tumors. These tumors include Astrocytoma, Oligodendroglioma, and ependymomas. Malignant gliomas comprise Glioblastoma – IDH (Iso citrate dehydrogenase) mutation wild type and mutant type [World Health Organization (WHO) grade IV], diffuse midline glioma (WHO grade IV), anaplastic astrocytoma – IDH mutant (WHO grade III), anaplastic oligodendroglioma – IDH mutant and 1p/19q co-deleted (WHO grade III) and anaplastic pleomorphic xanthoastrocytoma (WHO grade III)

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Magnetic Resonance Imaging (MRI) of brain with contrast is the diagnostic modality of choice when a brain tumour is suspected. The current standard therapy is maximal safe neurosurgical resection, removing as much tumour tissue as possible without causing new neurological deficits. Adjuvant therapy is based on the histopathological report. Radiation therapy (RT) plays an integral role in treating Glioblastoma (GBM), It also reviews the ideal dose-fractionation and target volume design. RT account for tumour-specific and patient specific factors.

HRQOL is a multi- dimensional concept that includes domains related to physical, mental, emotional, social functioning and other domains such as cognitive functioning, sexuality and spirituality.

AIM

Study of Clinical Profile, Toxicity and Quality Of Life In High Grade Gliomas Receiving Chemoradiation

Objectives of the study are as follows

- To assess the clinical response of treatment using RECIST criteria.
- To assess the toxicities among study population during chemo radiation.
- To assess quality of life among study population before, during and after 6 months of treatment by using EORTC questionnaire.

MATERIALS AND METHODS

It is an Observational prospective study done from Feb 2023 to Dec 2023 at Siddhartha Medical College GGH Vijayawada to Assesses Clinical profile.

Study Design

This hospital based Observational prospective study was conducted on out patients diagnosed with high grade glioma who underwent surgical excision and willing for adjuvant treatment with concurrent chemo-irradiation and adjuvant chemotherapy. The study was approved by Ethical committee, Informed consent from all the patients.

Inclusion Criteria

- Age greater than 18 less than 75 years
- ECOG: Performance status 0-2 (scale of 0-4)
- Histopathologically diagnosed Grade III and Grade IV Gliomas
- Hematological parameters: Hemoglobin>10gm/dl, Total leukocyte count: greater than 4000 cells/cu.mm, platelet count greater than 1.5 lakh/cu.mm, Liver function test and renal function test.

Exclusion Criteria

- Any prior treatment received for tumor.
- Patients with altered liver function tests.
- Patients who do not give informed consent.
- Renal parameters serum creatinine above 2mg/dl.

STUDY PROCEDURE

External beam radiation therapy was delivered using linear accelerator with 6 MV photons. A dose of 60 Gy was delivered in 30 fractions, using a four shrinking field technique and was treated 5days/week. Concurrent chemotherapy was administered using Cap. Temozolomide 75mg/m2. Followed by monthly TMZ at a dose of 150- 200mg/m2 on 5 out of every 28days for 6 cycles**.** Weekly assessment was carried out and toxicity was graded according to the common criteriaversion3.0 Hemogram, renal and liver function tests were repeated every week prior to clinical examination. Assessment of tumor response was done using clinical assessment and response evaluation criteria in solid tumors RECIST criteria by doing MRI Scan and CT scan.

A clinical complete response was documented if there was no evidence of residual disease on CNS examination at the end of 6 months. CT scan and MRI Brain was performed before starting treatment and 6 months after completion of treatment The tumor response was reported as per RECIST criteria. Intention to treat analysis is used in reporting results.

Statistical analysis

Data was analyzed by obtaining rates and proportions. Chi-square test and T test was used to find the significance. This whole analysis was done using SPSS software version 26.

RESULTS

All patients presented to Department of Radiation Oncology for Adjuvant therapy between February 2023 to December 2023 was screened for eligibility to the inclusion into study 20 patients are taken.

Patient characteristics

Patients' age ranged from 30 to 68 years. Mean age is 47 years. Out of 20 patients Female 7 (35%), Male 13 (65%). The performance status was PS1 (11), PS2 (9) members. Education status of the patient out of 20, 11 members are literate (55%), and 9 members are illiterate (45%).

