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SINGLE-CENTER DESCRIPTIVE STATISTICAL ANALYSIS OF GLIAL TUMORS WITH REFERENCE TO GLIOBLASTOMAS

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Abstract

Gliomas are the most common primary intracranial brain neoplasms composing almost 80% of all cancerous brain tumours. Glioblastoma is the most common malignant brain tumour in the adult population and accounts in about 15% of all intracranial neoplasms. This observational analytical study gives a better overview of the current state of glial tumours in North Macedonia from 2021 to 2022 with special reference to glioblastomas.

Epidemiological and statistical analysis of glial and other brain tumours in a specific time period with special reference to glioblastomas.

This research is an observational statistical analysis that takes place on the Institute for Pathology in the Medical Faculty of ''Ss. Cyril and Methodius'' University in Skopje using the digital data base of patients that had undergone surgery in the University Clinic of Neurosurgery and were diagnosed at the Institute of Pathology during the time period 2021-2022.

In the period from 2021 and 2022, at the Institute of Pathology were diagnosed 106 (62%) glioblastomas out of which classic glioblastoma histomorphology confined 85 (80.19%) cases; 9 (8.49%) glioblastomas showed oligodendroglial component, 5 (4.72%) cases were gliosarcomas and 4 (3.77%) cases were diagnosed as giant cell glioblastomas. Three (2.83%) cases showed glioblastoma histomorphology with radionecrosis.

The results of this descriptive statistical analysis show that glial tumours, especially glioblastomas as most prevalent malignant tumour type deserves greater scientific attention which beside the impact on their diagnostic complexity, will expand the knowledge of this pathology field and strongly reflect on future scientific and diagnostic work.

When it comes to global statistics, we can conclude that Republic of North Macedonia follows the global trends regarding the incidence of glioblastoma associated with gender and age. Our results show that glioblastoma is more prevalent in males than females with the ratio male to female being 1.2:1, and this tumour is more prevalent in patients older than 55 years with the average age of diagnosis being 61 years.

Keywords: Glioblastoma, glial tumours, statistics, analysis, epidemiology.

Introduction

Gliomas are the most common primary intracranial brain neoplasms composing almost 80% of all cancerous brain tumours. Glial tumors originate from glial cells such as astrocytes, oligodendroglial and ependymal cells, whose main function consists of providing structural, metabolic and immune support to the neurons. The WHO Classification of central nervous system distinguishes four WHO grades (I-IV or 1-4) of CNS tumours based on histomorphological criteria, like histological anaplasia (degree of differentiation), mitotic activity, microvascular proliferation and presence or absence of necrosis. Lower-grade gliomas (WHO grade II), such as diffuse astrocytoma or oligodendroglioma morphologically differs from higher-grade gliomas (WHO grade III or IV) by lower mitotic rate, low microvascular proliferation and absence of necrosis.

Glioblastoma is a high grade (WHO grade IV), diffusely infiltrating and highly cellular glioma composed of poorly differentiated tumour cells that shows nuclear atypia and marked pleomorphism. Mitotic rate in glioblastoma can vary in different tumour parts, and it can be as low as 5-10% and can go up to 60-70%. The two most distinguishable histomorphological characteristics of this tumour are microvascular proliferation and necrosis, which can present with perinecrotic palisading of tumour cells . The outdated term ‘’glioblastoma multiforme’’ may still best describe the variations of morphologies which can be found in the same sample of tumour tissue. There are several histological subtype/variants of glioblastoma, such as giant cell glioblastoma, gliosarcoma and epithelioid glioblastoma.

According to the latest World Health Organization (WHO) classification of Central nervous system (CNS) [1], tumours, gliomas are categorized in six groups:

Adult-type diffuse gliomas
Pediatric-type diffuse low-grade gliomas
Pediatric-type diffuse high-grade gliomas
Circumscribed astrocytic gliomas
Glioneuronal and neuronal tumours
Ependymal tumours

Glioblastoma is the commonest glial tumour (approximately 45% of all glial tumours) and the most common cancerous brain tumour in the adult population composing 15% of all intracranial neoplasms and 45-50% of all primary malignant brain tumours with peak age incidence between 55-85 years [1].

The epidemiological analyses of glial tumors which were published in the last couple of years showed that the median global glioma incidence ranged from 4.80 (National Cancer Intelligence Network – England) to 7.70 (Finish Cancer Registry – Finland) per 100,000 person yearly, while the global incidence of glioblastoma ranged from 2.82 (Korean Central Cancer Registry) to 5.10 (Danish Neuro-Oncology Registry – Denmark) per 100,000 person yearly [2].

