



CLINICAL AND HISTOPATHOLOGICAL CHARACTERISTICS OF PRIMARY BRAIN TUMOR DISEASE IN RSUP DR. KARIADI SEMARANG

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ABSTRACT

Introduction: Primary brain tumour is one of the non-communicable diseases that ranks 17th of all types of cancer in the world with an estimated 256,000 new cases each year. The incidence in North America, Europe and Australia is quite high with an estimated 4-8 new cases per 100,000 population per year. The incidence in continental countries of Asia and Africa is less compared to developed countries. The low incidence and mortality of brain tumours in the continents of Asia and Africa, especially in Indonesia, is thought to be due to the low reports of brain tumour disease from some of these countries, so as to increase knowledge and management of brain tumour plenary services in Indonesia, accurate hospital clinical data is needed. **Objective:** This study aims to look at the frequency of events, symptoms and clinical signs, histopathological characteristics, the stage at diagnosis, and compare the incidence of primary brain tumours in men and women. **Methods:** This study used a descriptive observational study design that uses data on primary brain tumour patients in the period of January 2017 - December 2018. Data collected includes clinical symptoms and signs, histopathological characteristics, and tumour tissue characteristics. **Results:** From 72 patients with primary brain tumour, only 36 (50%) of data can be used as samples due to the completeness of the medical record. The most common clinical symptoms and signs are headache, followed by limb disorders, and visual impairment. The most common histopathological features are Astrocytic tumour with a ratio of 17: 5 for men and women respectively. **Conclusion:** Primary brain tumours in RSUP Dr. Kariadi Semarang is often found with symptoms of headache followed by limb disorders and visual impairment, with a type of Astrocytic tumour that is more commonly found in men.

Keywords: Primary brain tumours, clinical features, histopathological

INTRODUCTION

The incidence of primary brain tumours and other central nervous systems in the age group of 15-39 years is 10.94 per 100,000 population, while the age group of 40 and above is 40.82 per 100,000 population¹. Data obtained by Arora et al² shows that the overall incidence in 1995-2003 was 9.21 per 100,000 population with an incidence rate for males more than females of 9.96 and 8.52 per 100,000 population respectively. Data obtained by EDY et al³ showed that from 2009-2013, 173 primary brain tumour cases occurred in two hospitals in Bandar Lampung with meningioma was the most in 100 cases.

Until now, the risk factor for primary brain tumours that have been shown to have a causal association is ionizing radiation⁴⁻⁷. The other potential risk factors include exposure to chemicals, diet, non-ionizing radiations, hereditary, hormonal, and ages^{1,8-11}.

Based on its location, primary brain tumours are classified into 2, namely Supratentorial and Infratentorial. Supratentorial locations include the hemisphere, sellar, and pineal, while the infratentorial covers the area of the brain stem and cerebellum¹². In 2007 WHO classified primary brain tumours into several groups, i.e. astrocytic, oligodendroglial,



oligoastrocytomas, ependymal, choroid plexus, other neuroepithelial, neuronal and neuronal-gliial, pineal, embryonal, tumour in cranial and paraspinal nerves, meningeal, and sellar¹³.

The manifestation of primary brain tumours include; headache, seizures, disturbance of consciousness, vision disorders, cranial nerve disorders, cognitive disorders, personality disorders, papilloedema, limb disorders, and nausea and vomiting^{3,14}. Tumours that occur in several functional areas of the brain will give a different clinical feature of neurological deficits¹⁴.

METHOD

This study used an observational study design with a descriptive retrospective approach. The data in this study used secondary data in the form of medical records of primary brain tumour patients who are treated at RSUP Dr. Kariadi

Semarang during the period of January 2017 - December 2018 with the inclusion criteria of patients aged 18 years and over and has histopathological data. The variables of this study are clinical features of primary brain tumour disease which include age, sex, symptoms and signs, and tumour characteristics based on histopathological examination.

HASIL

The incidence of primary brain tumours in males is more common (26 cases, 72.2%) compared to females (27.8%). The frequency of primary brain tumours by age group can be seen in Figure 1. The most common age group with the incidence of primary brain tumours in men is the age group of 50-59 years by 7 people (19%), followed by the age group of 40-49 by 6 people (16%).

