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Enhancing Quality of Life, Alleviating Anxiety, and Mitigating Depression through a Specific Physiotherapeutic Program in Individuals Diagnosed with Glioblastoma Multiforme and Astrocytoma

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Abstract:-

- ***Objectives:***

To investigate impact of specific physiotherapeutic program on quality of life, anxiety and depression in patients with glioblastoma multiforme and astrocytoma.

- ***Materials and Methods:***

20 post surgical Patients with Glioblastoma Multiforme (GBM) and Astrocytoma, aged 45-60 years mean age (55.30 and 53.80), both males and females were randomly included in the study and divided into two groups, group A and group B comprising 10 patients each. All the Patients were assessed for Quality of life using WHO Quality of Life Scale (WHOQOLs) and Functional Assessment of Cancer Therapy- Brain (FACT-BR), anxiety and depression using Hospital based Anxiety and Depression Scale (HADS). The patients of Group A received Specific Physiotherapeutic program, whereas Group B patients received home based exercise regimen. The Patients received interventions for 6 weeks, with 5 weekly sessions.

- ***Results:***

A statistically significant difference was observed in HADS (anxiety and depression) score in Group A (p=0.034) and Group B (p=0.00) whereas statistically non-significant difference was found in WHOQOL scores in Group A (p=0.74) and in Group B (p=0.035) statistically significant difference was observed. The statistically non-significant difference was also documented in FACT-BR (p=0.168) Scores in Group A, FACT-BR (p=0.633) Scores in Group B.

- ***Conclusion:***

Home based regimen was effective in improving the QOLs and reducing the effect of anxiety and depression in patients with GBM and astrocytoma whereas specific physiotherapeutic program was effective in improving the anxiety and depression.

Keywords:- *Glioblastoma Multiforme, Astrocytoma, Cancer, Quality of Life, Anxiety and Depression.*

Abbrevations:- WHOQOL= WHO quality of life **,** FACT-Br= Functional Assessment of Cancer Therapy-Brain

I. INTRODUCTION

Brain tumor is a collection of abnormally grown cells in brain, contributing total 256,213 new cases reported globally in 2012. Tumors of the central nervous system (CNS) are rare neoplasm constituting 1–2% of all neoplasm. They are however quite heterogeneous with a wide variety of primary tumors and a large number of secondary tumors. [1]

Glioblastoma multiforme (GBM) accounts for 50% of all gliomas in all age groups.[2] The most common adult primary malignant brain tumor with a peak incidence between 55 and 84 year of age.[3] Fifty percent of adult GBM patients die within 10–12 months after diagnosis. Approximately 10% of adult patients survive 24 months after diagnosis.[4] Its poor prognosis with survival rate of 14-15 months after diagnosis makes it a crucial public health issue.[5]

The common problems in patients with glioblastoma multiforme and astrocytoma are pain, fatigue, balance, poor independence, anxiety and depression. Majority of these problems along with other manifestation occur after surgery. All these manifestation contribute to inability to do activities of daily livings along with psychological distress.

These problems are often ignored and understated; moreover there is paucity of published literature regarding physiotherapeutic strategies for these manifestations in Indian population especially in rural facilities. There are limited resources available regarding the clinical evidence of role of physiotherapeutic techniques in patients with

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glioblastoma and astrocytoma receiving chemotherapy and radiotherapy.

In recent years, increased attention has focused on exercise as a rehabilitative intervention for cancer survivors both during and after the cessation of cancer therapy. [6-8] Therefore there is dire and urgent need, especially considering the huge number of patients affected by these disorders to explore the role of physiotherapeutic strategies in patients with brain cancer.

Consequently, the purpose of the study is to investigate the efficacy of a specific physiotherapeutic program in improving quality of life, and reducing anxiety and depression in patients with glioblastoma multiforme and astrocytoma.

II. MATERIALS AND METHODS

- *Ethics:*

The study was duly approved by the faculty of physiotherapy as well as Board of study of physiotherapy of Baba Farid University of Health and Sciences, Faridkot, Punjab, India (letter no. BFUHS/2K21p-TH/4954, Dated-19-04-2021). All the procedures followed were in accordance with Helsinki Declaration (JAMA 2000;284:3043-3049).

- *Study Design:*

The study has been conducted in Indoor Patient Department (IPD), Outdoor Patient Department (OPD) of Nuclear medicine and Department of Radiation Oncology of Guru Gobind Singh Medical College and Hospital, Faridkot, Punjab, India and Outdoor Patient Department (OPD) of University College of Physiotherapy, Faridkot. The design of the study was Quasi-experimental in nature.