To overview and follow the current prevalence and incidence of glial tumours, with reference to glioblastomas in North Macedonia, a descriptive statistical analysis was made using the data of a single center in the period from 2021 and 2022.

Objectives

Epidemiological and statistical analysis of glial and other brain tumours in a specific time period with special reference to glioblastomas, which can create a scientific data base that can serve as a foundation for deepening the research in the neuropathology field.

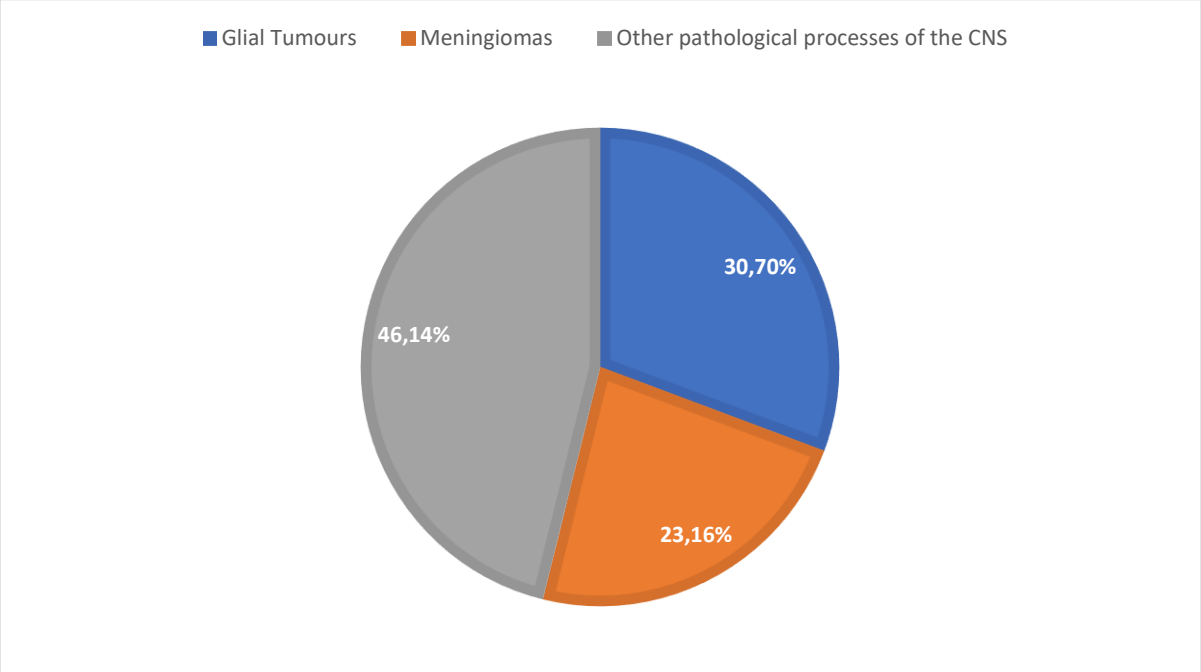
Materials and Methods

This research is an observational statistical analysis that takes place in the Institute of Pathology in the Medical Faculty of ‘’Cyril and Methodius’’ University in Skopje. The data used for this study was extracted from the digital data base of patients that had undergone surgery at the University Clinic of Neurosurgery and were diagnosed at the Institute of Pathology during the time period 2021-2022. Data was analyzed based on the following parameters: age, gender, tumour histomorphology (type and subtype).