Tumor location and characteristics

Site of tumor	Number of cases	Percentage
Rt Frontal	5	25%
Lt Front-temporal	2	10%
Rt parietal	1	5%
Rt parietal -occipital	2	10%
Lt front-parietal	2	10%
Lt frontal	3	15%
Lt temporal	2	10%
Lt parietal-occipital	1	5%
Rt front -parietal	2	10%

Presenting symptoms

Most common presenting symptom was headache and vomiting. Only headache in 3 patients, Headache with seizures and vomiting in 5 patients, Difficulty in speech in 2 patients, Limb weakness in 2 patients, only seizures in 1 patient, Altered sensorium in 1 patient, Loss of consciousness in 1 patient and Seizure and Speech difficulty in 2 patients.

Details of surgery

All the patients had maximal safe resection of tumor which is the current standard of care. Out of 20 patients .2 patients underwent for gross tumor excision (10%), subtotal excision in 18 patients (90%). Patients do not have re-exploration surgery and post-operative infection.

Gap between Surgery and adjuvant treatment

The median gap between surgery and starting radiotherapy was 17 days (12–31 days). six patients (10%) started radiotherapy within two weeks of surgery, whereas four patients (10%) started radiotherapy after four weeks. Rest of the patients (70%) were started within three weeks from the date of surgery. The delay in starting radiotherapy was due to personal reasons.

Details of chemo-radiotherapy

All the patients received concurrent chemo-radiotherapy with Temozolomide (75mg/m2) based stupp regimen. The technique of delivering radiation therapy was Conformal by using Intensity modulated radiation therapy (IMRT) in all 20 patients.

Radiotherapy Doses

All 20 patients received a dose of 60Gy in 30 fractions. Each radiotherapy fraction 2Gy over 6 weeks. None of the patients developed grade 3 or 4 toxicity or required any break in radiotherapy.

Effect Modifiers during adjuvant therapy

All the patients received Dexamethasone 4mg during radiotherapy, tapered gradually and stopped. All the regular medications including anti-epileptic drugs were continued during adjuvant therapy. All the patients (100%) were on anti-epileptic drugs and most commonly on Levetiracetam 500mg twice daily.

Follow up and Response

Out of the 20 patients recruited for study, 19 patients came for first follow up after completion of chemo radiation and advised adjuvant chemotherapy. Only 18 patients completed adjuvant chemotherapy. Out of 20 patients, two persons did not go for adjuvant chemotherapy. The median follow up duration was 10 Months (Range 6-16 months). After 6 months MRI was done for all 20 patients, out of 20 patients in 11members has complete response of tumor (27 %), Partial response in 7 (18%), and 2 patients has Progressive disease (5%).

Toxicities

Headache, Vomiting's and Nausea

Out of 20 patients, 8 patients had Grade 1 headache (40%) during Chemo radiation, 5 patients had Grade 1 vomiting's (25%) and 4 patients had Grade 1 nausea (20%).

QOL measures

Patients QOL were measured with the EORTC QLQ-C30. It is a 30-item questionnaire and consists of five functional scales (physical, role, cognitive, emotional and social), The additional symptoms commonly reported by cancer patients including: Dyspnea, lack of appetite, sleep problem, constipation, some financial difficulties (FI) of the disease and treatment. The global questions on general health and QOL area 7-point visual analogue scale ranging from 1 (very poor) to 7 (excellent).

Table 1 Quality of life score

	Mean QL2 score		Comparison of Mean Scores before and during RT		Comparison of Mean Scores during and after RT	
	MEAN	**SD**	**t-value**	**P value**	**t-value**	**P value**
Before RT	64.58	7.09	0.842	0.4 NS	2.296	0.02
During RT	66.67	8.55				
After RT	74.58	12.82				

Global health status (QL2) was compared Before RT, during and after completion of RT. It was statistically Significant (P value 0.02)

Table 2 Physical functional score

	Mean PF2 score		Comparison of Mean Scores before and during RT		Comparison of Mean Scores during and after RT	
	MEAN	**SD**	**t-value**	**P value**	**t-value**	**P value**
Before RT	68.07	29.11	0.061	0.95 NS	1.278	0.2 NS
During RT	68.67	33.31				
After RT	80.00	21.52				

Physical functional status (PF2) was compared Before RT and during RT vs during and after completion of RT. It was not statistically significant. Before and during RT before (P value 0.95), during and after RT (P value0.2)