The post surgical Patients with diagnosis of brain astrocytoma and glioblastoma multiforme (GBM), aged 45-60 years, mean age (55.30 and 53.80); both males and females were included in the study. The patients were referred for chemotherapy along with radiotherapy with minimum score of 22 as per mini mental state examination. The patients voluntarily enrolled in the study and were co-operative as well as understandable.

Patients were excluded from the study if they had co-morbid conditions such as diabetes mellitus, hypertension and any other cardiovascular conditions, secondary metastasis of tumor, focus of tumor in spinal cord and other system of body excluding brain, neurological disorders such as stroke, brain hemorrhage, aneurysm, infection of brain, history of trauma and recent history of major surgery in the last 1 year.

After obtaining their signed informed consent, the patients were assessed for the baseline parameters.

A total of 30 Patients undergoing intervention at the OPD and IPD of Department of Radiation Oncology were screened for the study. The study was performed in compliance with the ethical principles of the institutional ethical committee of Baba Farid University of Health and Sciences. Among them 20 Patients fulfilled the selection criteria and were thus selected for the study. They were randomly allocated in two different groups, Group A and Group B. Group A received specific physiotherapeutic program whereas Group B received home based exercise regimen.

The selected patients were assessed for two outcome measures namely quality of life (QOL) and Anxiety and depression; Quality of life was measured using WHO Quality of life scale (WHOQOL) and Functional Assessment of Cancer Therapy-Brain (FACT-BR) whereas Anxiety and depression were measured using Hospital Anxiety and Depression scale

WHOQOL[9] is 26 items scale with minimum scoring of 1 and maximum scoring 5 and the Functional Assessment of Cancer Therapy-Brain (FACT-Br)[10] is a commonly used instrument measuring general quality of life (QOL) that reflects symptoms or problems associated with brain malignancies across 5 scales. HADS [11] is fourteen item scale that generates: seven of the items relate to anxiety and seven relate to depression. Each item on the questionnaire is scored from 0-3 and this means that a subject can score between 0 and 21 for either anxiety or depression.

The baseline assessment was done before starting the intervention whereas 2nd assessment was conducted at 4th week and final assessment at 6th week post-interventional.

- *Interventions*

Interventions were provided for 5 days a week for six weeks.

- *Specific Physiotherapeutic Program*

The patients of Group A were given specific physiotherapeutic program. It compromised of warm up phase, specific phase and cool down phase in the hospital setting. Warm up exercise sessions should start with a 5-10 minutes low-intensity exercise incorporating light stretching exercises. Specific phase includes the aerobic, resistance and flexibility exercise. Resistance exercise included the lateral arm raise, biceps curls, shoulder press, seated row, leg extension, leg curls, calf raise etc. Cool down phase includes light stretching and walking exercise.

- *Home based Regimen*

Group B patients were taught home based regimen. It comprised of same warm up phase, specific phase and cool down phase in home based setting. Same interventions were given to the patients of group B but in home setting. Warm up phase include the walking and cycling. Resistance exercise includes biceps curls, triceps extension, standing row, chair rise, calf raise etc. Cool down phase includes slow walking.

- *Statistics*

Data analysis was done by SPSS software. Baseline characteristics were compared between groups using

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independent t- test. For all the outcome measures, One- way ANOVA was used to assess the interventions effects within the groups. Alpha was set at 0.05, and the 95% confidence interval (CI) was calculated. If the significant difference was detected, then post hoc tests with the scheffe methods were conducted.

III. RESULTS

The mean age (years) of the patients in group A was 55.30±5.77 whereas in group B was 53.80±5.69. The comparison of baseline parameter namely age, BMI and MMSE score were found to be having statistically insignificant difference (p> 0.05).

The analysis for WHOQOL score, upon application of one-way Anova at three different intervals (0 week, 4 weeks and 6 weeks) was found to be having statistically significant difference in group B (p=0.035) (table 1) (figure 1). Whereas the analysis of FACT-Br score at three different intervals (0 week, 4 weeks and 6 weeks) was found to be statistically non-significant difference in both group A as well as group B (table 1).

The second major outcome parameter assessed in the study was anxiety and depression through HADS score. The comparison of mean HADS score at the same three different intervals (0 week, 4 weeks and 6 weeks) was found to be having statistically significant difference in both the Groups A as well as Group B for anxiety (figure 2) and depression both. Further, the analysis of improvement in HADS score for anxiety and depression was found to be having statistically non-significant difference in both Groups A as well as Group B (table 5).