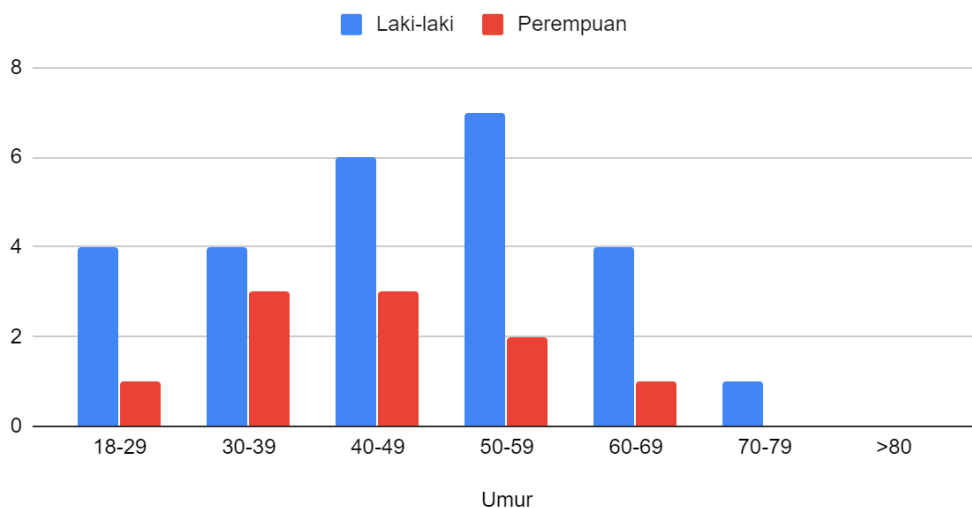


Figure 1. Age Group Frequency Distribution based on Gender



Table 1. Frequency Distribution of Primary Brain Tumors based on Clinical Signs

Clinical Manifestation	Cases (n)	Percentage (%)
General Symptoms		
Headache	25	69.44
Changes in consciousness	8	22.22
Seizures	4	11.11
Cognitive changes	1	2.78
Focal Symptoms		
Motor deficit	12	33.33
Visual problems	9	25
Cranial nerve deficit	8	22.22

Based on table 1, the most common symptom found in primary brain tumour patients is headache as many as 25 people (69.44%), other symptoms that can be found in brain tumour patients are limb disorders as much as 12 people (33.33%), visual impairment as much as 9 people (25%), and awareness disorders as many as 8 people (22.22%).

Based on anatomic location, primary brain tumours are more commonly found in

the frontal lobes (12 cases, 33.3%), and other locations that can be found in the incidence of primary brain tumours are the temporal lobe (5 cases, 13.9%) and occipital lobes in (4 cases 11.1%), this can be seen in Figure 2. The incidence of primary brain tumours is more commonly found on one side, the left side as many as (14 cases, 38.9%) and the right side alone as many as (16 cases, 44.4%). This can be seen in Figure 3.

