(International Print/Online Journal)

SJIF IMPACT FACTOR: 5.565
PUBMED-National Library of Medicine ID-101739732

ISSN (Print): 2209-2870
ISSN (Online): 2209-2862

International Journal of Medical Science and Current Research (IJMSCR)
Available online at: www.ijmscr.com
Volume 5, Issue 3, Page No: 335-340
May-June 2022

IJMSCR

Impact of P 53 Tumor Suppressor Gene On The Survival Of The Patients Of Glial Tumor In A Tertiary Care Teaching Institute, Ranchi, Jharkhand

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Type of Publication: Original Research Paper
Conflicts of Interest: Nil

Abstract

Background: The p53 gene often referred to as the "guardian of the genome" is a tumor suppressor gene, disturbance in the function of which leads to carcinogenesis. P53 expression can be helpful in tailoring the therapeutic modalities in individual cases.

Objective: To analyze histopathological spectrum of glial tumour & role of p53 in their prognosis.

Materials and Methods: The design of the study was hospital based cross-sectional study conducted among 50 patients. Patients visiting at RIMS whose clinical findings and Radiological Reports are suggestive of primary brain tumors were selected and their surgically obtained biopsy specimens were graded according to WHO classification. Out of 50 cases, 38 cases were found to be glial tumors. Further, 38 glial tumors were taken up for study and IHC staining with p53.

Result: Fisher Exact Test showed that proportion of patients with p53 positive died within 6 months were 34.2% whereas, 65.8% survived more than 6 months.

Conclusion: There was no any significant association between histopathological grade of tumors and status of P53 of the patients (P<0.104)

Keywords: Glial tumors, IHC, P53 gene, cross-sectional study

Introduction

Human brain is the most complex and powerful part of the body. Commonly tumours are caused by mutagens and carcinogens. Primary brain tumours are the most common solid tumour of childhood after leukaemia and sixth most common in adults. They account for 20% - 30% of all paediatric malignancies and the leading cause of death in children.[1] Primary brain tumours can be either glioma or non-glial tumours. Gliomas are tumours of the brain parenchyma that histologically resemble different type of glial cells. The major types of tumour in this category are astrocytoma, oligodendroglioma & ependymoma. Among astrocytoma, pilocytic astrocytoma is the most common glioma in children.[2]

The primary brain tumours account for less than 2% of all human cancer, but cause a disproportionate burden of cancer related to morbidity and mortality. Even the most highly malignant glioma rarely metastasizes outside the CNS. Tumors are able to spread through the CSF if they encroach upon the subarachnoid space, and thus may be associated with implantation along the brain and spinal cord at a distance from the original tumour site.[3] Disturbances in p53 function are strongly associated with carcinogenesis.[4] P53 have been widely used as a marker to predict outcome in various malignancies.[5] The p53 gene, often referred to as the "guardian of the genome" is a tumor suppressor gene[6] located on the short arm of Chromosome 17, It acts as a

"molecular policeman" in preventing the propagation[7] of genetically damaged cells; either directly, by its participation in mechanisms of DNA repair, or indirectly by its induction of cell cycle arrest and/or apoptosis in damaged cells. Further, recent data indicate its role in angiogenesis and tumor invasion.[8] In keeping with its critical "gatekeeper" function; mutations of this gene are now implicated in the genesis of a variety of malignancies. P53 expression can be helpful in tailoring the therapeutic modalities in individual cases.

Objective:

To analyze histopathological spectrum of glial tumours & role of p53 in their prognosis.

Materials and methods:

The design of the study was hospital based cross-sectional study conducted among 50 patients. The study was conducted in the department of Pathology, Rajendra Institute of Medical Sciences, Ranchi after the approval of institutional ethics committee (Rajendra Institute of Medical Sciences, Ranchi). Patients visiting at RIMS whose clinical findings and Radiological Reports are suggestive of glial tumours were selected and their surgically obtained biopsy specimens were graded according to WHO classification was taken up for study and IHC staining with p53 was performed.

