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UNVEILING THE NEUROPATHOLOGY TUMOUR LANDSCAPE: 10-YEAR STATISTICAL ANALYSIS WITH GLOBAL COMPARISON – SINGLE CENTRE EXPERIENCE

Panche Zdravkovski[1], Boro Ilievski[1], Vladimir Rendevski[2], Aleksandar Chaparoski[2], Venko Filipce[2], Aleksandar Zupanoski[2], Aleksandra Dimovska Gavrilovska[2], Blagoj Shuntov[2], Vlado Stolevski[5], Igor Stojkovski[3], Menka Lazareska[4], Ana Mihajlovska Rendevska[4], Gordana Petrushevska[1]

[1] Institute of Pathology, Medical Faculty, University "Ss. Cyril and Methodius" in Skopje, RN Macedonia

[2] University Clinic for Neurosurgery, Medical Faculty, University "Ss. Cyril and Methodius" in Skopje, RN Macedonia

[3] University Clinic for Radiotherapy and Oncology, Medical Faculty, University "Ss. Cyril and Methodius" in Skopje, RN Macedonia

[4] University Clinic for Radiology, Medical Faculty, University "Ss. Cyril and Methodius" in Skopje, RN Macedonia

[5] University Clinic for Surgical diseases "St. Naum Ohridski", Medical Faculty, University "Ss. Cyril and Methodius" in Skopje, RN Macedonia

Corresponding author: Panche Zdravkovski, Institute of Pathology, Medical Faculty, University "Ss. Cyril and Methodius" in Skopje, R. of Macedonia. E-mail: panche.zdravkovski@medf.ukim.edu.mk

ABSTRACT

Introduction: Central nervous system (CNS) tumours represent a significant public health issue worldwide, and their incidence and distribution vary across different populations. Although studies on CNS tumours have been conducted in various countries, there is a lack of information regarding their patterns in Macedonia. Therefore, this study is aimed at investigating the distribution, histopathological types and subtypes and demographic features of CNS tumours in our country.

Materials and Methods: A cross sectional study was conducted using the electronic database of the Institute of Pathology – Medical Faculty, University "Ss. Cyril and Methodius" in Skopje which contains data from 3286 received and analysed surgical specimens, mainly from the University Clinic of Neurosurgery in Skopje, and a smaller number of surgical specimens from the University Surgical Centre "St. Naum Ohridski" in Skopje between 2012 and 2022. The collected and analysed data includes patient age, sex and histopathological types and subtypes of the tumours.

Results: The majority of CNS tumours were diagnosed in adults aged between 50-70, with a male to female ratio of 1.5:1. The most common location of the tumours was the cerebrum, followed by the pituitary gland and cerebellum. The most frequent histological groups were gliomas, with glioblastoma as the most common diagnosis, followed by meningiomas.

Conclusion: Following a detailed and thorough review of the CNS tumours in our study, we can conclude that the R. of Macedonia follows global statistics and trends regarding brain tumours.

Keywords: neuropathology, CNS tumours, prevalence, analysis, global trends

INTRODUCTION

The importance of neuropathology tumour diagnostics cannot be stressed enough, as an accurate and timely diagnosis is crucial for effective treatment planning and prognosis assessment. This process poses several challenges that need to be addressed to ensure optimal patient care. One

of the main hurdles in neuropathology tumour diagnostics lies in achieving accurate diagnoses, which can be quite challenging due to various factors. Obtaining very small or insufficient tumour samples, sampling from areas near the neoplasm, necrosis and overlapping morphologies, all contribute to the complexity of achieving a precise diagnosis. The variety of brain tumours complicates correct diagnosis even more. Due to their similarities, identifying tumour cells from normal brain tissue might be difficult in some situations. This is especially true for low-grade or early-stage tumours when the distinctions between tumour cells and normal brain tissue can be modest. Another barrier is the scarcity of tissue samples. Obtaining tissue samples might be difficult due to the delicate nature of the brain and the possible complications associated with invasive surgical techniques. Limited availability to tissue samples may impede a correct diagnosis and, as a result, treatment decisions. Addressing all these issues in neuropathology tumour diagnostics is critical for improving diagnostic accuracy and efficiency.

Tumours of the central nervous system (CNS) are a broad group of neoplasms that develop from different types of brain and spinal cord cells. Globally, CNS tumour patterns differ greatly and are impacted by a variety of variables, including genetic, environmental, and lifestyle factors[1] [2]. Because developed nations like the United States, Canada, and the region of Western Europe have better access to healthcare and medical technologies, like advanced radiological imaging techniques, this may result in an increased incidence of diagnosed brain tumours[2][3]. The incidence of CNS tumours is lower in developing countries, such as in most African countries, India, Malaysia and Indonesia. The different levels of exposure to environmental factors, including industrialization and environmental pollution, which produce various carcinogens, ionizing radiation, specific chemicals, and electromagnetic fields, may also raise the risk of developing brain tumours. In addition, lifestyle elements including nutrition and exercise may be important. Obesity and a diet heavy in processed foods are more prevalent in developed nations[3][5].