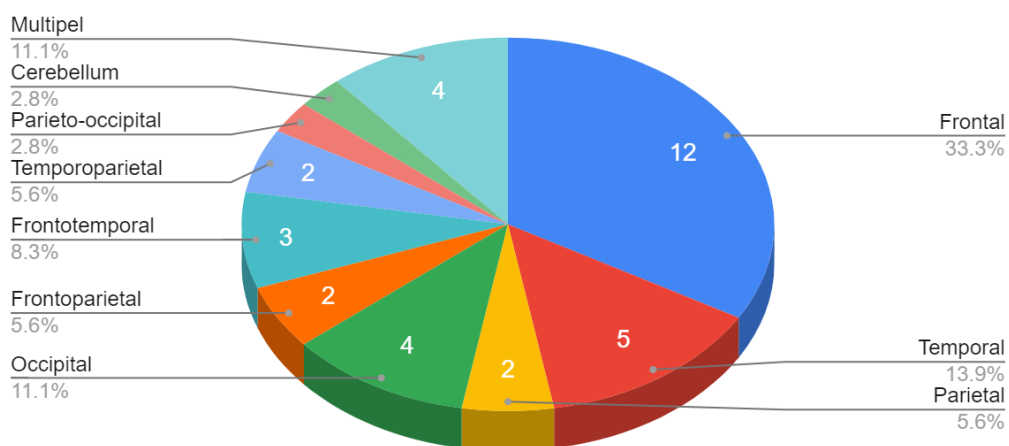


Figure 2. Frequency Distribution of Primary Brain Tumor Events by Tumor Type

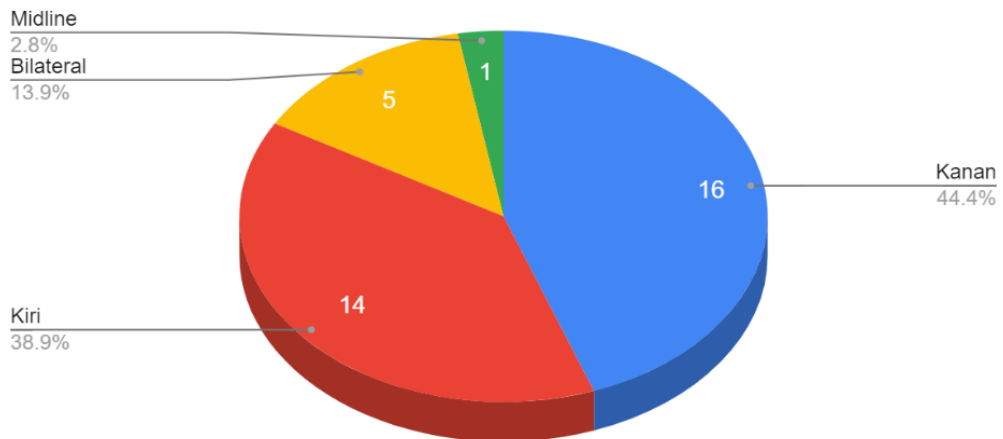


Figure 3. Frequency Distribution of Primary Brain Tumor Occurrence by Head Side

The most common type of primary brain tumour is astrocytic tumours (22 cases, 61.1%), followed by meningeal (6 cases,

16.7%), oligoastrocytomas (4 cases, 11.1%). This can be seen in Figure 4.

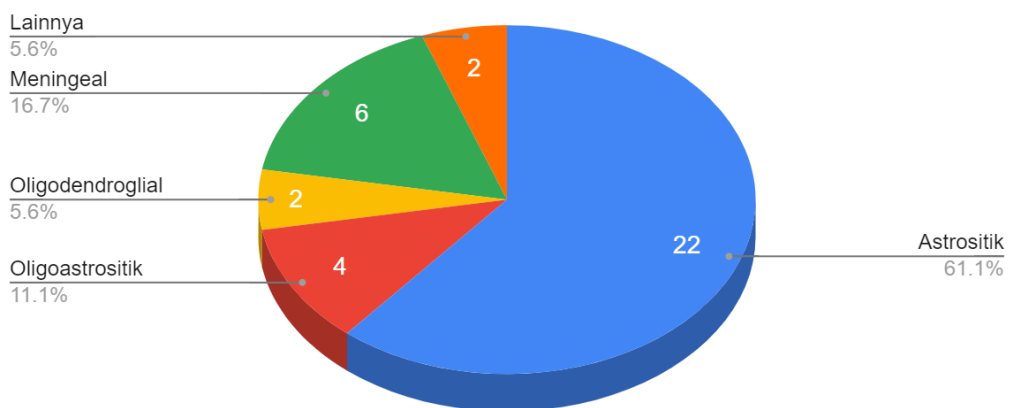


Figure 4. Primer Brain Tumor Frequency Distribution based on Tumor Type

Astrocytic tumours are more common in men as many as 21 people compared with women as many as 7 people,

the ratio between men and women is 17:5. Meningeal tumours are found in 3 people in each sex.

