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*RESEARCH ARTICLE*

# HEMORRHAGIC GLIOBLASTOMA MULTIFORM: PREVALENCE, PREDISPOSING FACTORS AND PROGNOSIS AMONG ADULT KFMC PATIENTS.

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## *Abstract*

**Context**: glioblastoma multiform (GBM) is the stage four of glioblastoma tumor(1). It is the most common primary intra-cranial tumors(2). GBM can be presented by intracranial hemorrhage (ICH) with an incidence between 1 – 10 % and usually occur in the late course of the disease. The general prognosis of GBM with ICH is poor and worsen in elderly(8)(5).

**Aims**: Determining the effect of the hemorrhage on the disease prognosis, exploring the prevalence and predisposing factors.

**Methods**: A retrospective medical record review had performed for patients diagnosed with GBM between 2008 through 2013 at national neuroscience institute in King Fahad Medical City. Inclusion criteria are male and female with age more than 18 years old diagnosed with glioblastoma multiform grade four and were followed in the King Fahad Medical City Clinic. The exclusion criteria is any patients with the hemolytic disorder.

**Results**: . A total of 87 out of 530 patients with GBM were identified. 15 (17.2%) of GBM patients have ICH while 72(82.8%) non-hemorrhagic. 61 (70.1%) were male while 26 (29.9%) were female. No difference between prognosis between hemorrhagic and non-hemorrhagic GBM patients. Tumor size, and gender are not predisposing factors.

**Conclusion**: there were no difference in the prognosis and between hemorrhagic glioblastoma multiform and non-hemorrhagic and gender and Tumor size are not predisposing factors.

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## Introduction:-

Gliomas is a collection of tumors arising from glia or their precursors within the central nervous system. Histopathologically, gliomas are divided into four grades; the most aggressive of these grades is 4 or GBM.(1)
GBM is the most common primary intracranial neoplasm of the central nervous system. It has an incidence for 15% to 20% of all primary central nervous tumors. These GBM tumors can be presented in different forms. Intracranial hemorrhage (ICH) is one of these forms, which can happen to different degrees and extension with variation in degree of prognosis. It has been reported that GBMs can masquerade as traumatic ICH, or intraventricular hemorrhage (IVH).(2)

The prognosis and clinical manifestation depend on multiple factors which share together according to their severity and their stage, namely; tumor size, location, infiltration range, eloquent area involvement, and the extent of the surgical resection. The main histopathological features include micro vascular proliferation, pleomorphic cells, necrosis, increased cellularity ,mitoses and microscopic intra-tumoral hemorrhage.(3)

Intracerebral hemorrhage (ICH) is defined as bleeding into the brain parenchyma.(4)
ICH is a common neurological emergency in patients with intracranial tumor, which usually occurs late in the course of disease, in some time it heralds the cancer diagnosis. The presence of ICH in patients of GBM usually occurs by unique mechanisms, especially intratumoral hemorrhage or coagulopathy, whereas hypertensive hemorrhage is rare.(5)
A highly vascularized, malignant primary brain tumor (BT) like a GBM and metastatic BT tends to bleed spontaneously. Gliobastoma multiform should be included in the differential diagnosis of non-traumatic ICH.(6)
In pathogenesis of sudden massive bleeds into cerebral tumors, the ischemic necroses areas are formed.(7)

The general, prognosis for GBM associated with ICH worsens with increasing age in elderly patients. The surgical removal of both the hematoma and the tumor with adjuvant treatment are associated with prolonged survival rate.(8)
In the short-term prognosis of ICH patients with GBM the report demonstrates about 22 % to 31 % mortality at 1 month, and 48 % to 75% have partial or complete independence at discharge. However, in the long-term prognosis of ICH with GBM, the underlying malignancy prognosis are often poor (78 % mortality at 1 year), and ICH generally occurs late in the neoplastic course.(5)

For the median survival rate in the GBM Alone is about 12 months. In 2-3% of the patients have long survival rate with more than 3 years. (22)

In this study we want to see if there is any significant difference between the prognosis of hemorrhagic GBM compare with non hemorrhagic GBM and the predisposing factors.