Beside the cancer registry basic reports from the Macedonian Institute of Public Health, there are no thorough epidemiological studies regarding the incidence and distribution of brain tumours. The Institute of Pathology – Faculty of Medicine, University "Ss. Cyril and Methodius" in Skopje, as the oldest and continuously operating public institution, for over six decades has been at the forefront of diagnosing tumours of the CNS, contributing significantly to the understanding, treatment, and management of these complex diseases. From its inception in 1947, the Institute has remained dedicated to advancing the knowledge and practice of pathology, it has nurtured generations of pathologists and has become the cornerstone of diagnostics excellence in this country. The Institute of Pathology – University "Ss. Cyril and Methodius" in Skopje recognizes the significance of collaboration and multidisciplinary approach in providing comprehensive care for patients with brain tumours, and maintains close collaboration with neurosurgeons, neuro-oncologists, neuro-radiologists, and other specialists to ensure seamless integration of diagnostic findings into treatment strategies.

The aim of this statistical analysis was to examine the epidemiology and histology of CNS tumours and non-neoplastic disorders within the context of the public health system.

MATERIALS AND METHODS

This cross-sectional study was conducted using the electronic database of the Institute of Pathology – Medical Faculty, University "Ss. Cyril and Methodius" in Skopje which contains data from 3286 analysed surgical specimens mainly received from the Public Health Institution – University Clinic for Neurosurgery – Skopje, University Clinic "Mother Teresa", the neurosurgical core and the oldest public neurosurgical institution in the country. We also used a smaller number of surgical specimens (n=178) from the Public Health Institution - University Clinic for Surgical Diseases "St. Naum Ohridski" in Skopje, which mainly focuses on spinal surgery and intervertebral-disk disorders, between 2012 and 2022. The collected and analysed data include patient age, sex and histopathological types and subtypes of the tumours. The statistical methods and tests used in this study comprise descriptive statistics, correlations, and cluster analysis.

RESULTS

Over the course of the last ten years (2012–2022), the Institute of Pathology have received and patohistologically analysed 3108 operative materials from 2836 patients, operated once or multiple times at the University Clinic of neurosurgery in Skopje. There were 272 operative materials taken from recurrent or residual diseases, 352 from non-neoplastic diseases, and 2484 from neoplastic disorders. (Fig. 1.)

Of the 2836 patients, 352 had non-neoplastic diseases, the most prevalent of which were cerebrovascular diseases, followed by inflammatory and infectious diseases, and the least prevalent of which were spinal cord disorders. (Fig. 2.)

Among the entire patient cohort, 2484 individuals had a diagnosis of neoplastic disease. Within this group, there were 1785 cases of primary tumours, 463 cases of secondary (metastatic) tumours, 161 cases of pituitary gland tumours (16% of total neoplastic diseases), and 75 cases of neoplasms originating from various sites and origins (e.g., basal cell carcinoma – scalp, chordoma – vertebrae, giant cell tumour of bone – vertebrae, trichofolliculoma – scalp, osteochondroma – vertebrae). (Fig. 3)

In terms of malignant brain neoplasms, there was a male-to-female ratio of 1.5:1. The age range of patients varied from one to 94 years, with a median age of 65. (Fig. 10)

The most prevalent primary tumours were diffuse astrocytic and oligodendroglial tumours, followed by meningiomas, and the least common being neuronal and mixed neuronal tumours, choroid plexus tumours and germ cell tumours. (Fig. 4.)

The most common types of diffuse astrocytic and oligodendroglial tumours were those classified as WHO Grade IV, specifically glioblastoma and its variants. The second most prevalent types were those classified as WHO Grade II, which included diffuse astrocytoma, oligodendroglioma, oligoastrocytoma, and pleomorphic xanthoastrocytoma. The least prevalent types were those classified as WHO Grade III, which encompassed anaplastic astrocytoma, anaplastic oligodendroglioma, anaplastic oligoastrocytoma, and anaplastic pleomorphic xanthoastrocytoma. These findings are represented in Figure 5 and Figure 6.

Meningiomas were the second most frequent primary tumours, with a total of 629 cases. Among meningiomas, the most prevalent type was classified as WHO grade I, while the least common type was represented by WHO grade III meningiomas. These statistics can be observed in Figure 7 and Figure 8.

Metastatic carcinomas accounted for the majority (86%) of secondary brain tumours, while metastatic melanomas constituted a smaller portion (14%) of such tumours (Fig. 9). Interestingly, secondary brain tumours were less common than primary brain tumours. This information diverges from the global trend, where a larger proportion of brain tumours are typically secondary in nature.