Emotional functional score

Emotional functional status (EF) was compared Before RT And during RT vs. during and after completion of RT. It was not statistically significant. Before and during RT before (P value 0.89), during and after RT (P value0.39)

Table 3 Role functional scale

	Mean RF score		Comparison of Mean Scores before and during RT		Comparison of Mean Scores during and after RT	
	MEAN	**SD**	**t-value**	**P value**	**t-value**	**P value**
Before RT	83.33	18.73	0.136	0.89 NS	0.718	0.47 NS
During RT	82.50	19.85				
After RT	86.67	16.75				

Role functional status (RF) was compared Before RT And during RT vs. during and after completion of RT. It was not statistically Significant. Before and during RT before (P value 0.89), during and after RT (P value0.47)

Table 4 Social functional scale

			Comparison of Mean Scores before and during RT		Comparison of Mean Scores during and after RT	
	MEAN	**SD**	**t-value**	**P value**	**t-value**	**P value**
Before RT	80.83	19.70	0.267	0.79 NS	1.219	0.23 NS

During RT	82.50	19.85				
After RT	90.00	19.04				

Social functional status (SF) was compared Before RT And during RT vs. during and after completion of RT. It was not statistically Significant. Before and during RT before (P value 0.79), during and after RT (P value0.23)

Table 5 Cognitive functional score

	Mean CF score		**Comparison of Mean Scores before and during RT**		**Comparison of Mean Scores during and after RT**	
	MEAN	**SD**	**t-value**	**P value**	**t-value**	**P value**
Before RT	89.17	18.95	0.63	0.52NS	0.636	0.52 NS
During RT	92.50	13.76				
After RT	93.33	13.68				

Cognitive functional status (CF) was compared Before RT And during RT vs. during and after completion of RT. It was not statistically Significant. Before and during RT before (P value 0.52), during and after RT (P value0.52) Fatigue score status was compared Before RT And during RT vs. during and after completion of RT. It was not statistically Significant. Before and during RT before (P value 0.98), during and after RT (P value0.33)

Table 6 Nausea score

	Mean Nausea score		**Comparison of Mean Scores before and during RT**		**Comparison of Mean Scores during and after RT**	
	MEAN	**SD**	**t-value**	**P value**	**t-value**	**P value**
Before RT	3.33	10.26	NA	NA	NA	NA
During RT	0	0				
After RT	0	0				

Nausea was compared Before RT and during RT vs during and after completion of RT. It was not applicable.

Pain score

Pain score was compared Before RT And during RT vs during and after completion of RT. It was not statistically Significant. Before and during RT before (P value 0.72), during and after RT (P value0.33).

Insomnia score

Insomnia score was compared Before RT And during RT vs During and after completion of RT. It was not statistically Significant. Before and during RT before (P value 0.64), during and after RT (P value0.33)

Table 7 Financial Difficulties score

	Mean Financial Difficulties score		**Comparison of Mean Scores before and during RT**		**Comparison of Mean Scores during and after RT**	
	MEAN	**SD**	**t-value**	**P value**	**t-value**	**P value**
Before RT	28.83	22.43	0.07	0.94 NS	0.116	0.9 NS
During RT	28.33	22.20				
After RT	27.50	22.96				

Financial difficulty score was compared Before RT And during RT vs During and after completion of RT. It was not statistically Significant. Before and during RT before (P value 0.94), during and after RT (P value0.9)

Future uncertainty score

In the present study, Future uncertainty score was compared Before RT And during RT vs During and after completion of RT. It was not statistically Significant. Before and during RT before (P value 0.85), during and after RT (P value0.46)

Table 8 Visual disorder score

	Mean Visual disorder score		**Comparison of Mean Scores before and during RT**		**Comparison of Mean Scores during and after RT**	
	MEAN	**SD**	**t-value**	**P value**	**t-value**	**P value**
Before RT	2.72	7.90	0.43	0.66 NS	NA	NA
During RT	1.67	7.45				
After RT	1.67	7.45				

In the present study, Visual disorder score was compared Before RT And during RT vs During and after completion of RT. It was not statistically Significant. Before and during RT before (P value 0.66), not applicable during and After RT