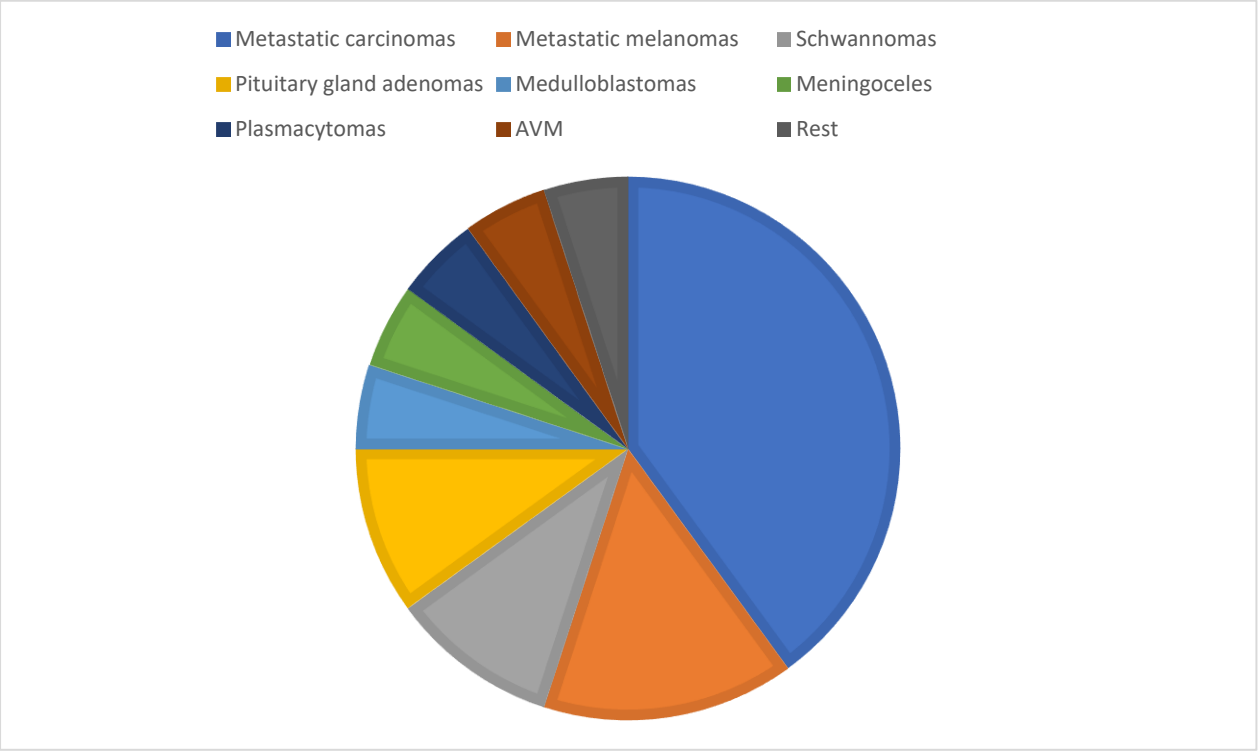
Results

In the period from 2021 to 2022, a total of 557 surgical specimens were collected from the University Clinic of Neurosurgery in Skopje which were diagnosed at the Institute of Pathology in Skopje using the WHO classification of CNS tumors published in 2016. Of the total of 557 surgical specimens, 171 (30.7%) were glial tumors, second most frequent were meningiomas with 129 (23.16%) diagnosed cases and, the rest 257 (46.14%) comprised other pathological processes of the central nervous system, such as: metastatic melanomas 12 (2.15%), metastatic carcinomas 78 (14%), schwannomas 21 (3.77%), pituitary gland adenomas 27 (4.85%), medulloblastomas 3 (0.54%), meningoceles 3 (0.54%), plasmacytomas 2 (0.35%), arterio-venous malformations 6 (1.07%).

(Pie Chart 1.), (Pie Chart 2)