## Methodology:-

Retrospective medical record review has performed from 2008 through 2013 on 53 existence data recorded at the national neuroscience institute in King Fahad Medical City. Inclusion criteria was any patients diagnosed with Glioblastoma multiform world health organization grade four both male and female with age more than 18 years old who Fellow in the King Fahad Medical City clinic. The exclusion criteria was any patients have any hemolytic disorder. The research team has reviewed how many patients presenting with ICH among GBM, data of the predisposing factor which is common between ICH GBM (gender, tumor size) and compared it with non hemorrhagic GBM patients. In addition, the study reviewed the prognosis of ICH GBM patients and compare it with non hemorrhagic GBM patients (post operative survival rate, partial or full resection). To look for differences of either age, tumor size and survival rate with hemorrhagic and non hemorrhagic condition, we used (T-test ) analytic method. For the association between the location of tumor and gender with hemorrhagic and non hemorrhagic condition, we used (Chi-square) analytic method.

## Results:-

The study involved 87 subject with GBM divided into two groups hemorrhagic or non-hemorrhagic. The most frequent location of for Hemorrhagic and non-Hemorrhagic GBM is in frontal lobe by 37.8% and the frequent location in hemorrhagic GBM is Temporal. (see CHART 1). 15 (17.2%) of the study population that attended National Neuroscience Institute at King Fahad Medical City in Riyadh City had intracranial hemorrhage and 72(82.8%) had non-hemorrhagic GBM. Most of them were male 61 (70.1%) and 26 (29.9%) were females. The distribution of Hemorrhagic or non-Hemorrhagic GBM and sex is summarized in **Table 1.**

**Table 1:** Distribution of patients in both groups

| Hemorrhagic or non-Hemorrhagic | Gender | | Total |
|---|---|---|---|
| | Male | Female | |
| Hemorrhagic | 13 (14.6%) | 2 (2.3%) | 15 (17.2%) |
| Non Hemorrhagic | 48 (55.2%) | 24 (27.6%) | 72(82.8%) |
| Total | 61 (70.1%) | 26 (29.9%) | 87 (100.0%) |

Independent t-test was conducted to measure the difference between intra cranial hemorrhage and non-hemorrhagic GBM. ICH GBM age Median= 54.40 years with 18.157 standard deviation, tumor size Median= 105.19 $cm^3$ with 61.990 standard deviation and survival rate Median = 2.07 years with 1.387 standard deviation and non-hemorrhagic GBM age Median= 53.64 with 18.120 standard deviation, Tumor size Median= 106.60 $cm^3$ with 83.081 standard deviation and survival rate Median= 2.25 with 1.172 standard deviation.

A chi-square test was performed to know if there is significant relationship between the frequency of ICH GBM and non-hemorrhagic GBM in gender *X2 = 1.511 (1), p=.219*, tumor location *X2* = 15.012 (8), p =.059 and surgery type *X2 = .803 (3), p= .849*.

## Discussion:-

In this study, we aimed to find the prevalence of patients who are presented with intracranial hemorrhage and non-hemorrhagic, to find predisposing factors and which GBM group at high risk to develop ICH and difference in the prognosis of GBM with ICH compare with GBM without ICH.

In this study, we found that the prevalence of ICH as a complication of GBM was 17.2 % while the non-hemorrhagic was 82.8 % of 87 adult Patients attended National Neuroscience Institute at King Fahad Medical City in Riyadh. The prevalence of ICH in GBM in the other studies was between 1-2% and other studies reported it between 7% to 10%. (5)

There are no differences between hemorrhagic and non-hemorrhagic in prognosis. So, the survival rate is almost the same in each group with median survival rate of hemorrhagic 2.07 year and median of survival rate of non-hemorrhagic 2.25 year with P value .595. In literature review the prognosis of GBM patient with ICH are 78% mortality by 1 year (5). Chi-square has performed to look for the surgery type either partial or complete resection affect the prognosis and the result show no effect on the prognosis with P value .849. ICH is not affect the prognosis of GBM. Tumor size and gender are not predisposing factors that make the GBM more prone develop ICH. For confirm that we had performed T-test on tumor size and Chi-square on gender but they did not show any differences between hemorrhagic and non-hemorrhagic with .951 P value of Tumor and .849 P value for gender.

For age, we did T-test to see the Age distribution between each group. The results are 54.40 years old for hemorrhagic and 53.64 years old for non-hemorrhagic. So, the aging people are not high risk for GBM developing ICH than younger patients.

no difference between the prognosis of GBM with ICH compare GBM alone may be because the GBM itself has poor prognosis although The ICH alone is known to have poor prognosis. .(23) (22) we looked if ICH worsen the prognosis of GBM but the study show it is not.

There are some limitation of the studies as nonrandomized study which are the sample size is small but it is convenient, the study cover one city which is Riyadh City and as retrospective cohort study there is possible for selection bias.

## Conclusion:-

Our study show that ICH is no affect the GMB prognosis and tumor size and gender are not predisposing factors for developing ICH in GBM patients.

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