Most of the surgical specimens were obtained from patients within the age range of 60-70 years, whereas the fewest number of cases came from patients aged between 20-30 years. This distribution is illustrated in Figure 10.

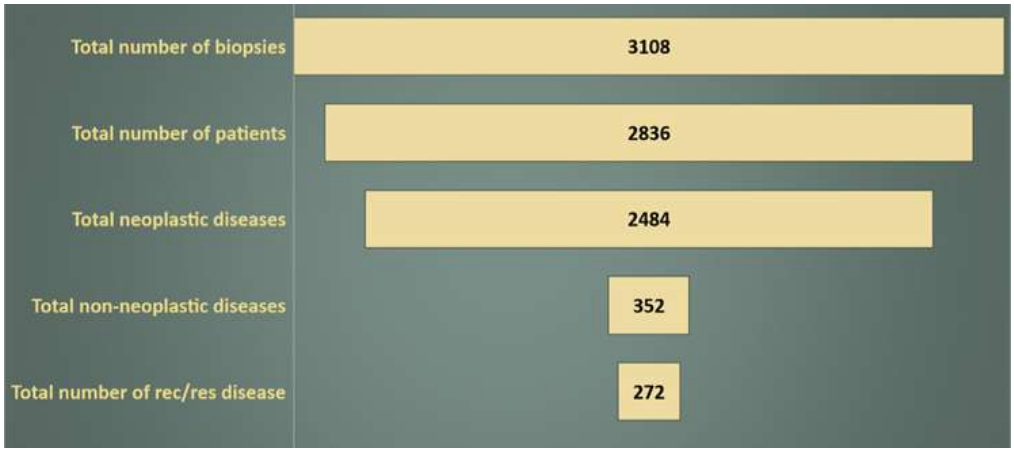

Figure 1. *Schematic 10-year overview of total analysed surgical specimens at the Institute of Pathology operated at the University Clinic of Neurosurgery in Skopje*

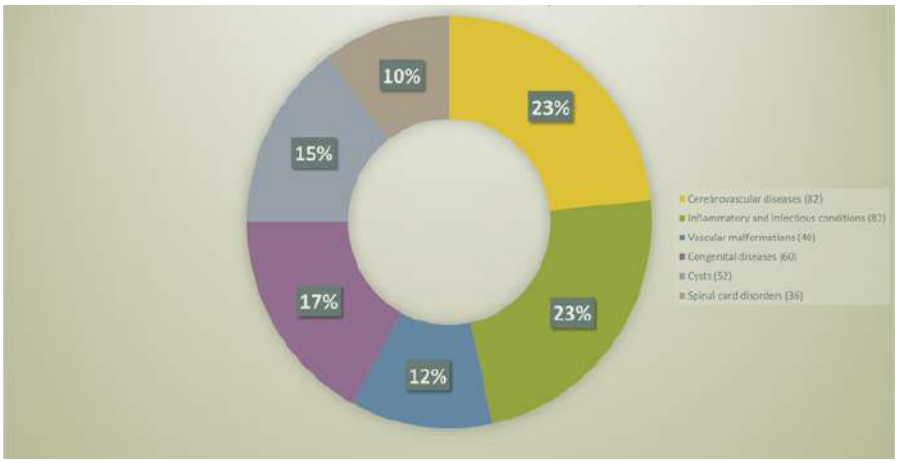

Figure 2. *Pie chart of non-neoplastic diseases (2012-2022) operated at the University Clinic of Neurosurgery in Skopje*

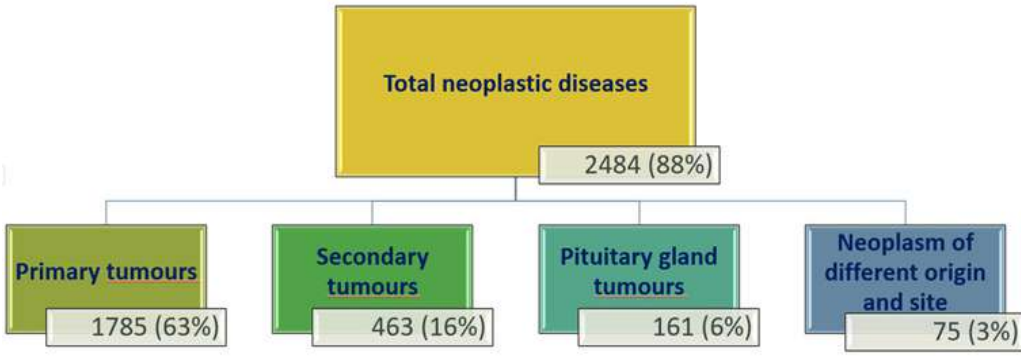

Figure 3. *Systematic preview of the total neoplastic diseases (2012 - 2022) operated at the University Clinic of Neurosurgery in Skopje*