Table 1 Comparison of mean value for WHOQOL scores and FACT- Br at different intervals (0 week, 4 weeks and 6 weeks) within Group A and Group B.

		Week 0 (Mean±SD)	**Week 4 (Mean±SD)**	**Week 6 (Mean±SD)**	**F value**	**p value**
WHOQOL	Group A	77.00±5.35	85.20±12.80	88.90±14.62	2.864	0.074(NS)
	Group B	75.30±5.91	79.30±5.74	82.50±5.93	3.792	0.035 (S)
FACT-BR	Group A	105.70±10.00	108±6.58	112.40±6.26	1.905	0.168(NS)
	Group B	106.60±9.83	103±8.01	103.20±10.14	0.466	0.633(NS)

Table 2 Post Hoc Scheffe Analysis for WHOQOL Scores at different intervals for Group B

WHOQOL Score	**Group B**	
	Mean Diff.	**p value**
(0 vs 4) Week	-4.00	0.33 (NS)
(04 vs 06) Week	-3.20	0.48 (NS)
(0 vs 06) Week	-7.20	0.04 (S)

Table 3 Comparison of mean value for HADS (anxiety) and HADS (depression) scores at different intervals (0 week, 4 weeks and 6 weeks) within Group A and Group B.

		Week 0 (Mean±SD)	**Week 4 (Mean±SD)**	**Week 6 (Mean±SD)**	**F value**	**p value**
HADS (anxiety)	Group A	13.30±1.57	9.70±4.19	9.10±4.51	3.837	0.034 (S)
	Group B	12.60±1.58	8.10±1.73	7.80±1.87	24.130	0.000 (S)
HADS (depression)	Group A	13.60±2.17	10.20±3.91	9.40±4.20	3.968	0.031 (S)
	Group B	13.00±1.83	8.70±1.77	8.30±1.57	22.859	0.000 (S)

Table 4 Post Hoc Scheffe Analysis for HADS (anxiety) and HADS (depression) Scores at different intervals for Group A and Group B.

		(0 vs 4) Week	**(4 vs 6) Week**	**(0 vs 6) Week**
HADS (anxiety)	Group A	0.11 (NS)	0.94 (NS)	0.05 (S)
	Group B	0.00 (S)	0.93 (NS)	0.00 (S)
HADS (depression)	Group A	0.12 (NS)	0.88 (NS)	0.04 (S)
	Group B	0.00 (S)	0.88 (NS)	0.00 (S)

Table 5 Comparison of improvement of mean value for HADS (anxiety) and HADS (depression) Scores at 0 vs 6 weeks interval between Group A and Group B

0 vs 6 Week		
	t- value	**p- value**
HADS (anxiety)	1.376	0.1858(NS)
HADS (depression)	1.397	0.1793 (NS)

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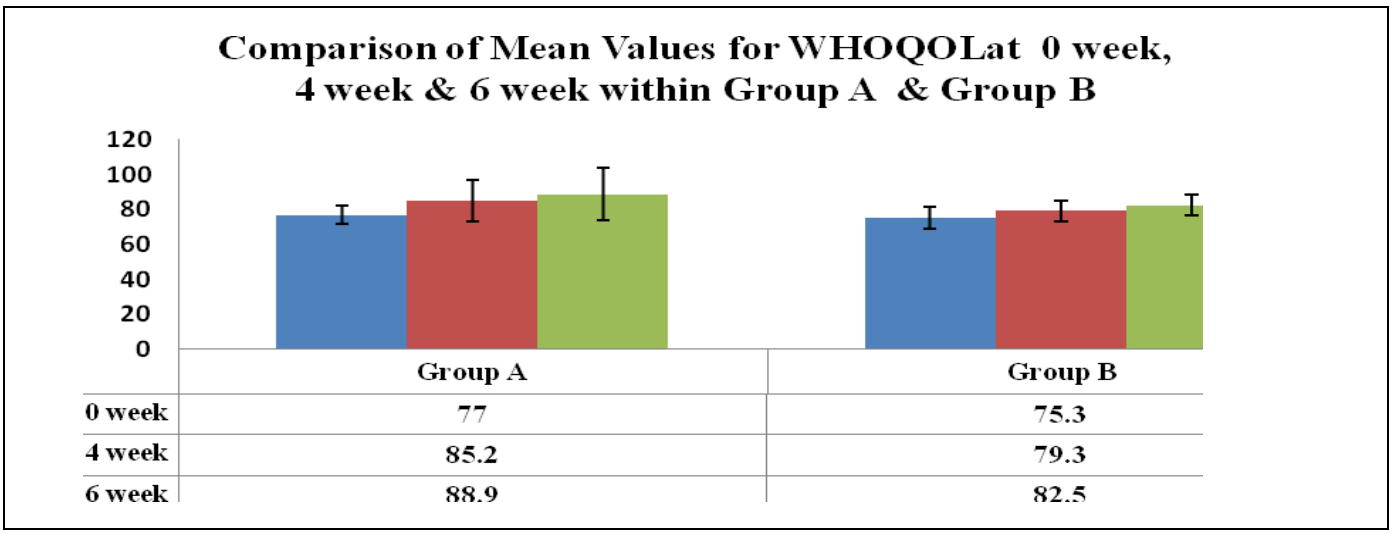