Table 9 MOTOR score

	Mean MOTOR score		**Comparison of Mean Scores before and during RT**		**Comparison of Mean Scores during and after RT**	
	MEAN	**SD**	**t-value**	**P value**	**t-value**	**P value**
Before RT	13.50	23.36	0.257	0.79 NS	0.05	0.95 NS
During RT	11.67	21.70				
After RT	11.25	25.40				

In the present study, Motor Functional score was compared Before RT And during RT vs. During and after completion of RT. It was not statistically Significant. Before and during RT before (P value 0.79), during and after RT (P value0.95)

Communication difficulty score

In the present study, Communication difficulty score was compared Before RT and during RT vs. during and after completion of RT. It was not statistically significant. Before and during RT before (P value 0.41), during and after RT (P value0.73)

DISCUSSION

A study entitled "Study of Clinical Profile, Toxicity and Quality Of Life in High Grade Gliomas Receiving

Chemoradiation." was undertaken at Department of Radiation Oncology, SIDDHARTHA Medical College and GGH Vijayawada, from Feb 2023 to Dec 2023. The standard of treatment is Gross total resection of tumor or subtotal resection of tumor followed by Adjuvant chemo radiation therapy for 6 weeks. This study was done to assess the response, toxicity profile during chemo radiation in high grade gliomas during chemo radiation and also to measure the Quality of Life. The Performance status was included before RT and after RT, patient had improved performance status after chemo radiation. GBM is most commonly located in the supra tentorial region (frontal, temporal parietal, and occipital lobes), with the highest incidence in the Frontal lobe, multiple lobes (Overlapping tumors), followed by the temporal and Parietal lobes. Most of the gliomas were located in the cerebral lobes (86%). Gliomas in the frontal lobe accounted for 40%, temporal lobe for 29%, parietal lobe for 14%, and occipital lobe for 3.0%. Gliomas were located more frequently in the right hemisphere (51%) than in the left (40%) as study done. The current standard of care for patients with GBM is maximum safe surgical resection followed by concurrent TMZ (75 mg/m2/day for 6 weeks) and RT (60 Gy in 30 fractions) and then six maintenance cycles of TMZ (150–200 mg/m2/day for the first 5 days of a 28- day cycle—sdTMZ), according to the results of the phase III EORTC 26981. Stupp et al. showed an OS and PFS improvement with the combination therapy relative to RT alone.

In our study concurrent chemotherapy with Temozolomide is 75mg/m2 and RT dose of 60Gy over 6 weeks, blood test was repeated weekly, whereas MRI scan was done after completion of adjuvant chemotherapy at 6month. Radiotherapy with concomitant and adjuvant temozolomide (six cycles) is the standard treatment after surgery in glioblastoma patients. In the present study response of the tumor is studied under RECIST criteria (1.0), in which out of 20 patients, 27% patient show complete response (CR), 15% show partial response (PR) and 5% had progression of disease (PD).

Our study has shown that they were 5 patients had Grade 1 vomiting's (25%), Grade 2 toxicity in 2 patients (10%) during chemo radiation. They were no Grade3 and 4 toxicities and 4 patients had Grade 1 nausea (20%), 1 patient had Grade 2 nausea (5%). In the present study, Global health status (QL2) was compared Before RT and during RT vs. During and after completion of RT. It was statistically significant (P value 0.02). Similar to my study patients in the GBM and malignant groups. Financial difficulties decreased at (12 months following radiotherapy) in the groups receiving curative therapy.
Fatigue is the most significant symptom with high-grade gliomas and may be more significant a problem compared to patients with low-grade tumors. In patients with recurrent malignant gliomas, the incidence of fatigue may approach 89%–94%.

CONCLUSION

Although there was statistically significant improvement in Global QOL, the present study demonstrated a moderately clinically relevant improvement to HRQOL although there were patients with toxicities like headache, nausea and vomiting during chemo radiation, but overall Quality of life not Deteriorated. About 50% of the patients had very good tumor response with concurrent Chemo radiation where the quality of life is good in this group.

HRQOL has become an important outcome measure in brain tumor patients, which may help both physicians and the patients and their family members to make decisions on (tumor) treatment and clinical care. Over the years, several validated questionnaires have been developed to measure HRQOL. Both in clinical trials and in daily practice, it is expected that its use will even increase now that new (combination of) treatments emerge for brain tumor patients.

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