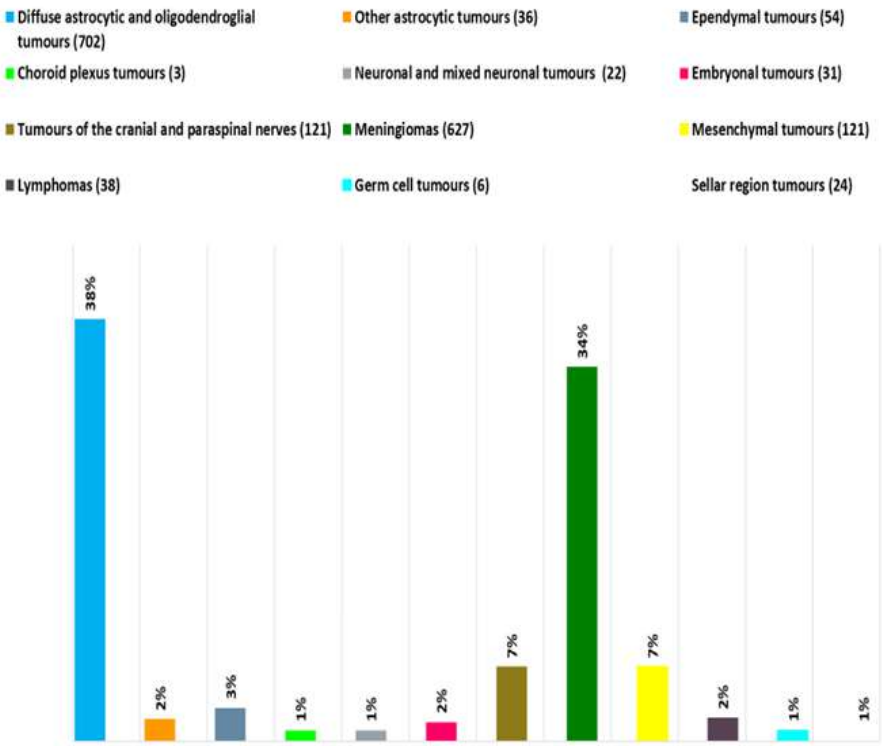

Figure 4. *Diagrammed overview of primary tumours (2012-2022) operated at the University Clinic of Neurosurgery in Skopje*

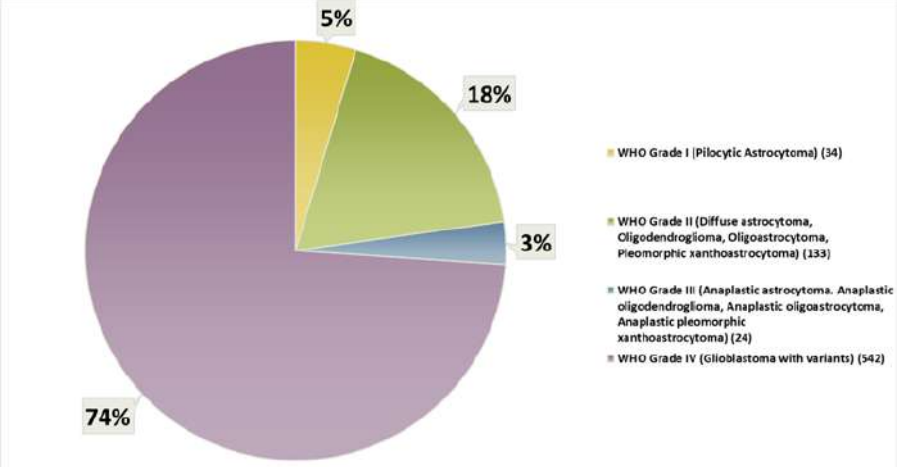

Figure 5. *Pie chart - diffuse astrocytic and oligodendroglial tumours – WHO I, II, III, IV (2012-2022) operated at the University Clinic of Neurosurgery in Skopje*