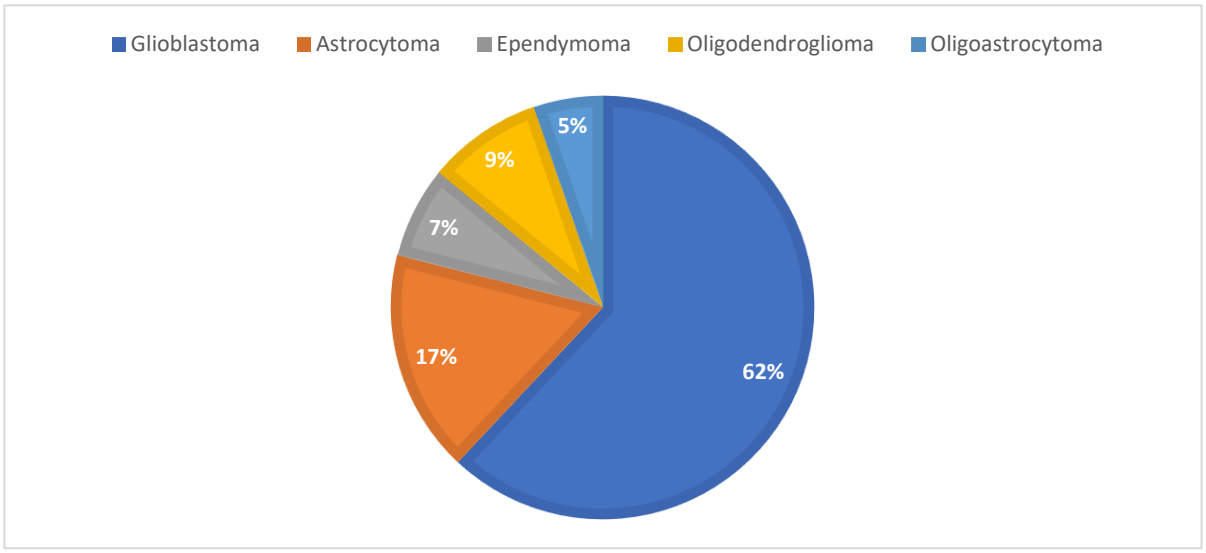


Pie chart 1. Surgical specimens collected from the University Clinic of neurosurgery in Skopje and diagnosed at the Institute of Pathology – UKIM from 2021 to 2022.



Pie chart 2. Representation of other pathological processes (46%) of the CNS from 2021 to 2022.

Out of all analyzed cases from 2021 to 2022, **171** of them were glial tumours out of which **106 (61.99%)** were glioblastomas, **29 (16.96%)** were astrocytoma (WHO grade I, II and III), **15 (8.77%)** were oligodendrogliomas (WHO grade II and III), **12 (7.02%)** were ependymomas and **9 (5.26%) were** oligoastrocytomas (WHO grade II and III).
(Pie Chart 3.)



Pie chart 3. Analysis of glial tumours from 2021 to 2022.

The deeper analysis of the 106 glioblastoma cases showed the that those materials came from 95 patients. Out of 106 surgical specimens, most of them were from newly diagnosed glioblastomas and only 18 of them were recurrent glioblastomas from previously diagnosed tumour in 2020. The demographic analysis showed that glioblastoma is more often diagnosed in patients older than 55 years **67 (70.69%)**, while the rest of the patients - **28 (29.31%),** were under 55 years of age, in addition **53 (55.7%)** were male and **42 (44.2%)** were female patients.
(Diagram 1.)