Inclusion criteria:

1. 38 consecutive cases with confirmed diagnosis of glial tumors.
2. Only cases which is graded according to WHO classification.

Exclusion criteria:

1. Insufficient tissue materials.
2. Degraded or autolyzed samples.
3. Cases with inconclusive diagnosis and/or without definite grading were excluded.

Collection of specimens:

Tissues for histopathological examination were obtained in the form of biopsies then placed in formalin for 24 hours and stained with Haematoxylin & Eosin after proper grossing.

Method of evaluation of p53 immunostaining:

The respective sections from all cases were studied by selecting the areas showing good cellularity. A minimum of 200 cells per sections were counted for p53 positivity and expressed as a percentage cell showing distinctive brown staining of the nuclei were counted as positive. P53 scoring was calculated by studying a minimum of five fields in the highest labeled areas and the scoring was assessed as follows: 0 = no positive nuclei, 1 = <5% positive, 2 = 5–30% positive, 3 = >30% positive. Survival was defined as the interval between biopsy proven diagnosis and death or date of last follow up, up to 6 months.

Results:

Table 1: Age and Gender distribution of the patients

Age Group (in years)	Male	Female	TOTAL
<1 yr	1	1	2
%	50%	50%	100%
10-19 yr	4	5	9
%	44.4%	55.6%	100%
20-29 yr	4	7	11
%	36.4%	63.6%	100%

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30-39 yr	9	4	13
%	69.2%	30.8%	100%
40-49 yr	5	2	7
%	71.4%	28.6%	100%
≥50 yr	4	4	8
%	50%	50%	100%
TOTAL	27	23	50
%	54.0%	46.0%	100.0%
Mean ± s.d.	33.25±13.77	30.50±15.25	
Median	33	28	
Range	10 months - 65 years	8 months - 64 years	

Chi-square (χ^2) test showed that there was no significant association between age groups and gender of the patients (p=0.57).

The mean age (mean± s.d.) of males was 33.25±13.77 years with range 10 months - 65 years and the median age was 33 years.

The mean age (mean± s.d.) of females was 30.50±15.25 years with range 8 months - 64 years and the median age was 28 years.

t-test showed that there was no significant difference in mean ages of males and females (t_{48}=0.66; p=0.51). Thus, male and female were with more or less equal distribution of their ages.

Table-2: Histopathological grade of tumors of the patients:

Histopathological Grade	Number	%
I	8	21.1%
II	16	42.1%
III	9	23.7%
IV	5	13.2%
Total	38	100.0%

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Most of the patients had tumor of Grade-II (42.1%) which was significantly higher (Z=2.76; p=0.0027) followed by Grade-III (23.7%). 13.2% of them had Grade-IV tumors.

Figure: 1 showing histopathological grade of tumors of the patients:

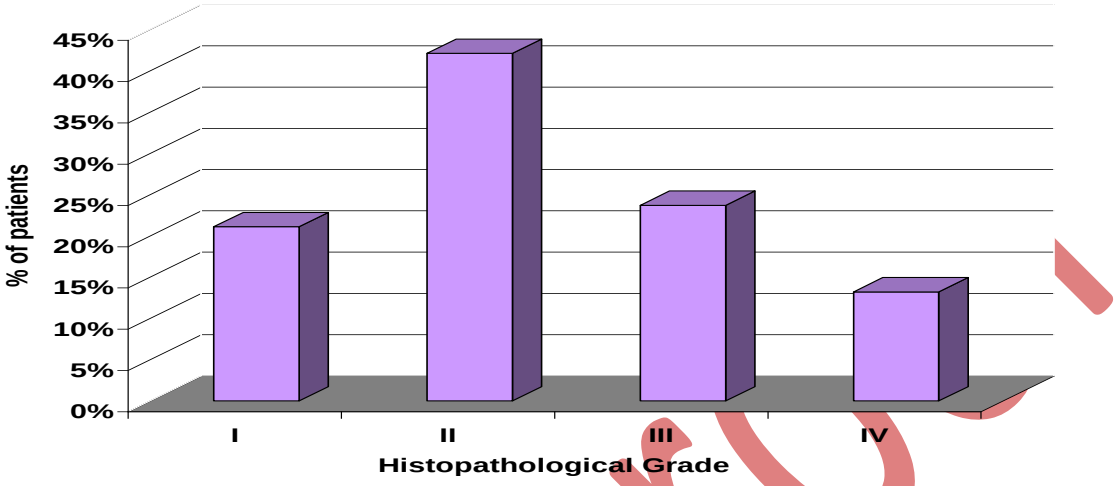

Table-3: Association between p53 and survivality of the patients

p53	**Length of survival**		**TOTAL**
	<6 months	**≥6 months**	
Negative **%**	6 31.6%	13 68.4%	19 100%
<5% **%**	4 50%	4 50%	8 100%
5% - 30% **%**	2 28.6%	5 71.4%	7 100%
>30%	1 25%	3 75%	4 100%
TOTAL %	13 34.2%	25 65.8%	38 100.0

Corrected Chi-square (χ^2) test showed that there was no significant association between histopathological grade of tumors and status of p53 of the patients (p=0.087). Fisher Exact Test showed that proportion of patients with p53<5% cells positive died within 6 month (50%) was equal to that of who survived more than 6 months (p=0.207).

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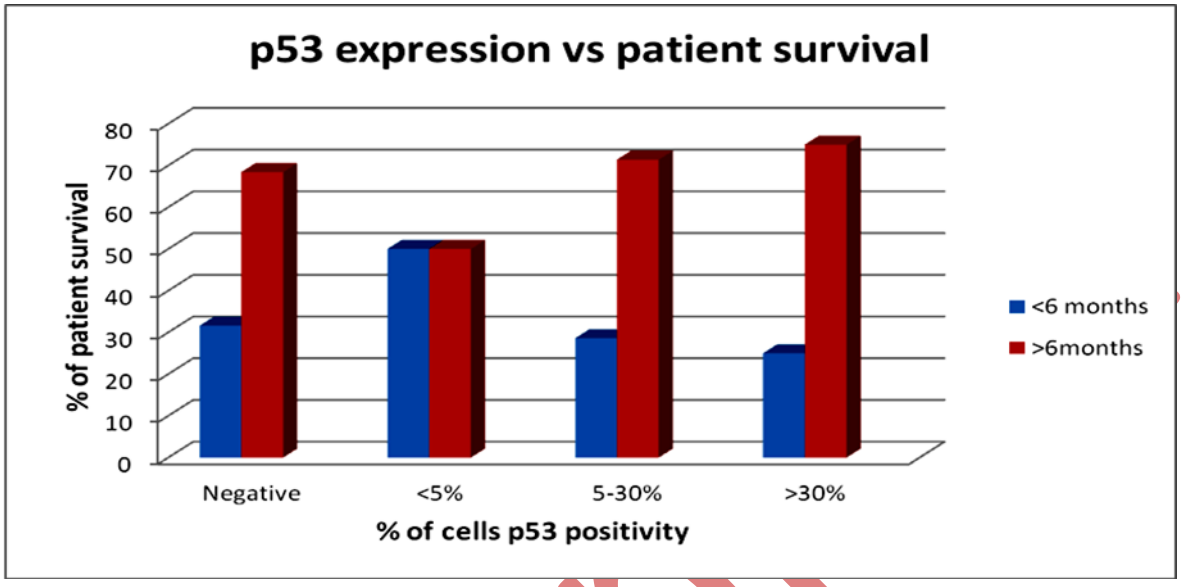
Figure 2: Showing association between p53 and survivality of the patients:



Discussion:

The present study was carried out on 50 patients aged 0 to 80 years. Patients were divided in six age groups viz. <1 year, 10-19, 20-29, 30-39, 40-49 and ≥50 years. It was clear from **Table1** that the mean age (mean± s.d.) of male was 33.25±13.77 years with range 10 months - 65 years and the median age was 33 years. The mean age (mean± s.d.) of female was 30.50±15.25 years with range 8 months - 64 years and the median age was 28 years. Arshad H et.al[9] had conducted a study on correlation of histopathological grade and p53 expression with patient survival in 2010. Fifty primary brain tumor cases were included in the study. Thirty-five cases (70%) were in males, while fifteen (30%) were in females. Ages of patients ranged from 5 to 67 years with a mean age of 35 years. Eleven patients (22%) were under 19 years of age. **Table 2** clearly depicts that most of the patients had tumor of grade-II (42.1%) which was significantly higher (Z=2.76; p=0.0027) followed by grade-III (23.7%). 13.2% of them had grade-IV tumors. **Table 3** showed that out of 38 glial tumor patients, 19 was found to be P53 negative; of which 6 patients (31.6%) died within 6 months and 13 patients (68.4%) survived more than 6 months; 8 patients was found to be less than 5% P53 expression, of which 4 patients (50%) died within 6 months whereas, 4 patients (50%) survived more than 6 months. 5% – 30% P53 expression was depicted by 7 patients, of which 2 patients (28.6%) died within 6 months while 5 patients (71.4%) survived more than 6 months. More than 30% P53 expression was shown by 4 patients, of which 1 patient (25%) died within 6 months whereas, 3 patients (75%) survived more than 6 months. Corrected Chi-square (χ^2) test showed that there was no significant association between histopathological grade of tumors and status of p53 of the patients (p=0.087). Fisher Exact Test showed that proportion of patients with p53 positive died within 6 months were 34.2% whereas, 65.8% survived more than 6 months.

Conclusion:

The p53 gene, often referred to as the "guardian of the genome" is a tumor suppressor gene which acts as a "molecular policeman" in preventing the propagation of genetically damaged cells; either directly, by its participation in mechanisms of DNA repair, or indirectly by its induction of cell cycle arrest and/or apoptosis in damaged cells. Mutations

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of this gene are now implicated in the genesis of a variety of malignancies. In this study, corrected Chi-square (χ^2) test showed that there was no significant association between histopathological grade of tumors and status of p53 of the patients (p=0.087). Whereas, Fisher Exact Test showed that proportion of patients with p53 positive died within 6 months were 34.2% whereas, 65.8% survived more than 6 months.

Refrences:

1. Baldwin RT, Preston-Martin S. Epidemiology of brain tumors in childhood – A review. Toxicol Appl Pharmacol. 2004; 199:118–31.
2. Clarke CRA. In: Neurological diseases in Kumar &Clark Clinical Medicine. 6th ed. Kumar P, Clark M, editors. Edinburgh: Elsevier Saunders; 2005. pp. 1244–45
3. Gerdes J, Lemke H, Baisch H, Wacker HH, Schwab U, Stein H. Cell cycle analysis of a cell proliferation-associated human nuclear antigen defined by the monoclonal antibody Ki-67. J Immunol. 1984; 133:165-66.
4. Hollstein M, Sidransky D, Vogelstein B, et al. p53 mutations in human cancers. *Science* 1991;253:49-53.
5. Cattoretti G, Becker MH, Key G, Duchrow M, Schlüter C, Galle J, et al. Monoclonal antibodies against recombinant parts of the Ki-67 antigen (MIB 1 and MIB 3) detect proliferating cells in microwave-processed formalin-fixed paraffin sections. J Pathol. 1992;168:357
6. Levine AJ, Momand J, Finlay CA. The p53 tumor suppressor gene. *Nature*1991;351:453-6.
7. Pardo FS, Hsu DW, Zeheb R, et al. Mutant, wild type or overall p53 expression: freedom from clinical progression in tumors of astrocytic lineage. *Br J Cancer*, 91, 2004; 1678-86.
8. Labit CB, Chinott O, Ochit C, et al. Prognostic significance of p53 and epidermal growth factor receptor immunostaining in human glioblastomas. *NeuropatholApplNeurobiol*, 24, 1998; 381-8.
9. Arshad H, AhmadZ, Hasan S. Gliomas: Correlation of Histologic Grade, Ki67 and p53 Expression with Patient Survival. *Asian Pacific Journal of Cancer Prevention*, Vol 11, 2010:1637-1639.

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