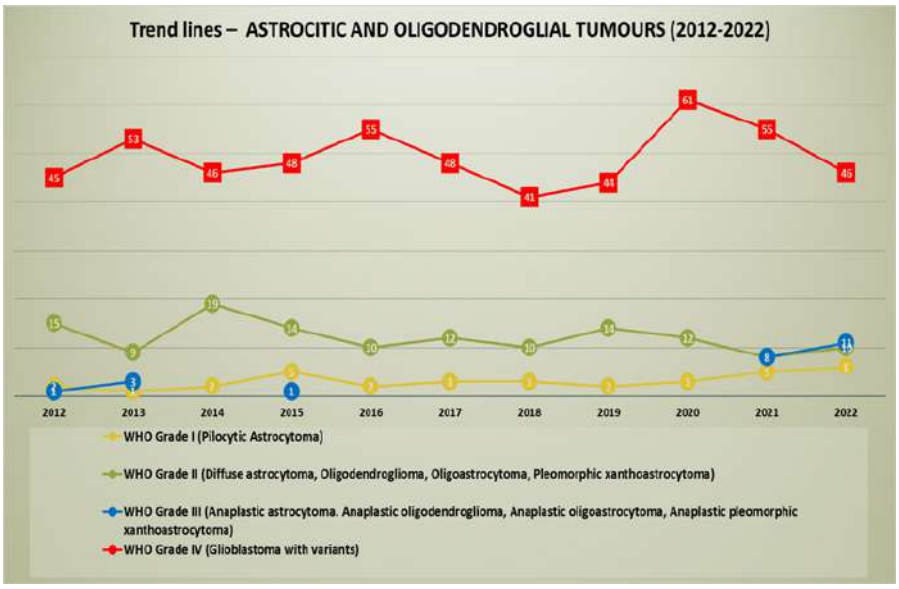

Figure 6. *Graphic overview of trend lines regarding astrocytic and oligodendroglial tumours (2012-2022) operated at the University Clinic of Neurosurgery in Skopje*

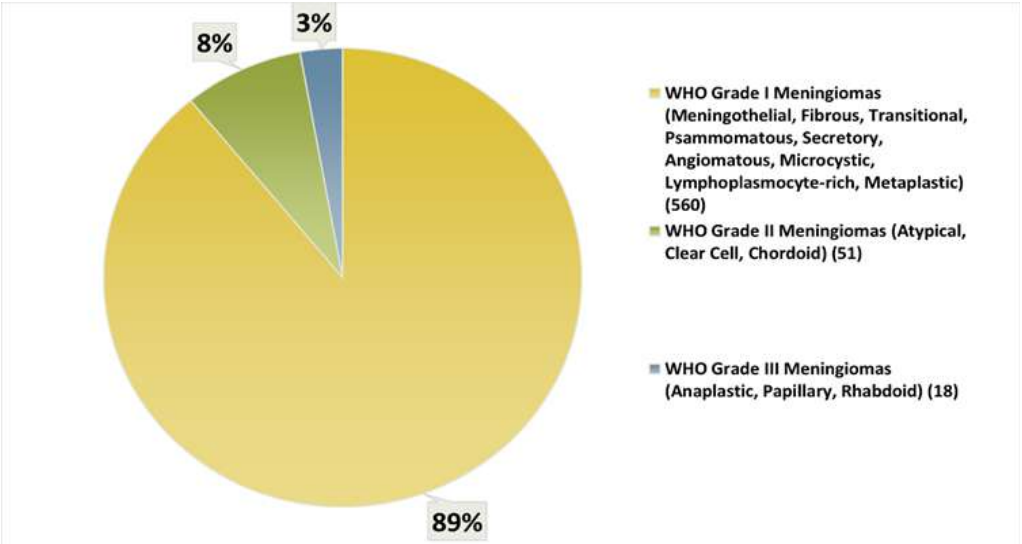

Figure 7. *Pie chart – meningiomas – WHO gr. I, II, III (2012-2022) operated at the University Clinic of Neurosurgery in Skopje*

Figure 8. *Graphic overview of trend lines regarding meningiomas (2012-2022) operated at the University Clinic of Neurosurgery in Skopje*

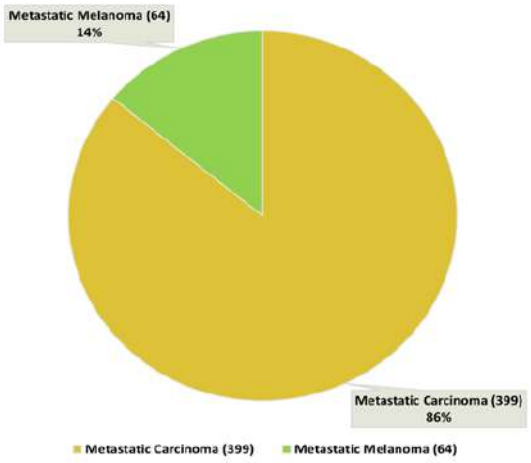

Figure 9. *Pie chart – secondary brain tumours (2012-2022) operated at the University Clinic of Neurosurgery in Skopje*