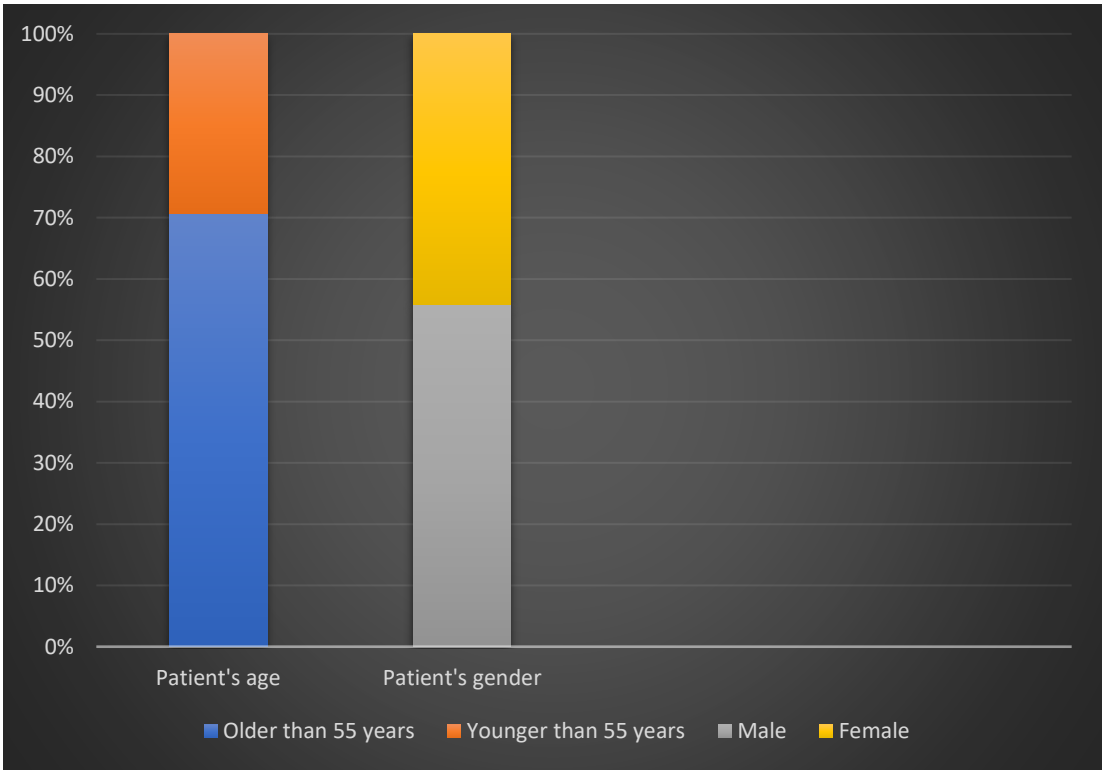
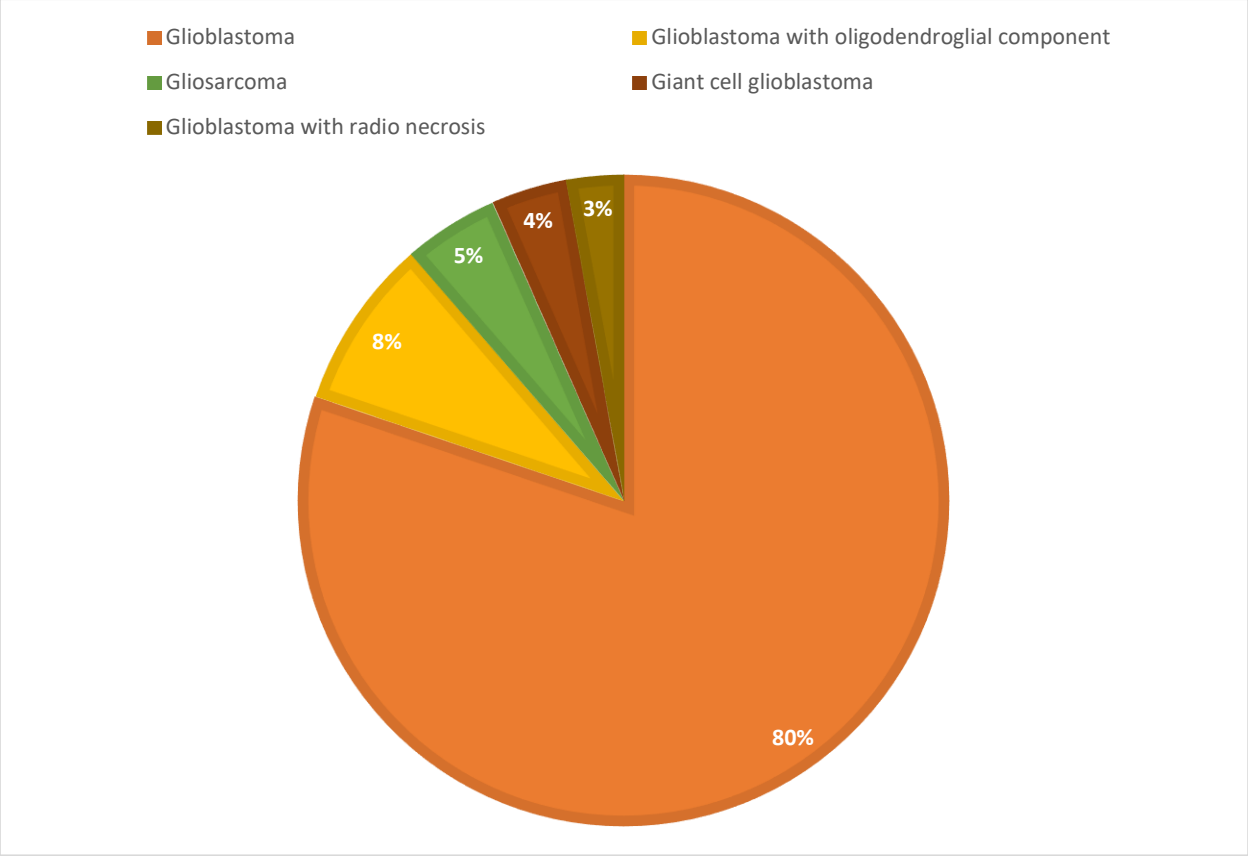


Diagram 1. Age and gender distribution of glioblastoma in 95 patients from 2021 to 2022.