Fig 1 Graphical display of Comparison of mean value for WHOQOL Scores at Week 0, Week 4, Week 6 within Group A and Group B patients

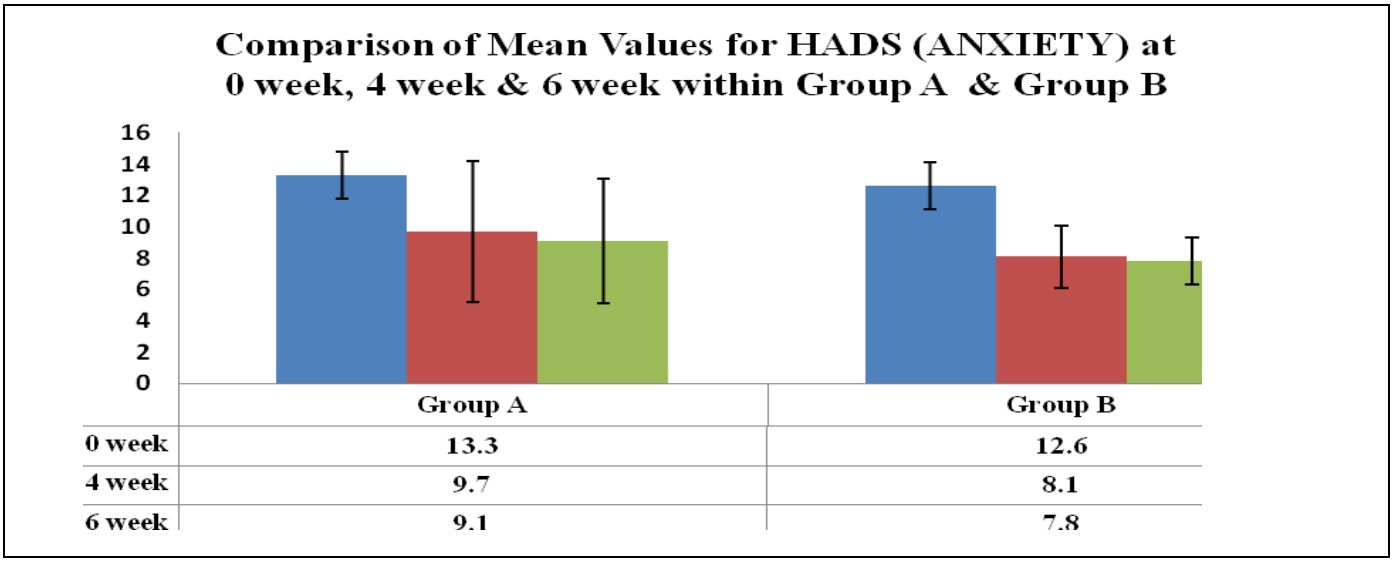

Fig 2 Graphical display of Comparison of mean value for HADS (anxiety) at Week 0, Week 04, Week 06 within Group A and Group B patients.

IV. DISCUSSION

This study compared the efficacy of specific physiotherapeutic program with home based regimen in patients with GBM and astrocytoma, on two parameters, namely, Quality of life (QOLs) and anxiety - depression. Patients with GBM and astrocytoma have to deal not only the problems of pain, fatigue, balance and independence but they also suffer from psychological distress, anxiety and depression which often get neglected. There is no doubt that physiotherapeutic interventions have an important positive role in these patients, especially during the period of chemotherapy and radiotherapy, but there are limited resources and paucity of published literature. Therefore, this study was an attempt to have a clear insight into the role of physiotherapy intervention in these patients. Consequently, the basic aim of the current study was to investigate the efficacy of a specific physiotherapeutic program in improving quality of life and reducing anxiety, depression in patients with glioblastoma multiforme and astrocytoma.