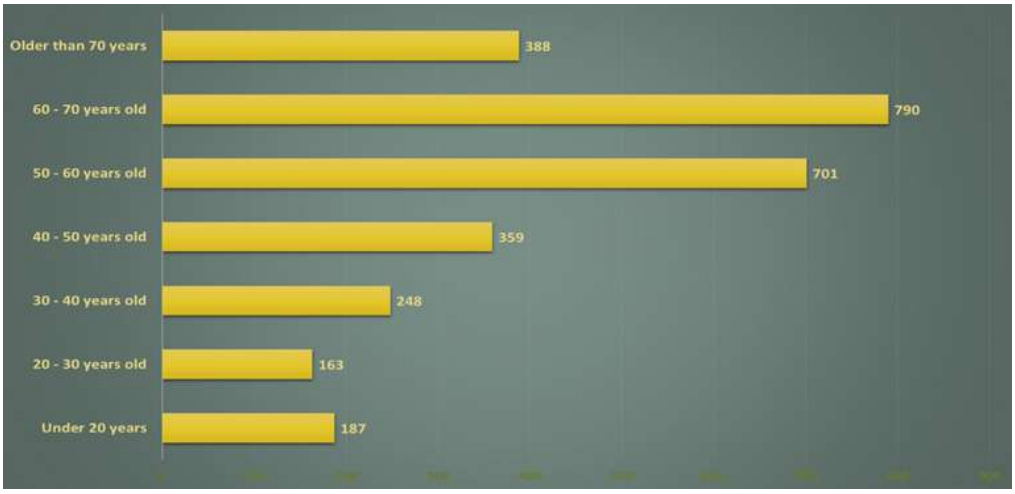

Figure 10. *Diagram – age distribution of total brain surgical specimens (2012-2022) operated at the University Clinic of Neurosurgery in Skopje*

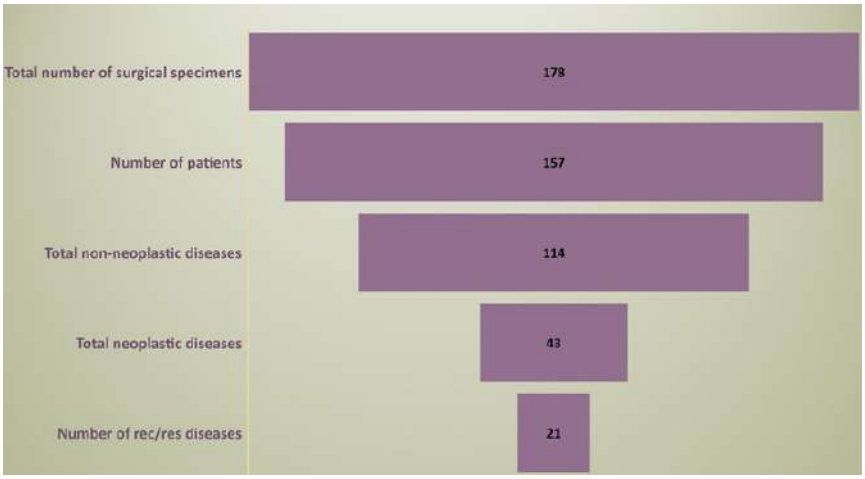

Figure 11. *General statistics from analyzed surgical specimens (2012-2022) operated at the University Clinic for Surgical diseases St. Naum Ohridski*

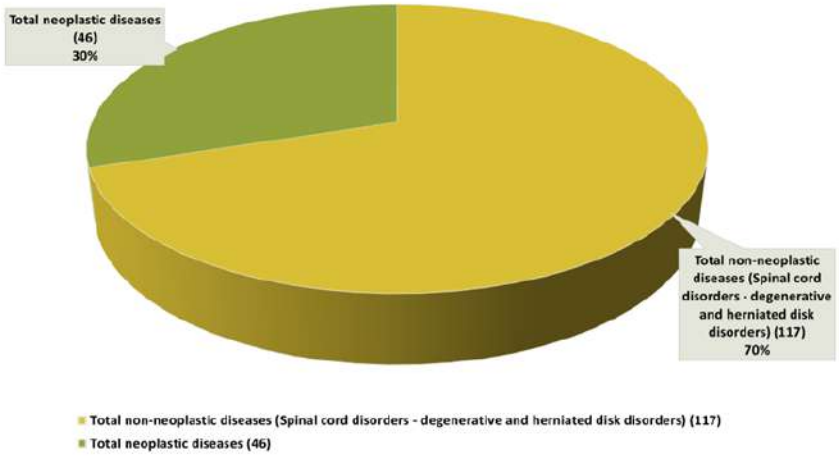

Figure 12. *Pie chart – non-neoplastic and neoplastic diseases (2012-2022) operated at the University Clinic for surgical diseases St. Naum Ohridski*