The most dominant histomorphology that was diagnosed in the given period was the classic Glioblastoma type tumour which was found in **85 (80.19%)** cases. **Nine (8.49%)** cases had the histomorphology of glioblastoma with oligodendroglial component, **5 (4.72%)** had the histomorphology of gliosarcoma and **4 (3.77%)** the histomorphology of giant cell glioblastoma. There were **3 (2.83%)** cases with morphological features of glioblastoma with radionecrosis which represents a post-irradiation effect on the tumour tissue. **(Pie chart 4.)**



Pie chart 4. Representation of glioblastoma and its histological variants in patients diagnosed from 2021 to 2022.

Discussion

Introducing the incidence and prevalence of glial tumours, with special reference to glioblastoma from the data collected from the leading diagnostic pathology center - Institute of Pathology, where almost all brain surgical specimens in the country, mainly from the University Neurosurgery Clinic are collected, analysed and diagnosed is a very important step in understanding the impact of these tumours on the population.

Almost all neurosurgery patients in North Macedonia are assessed and operated at the University Neurosurgery Clinic as part of the University Campus ‘’Mother Teresa’’ in Skopje, North Macedonia. The surgical specimens from the Neurosurgery Clinic are regularly sent to the Institute of Pathology and analysed by experienced and trained neuropathologists. Due to the heterogenic and diverse histomorphology of gliomas, especially glioblastoma, where sometimes the presence of lower grade glial elements in the high-grade neoplasms, can be very challenging. Also, the surgical specimens sometimes can contain only necrotic tumour tissue which is difficult for analysis.

The biggest burden for every pathologist or neuropathologists is the rapid developing molecular and genetic analyzes, which in the past couple of years have dramatically impacted and changed the traditional way of analyzing and diagnosing a tumour sample. The latest WHO classification of the Central nervous system tumours published in 2021 have made nosologycal changes of some entities based on their IDH mutational status , molecular profile and the prognosis of the disease. Currently, the term glioblastoma is used only for glial neoplasms that do not have a mutations in the *IDH* gene, do not have epigenetic mutations in the histones and have one or more than one of the following histological

or genetic characteristics: microvascular proliferation, necrosis, *TERT* promoter mutation, *EGFR* gene amplification, +7/-10 chromosomal change in the number of copies. That means that the glial tumours which have mutations in the *IDHI* gene and have histological characteristics of a WHO grade IV tumour (microvascular proliferation, necrosis, mitotic activity) are now classified as Astrocytoma IDH-mutant (CNS WHO grade 4). The median survival for patients diagnosed with Glioblastoma, IDH-wild type is 15-18 months after radiation and chemotherapy and these patients have a shorter median survival time in comparison to patients with IDH-mutant astrocytoma (CNS WHO Grade 4) with similar histological characteristics [1,3].

These new criteria and changes in the brain tumour classification made the neuropathological diagnostic process more dependent on additional techniques, such as immunohistochemical analysis, fluorescent in situ hybridization and molecular-genetic analysis. Because of its affability and affordability, immunohistochemical analysis with immunohistochemical markers like GFAP (Glial Fibrillary Acidic Protein)[4,5], IDH1/2 (Isocitrate dehydrogenase) [6,7], OLIG2 (Oligodendrocyte transcription factor that activates the expression of myelin-associated genes in the oligodendrocyte-lineage cells) [8,9] and ATRX (alpha-thalassemia/mental retardation syndrome X-linked) [10], beside the diagnostic, can have prognostic, even predictive impact and value for glioblastoma.

The results of this descriptive statistical analysis show that glial tumours, especially glioblastomas as most prevalent malignant tumour type deserves greater scientific attention which beside the impact on their diagnostic complexity, will expand the knowledge of this pathology field and strongly reflect on future scientific and diagnostic work.

Conclusion

According to the newest epidemiological statistical information from USA, Canada, United Kingdom and Australia, the annual incidence of glioblastoma in correlation to age is increasing in the last years to 3-6 cases in 100.000, meanwhile its incidence in the Asian and African countries is lower, possibly as a result of underdiagnosing. The most obvious difference associated with gender in glioblastoma is its incidence: the incidence of GBM is 1.6 times higher in men than women.

Whereas lower-grade gliomas incidence is nearly similar in men and women, malignant brain tumors, including glioblastoma occur more often in men. Regarding the age, it can occur at any age, but glioblastoma is more common in older adults. The average age of diagnosis is 64 [3].

When it comes to global statistics, we can conclude that Republic of North Macedonia follows the global trends regarding the incidence of glioblastoma associated with gender and age. Our results show that glioblastoma is more prevalent in males than females with the ratio male to female being 1.2:1, and this tumour is more prevalent in patients older than 55 years with the average age of diagnosis being 61 years.

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