In present study the average mean value of WHOQOL score increased from 77.00 pre-intervention to 85.20 at 4 weeks and 88.90 at 6 weeks in GBM and astrocytoma patients who received specific physiotherapeutic program. Similarly, this score increased from 75.30 pre-intervention to 79.30 at 4 weeks and 82.50 at 6 weeks in GBM and astrocytoma patients who received home based regimen. Thus only Group B revealed significant improvement in quality of life levels after receiving home based regimen. Previous Studies done by Mustian *et al*, 2011; [23] Galvao DA et.al, 2005; [22] Knols R et.al, 2005; [24] Stevinson C et al., 2004 [25] showed the significant improvement in the quality of life score in the patients receiving rehabilitation treatment in the setting as compared to home based regimen (ANCOVA $p<0.05$), the interventional group showed more positive result because patients was strictly adhere to exercise intervention then control group. Researchers have shown that physical exercise among cancer survivors during and after treatment produces improvements in QOL.

Further the average mean value of FACT-BR score increased from 105.70 pre-intervention to 108 at 4 weeks and 112.40 at 6 weeks in GBM and astrocytoma patients who received specific physiotherapeutic program. This score decreased from 106.60 pre-intervention to 103 at 4 weeks and then markedly increased to 103.20 at 6 weeks in GBM and astrocytoma patients who received home based regimen. Thus both groups showed non-significant improvement in quality of life levels, post intervention. (Babatunde *et al* 2016; Bergenthal *et al* 2014; Buffart *et al* 2017; Fong *et al* 2012) [26-29] reported significant improvement in the quality of life of the patients. Fong et. al, 2012 [29] revealed improvement in the quality of life score with p value <0.03. The findings of the present study indicated marked improvement in psychological distress in terms of statistically significant improvement in anxiety levels as well as depression in both different interventional groups. Thus both specific physiotherapeutic program and home based regimen were effective in improving in anxiety and depression in patients with GBM and astrocytoma.

Lee W Jones *et al*, [12] documented improvement in anxiety levels with the use physiotherapeutic rehabilitation program. In the present study the average mean value of HADS (anxiety) score decreased from 13.3 pre-intervention to 9.7 at 4 weeks and 9.10 at 6 weeks in GBM and astrocytoma patients who received specific physiotherapeutic program. Similarly, this score decreased from 12.60 pre-intervention to 8.10 at 4 weeks and 7.80 at 6 weeks in GBM and astrocytoma patients who received home based regimen. Thus both groups showed significant improvement in anxiety levels, post intervention whereas Berglund G et. al. 1994, [13] Burnham TR et al., 2002 [14] and Daley AJ et.al.2007, [15] did not documented significant improvement in anxiety score. Whereas, R. Segal et al., 2003 [30] found significant improvement due to exercised intervention as compared with control group where no exercise treatment was given to the patients.

Depression can be a very common co-morbid condition with cancer and impacts severely on patient's quality of life, recovery, and possibly even survival. Physiotherapeutic rehabilitation program has been previously applied in management of psychological distress like depression on patients with GBM and astrocytoma by different researchers (Segar ML et.al, 1998, Smith BD et.al,2009, Thorsen L et.al.2005) [16-18] Berglund G *et al.*,[13], documented improvement in depression levels with the use physiotherapeutic rehabilitation program. In present study the average mean value of HADS (depression) score decreased from 13.60 pre-intervention to 10.20 at 4 weeks and 9.40 at 6 weeks in GBM and astrocytoma patients who received specific physiotherapeutic program. Similarly, this score decreased from 13.00 pre-intervention to 8.70 at 4 weeks and 8.30 at 6 weeks in GBM and astrocytoma patients who received home based regimen. Thus both groups revealed significant improvement in depression levels after receiving specific physiotherapeutic rehabilitation and home based regimen. This fact has also been reported by other authors (Segar ML et al., 1998, Demark-Wahnefried W et al., 2006, Pinto BM et al., 2003, Singh NA et al., 2005). [16,19-21] All these studies showed the effects of either endurance or mixed exercise (endurance combined with progressive resistance training) training program prescribed at a moderate to vigorous intensity (50–75% of baseline exercise capacity) at least 3 days per week for 10–60 min per exercise session result in positive effect on depression.

The study was delimited to the geographical region of Faridkot (Punjab) and surrounding areas. Secondly, the sample size was also limited as result of Covid-19 pandemic as a result the patients were reluctant for elective treatment and participation. The finding can be concluded that Specific physiotherapeutic program and home based regimen are equally effective in improving the anxiety level as well as reducing the level of depression in patients with GBM and astrocytoma. Further, it is also acknowledged that home based regimen is far more effective in improving the quality of life (QOL) in these patients.

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