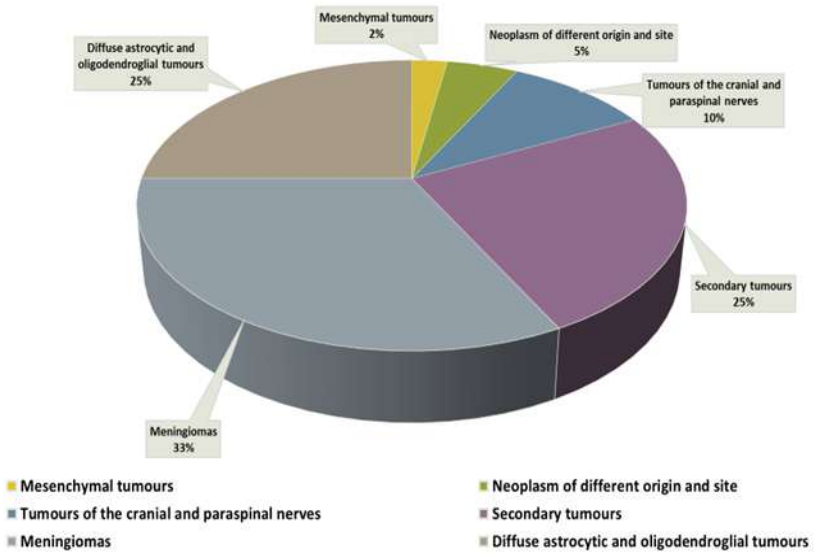

Figure 13. *Pie chart – neoplastic diseases (2012-2022) operated at the University Clinic for Surgical diseases St. Naum Ohridski*

During a 10-year period at the University Clinic for surgical diseases "St. Naum Ohridski", 157 patients were operated upon, and a total number of 178 cases were analysed. Out of these operative materials, 21 were recurrent or residual diseases (Fig. 11). Interestingly, in contrasting the previous statistics from the University Clinic for Neurosurgery in Skopje, the number of non-neoplastic surgical specimens exceeded the number of diagnosed neoplastic cases, as shown in Fig. 12. The most frequent non-neoplastic diagnosis was spinal cord disorders, specifically degenerative and herniated intervertebral-disk disorders. On the other hand, the most common neoplastic disease diagnosis was meningioma, followed by diffuse astrocytic and oligodendroglial tumours, as well as secondary tumours, as indicated in Fig. 13.

DISSCUSION

The findings and conclusions presented in this study derived from the analysis of surgical materials obtained from the University Clinic of Neurosurgery in Skopje and University Clinic for Surgical Diseases "St. Naum Ohridski" - Skopje.

The number of neoplastic disorders was six times higher than that of non-neoplastic diseases. Non-neoplastic conditions such as cerebrovascular, inflammatory, and infectious disorders were the most frequently encountered. On the other hand, spinal cord problems were the least prevalent non-neoplastic disorders.

Among CNS tumours, diffuse astrocytic and oligodendroglial tumours, specifically gliomas with a predominance of glioblastomas, were the most prevalent, which corresponds to the global predominance of this tumour types where they account for over 70% of all primary CNS tumours. WHO reports show that astrocytoma, oligodendroglioma, and ependymoma are the most common subtypes of gliomas.[4][6] Within the category of diffuse astrocytic and oligodendroglial tumours, in our study WHO grade IV neoplasms, particularly glioblastoma with variations, were the most prevalent, followed by WHO grade II gliomas. The most frequently observed recurrent/residual disease was glioblastoma (WHO grade IV), followed by meningiomas. Following the trend lines of astrocytic and oligodendroglial tumours, we confirm that glioblastoma (WHO grade IV) is the most prevalent glial tumour with peak of incidence in 2020 followed by 2021, and the lowest incidence occurred in 2018. Glioblastoma is followed by WHO grade II group of glial tumours with the peak incidence in 2014, and the lowest incidence in 2021. (Fig. 6)

Meningiomas and secondary (metastatic) tumours followed as the next commonly observed tumour types in the R. of Macedonia. Meningeal tumours are the second most common type of CNS tumours worldwide, also in our country, accounting for about 25% of all primary CNS tumours. The most common subtype of meningeal tumour is meningioma, which arises from the meninges [2][3][5][6], and the most diagnosed tumour grade was WHO grade I and the least common was WHO grade III. The trend lines regarding meningiomas show that the most diagnosed is the WHO grade I meningiomas with a continuous increase in incidence from 2018 to 2022, and the least diagnosed was WHO grade III meningiomas. (Fig. 8)

The incidence of CNS tumours tended to increase with age, with the highest incidence found in patients aged 60-70, followed by those aged 50-60. The age range and the incidence follow the global trends.

Secondary (metastatic) tumours account for 18% of the total number of all brain tumours which fall into range with the global epidemiology for secondary brain tumours, where they account for about 10-30% of all brain tumours. They are more common in adults than in children. The most common cancers that metastasize in the brain are lung cancer, breast cancer and melanoma. Annually, our analysis shows that in our country, seen solely from a public health system represented by the data from the Institute of Pathology – University "Ss. Cyril and Methodius" in Skopje, around 46 cases of brain metastases are diagnosed with an annual incidence of approximately 2.3 cases per 100,000. In comparison, there is an estimated number of 70,000 – 200,000 new cases of metastatic brain tumours in the United States of America with an approximate annual incidence of 21 new cases per 100,000 [7].

Hormone-producing pituitary adenomas (WHO grade I) predominated among pituitary gland tumours, with plurihormonal adenomas being the most common subtype. Globally, pituitary gland tumours are relatively common neoplasms, accounting for about 10-15% of all brain tumours. The annual incidence in Macedonia is 0.08 in 1000

people. This is lower than the incidence of 1 in 1000 people in the USA, and Western European incidence of 1 in 2000 people. As in our country, worldwide, the most common type of pituitary gland tumour is pituitary adenoma, which accounts for about 80% of all pituitary gland tumours [3][6].

The WHO and other referent studies report that lymphomas and germ cell tumours are less common CNS tumours, accounting for less than 5% of all primary CNS tumours [2][3][5][6]. This statistic is comparable to our results where primary CNS lymphomas (n=38) account for 2.1% of the total primary CNS tumours (n=1785). Diffuse large B-cell lymphoma in our study were the most prevalent subtype of primary CNS lymphomas. Choroid plexus and histiocytic tumours were the least common forms of tumours, observed with less than 1% from total primary CNS tumours.

CONCLUSION

Following a detailed and thorough review of the CNS tumours in our study, we can conclude that the R. of Macedonia follows the global statistics and trends regarding brain tumours. However, it is equally crucial to recognise some variances that exist. Exploring the reasons behind these variations could shed light on specific risk factors, genetic predispositions, or environmental influences that contribute to the unique tumour profile in our country.

These variances demand awareness in the sense of development of personalized preventive, diagnostic and treatment measures. More research and collaboration with international efforts will lead to a more thorough understanding of CNS malignancies, enhancing patient management and outcomes.

It is important to note that this study was conducted from a single centre perspective, and these results may differ if data from other pathology centres were included such as ones from private hospitals or independent laboratories.

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Резиме

РАЗОТКРИВАЊЕ НА ОПСЕГОТ НА ТУМОРСКА НЕВРОПАТОЛОГИЈА: 10 ГОДИШНА СТАТИСТИЧКА АНАЛИЗА И КОРЕЛАЦИЈА СО ГЛОБАЛНИТЕ ТРЕНДОВИ – ИСКУСТВА ОД ЕДИНЕЧЕН ЦЕНТАР

Панче Здравковски[1], Боро Илиевски[1], Владимир Рендевски[2], Александар Чапароски[2], Венко Филипче[2], Александар Жупаноски[2], Александра Димовска Гавриловска[2], Благој Шунтов[2], Владо Столевски[5], Игор Стојковски[3], Менка Лазареска[4], Ана Михајловска Рендевска[4], Гордана Петрушевска[1]

[1] Институт за патологија, Медицински факултет, Универзитет „Св. Кирил и Методиј“ во Скопје, РС Македонија

[2] Универзитетска клиника за неврохирургија, Медицински факултет, Универзитет „Св. Кирил и Методиј“ во Скопје, РС Македонија

[3] Универзитетска клиника за радиотерапија и онкологија, Медицински факултет, Универзитет ‘’Св. Кирил и Методиј’’ во Скопје, РС Македонија.

[4] Универзитетска клиника за радиологија, Медицински факултет, Универзитет „Св. Кирил и Методиј“ во Скопје, РС Македонија

[5] Универзитетска клиника за хируршки болести „Св. Наум Охридски“, Медицински факултет, Универзитет „Св. Кирил и Методиј“ во Скопје, РС Македонија

Вовед: Туморите на централниот нервен систем (ЦНС) претставуваат значаен проблем за глобалното јавно здравје и нивната дистрибуција и инциденца се различни кај различни популации. Во различни земји од светот се направени студии за туморите на ЦНС, а во Македонија се забележува нивен недостиг. Поради тоа, целта на оваа студија е да се истражи дистрибуцијата, хистопатолошкиот тип и поттип, како и демографските карактеристики на туморите на ЦНС во нашата земја.

Материјали и методи: Оваа пресечна студија е направена со користење на електронската база на податоци на Институтот за патологија при Медицинскиот факултет, Универзитет „Св. Кирил и Методиј“ во Скопје, од која се обработија податоци од вкупно 3286 патохистолошки анализирани оперативни материјали, испратени главно од Универзитетската клиника за неврохирургија во Скопје, и помал број на анализирани оперативни материјали испратени од Универзитетската клиника за хируршки болести „Св. Наум Охридски“ во период од 2012 до 2022 година. Анализираните податоци се состојат од возраст на пациентите, пол и хистолошки тип и поттип на туморот.

Резултати: Повеќето од туморите на ЦНС се дијагностицирани кај пациенти на возраст од 50 до 70 години, со сооднос меѓу мажите и жените 1,5 : 1. Најчестата локација на туморите е големиот мозок, по што следуваат хипофизата и малиот мозок. Најчестата хистолошка група тумори кај пациентите се глиомите, односно глиобластомот, а по него – менингиомот.

Заклучок: Од резултатите од направената статистичка анализа за мозочни тумори можеме да заклучиме дека Р Македонија ги следи глобалните статистики и трендови во однос на мозочните тумори.

Клучни зборови: невропатологија, тумори на ЦНС, преваленца, анализа, глобални трендови