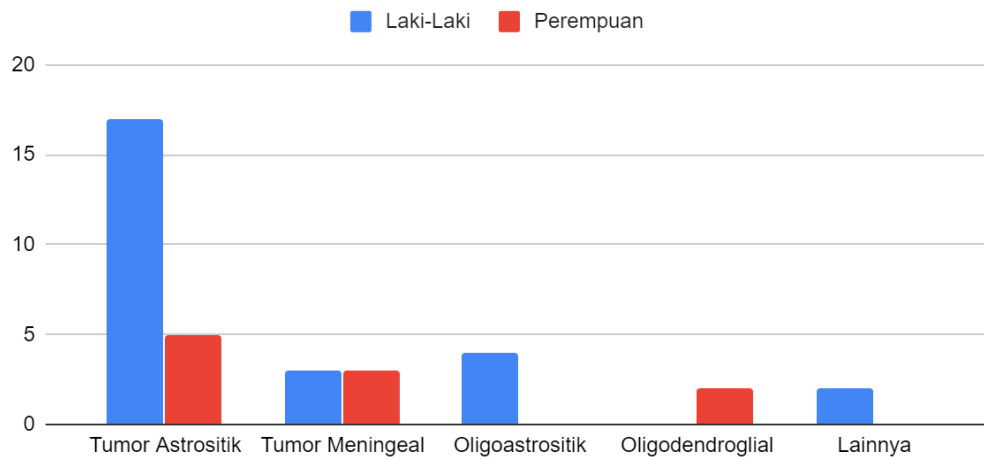


Figure 5. Frequency Distribution of Primary Brain Tumor Types based on Gender

Table 2. Frequency Distribution of Primary Brain Tumors based on Stadium

Stages	Astrocytic		Meningeal		Oligoastrocytic		Oligodendroglial	
	Cases (n)	Percentage (%)	Cases (n)	Percentage (%)	Cases (n)	Percentage (%)	Cases (n)	Percentage (%)
WHO I	1	3.57	2	33.33	0	0	0	0
WHO II	4	14.28	2	33.33	1	25	0	0
WHO III	8	28.57	2	33.34	3	75	2	100
WHO IV	15	53.57	0	0	0	0	0	0
Total	28	100	6	100	4	100	2	100

Based on the stage in each tumour type that can be seen in table 1, astrocytic tumours more commonly found with stage 4 (15 cases, 53.57%) followed by stage 3 (8 cases, 28.57%). Meningeal tumor stage was found in 2 people in each stage from stage 1 to 3.

DISCUSSION

The results obtained from studies in primary brain tumour patients in RSUP Dr. Kariadi showed that primary brain tumours were more often found in men compared to women. This can occur because sex

differences will affect the complementary sex chromosomes, the acute and epigenetic effects of sex hormone activity, thereby causing differences in development, metabolic, and genotoxic stress¹⁵. In addition, based on experimental research conducted by Kabat GC et al¹⁶ found that glial tumours implanted in female mice had slower tumour growth and a longer life expectancy in the group of rats given estrogen, both male and female rats.

Sex differences will cause differences in therapeutic response. This is based on differences in the initiation of



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tumour mechanisms, tumour development, and prognosis. Glioblastoma multiforme based on genetic disorders are divided into 4 subtypes, namely mesenchymal, proneural, neural, and classical. Mesenchymal, proneural and neural types have a ratio of male and female ratios of 2:1, while classically the number of events is the same for both men and women. Meningioma cases associated with sex hormones, this is based on several opinions; (1) meningiomas are rarely found in pre-puberty children where sex hormones have not reached optimal levels, (2) the incidence in women is twice higher than in men, (3) meningiomas express receptors for progesterone and estrogen¹⁵.

The incidence of primary brain tumours more commonly found in the age group of 50 and above can be explained by the theory of ageing which can lead to dysregulation of the cell cycle, causing tumours. The theory of ageing is generally divided into 2, namely the programmed theory and the theory of damage and error. Programmed theory consists of several theories, (1) programmed longevity in which ageing is a series of events arising or loss of certain gene functions causing genetic function imbalances, (2) endocrine theory states that hormones have a role in controlling the ageing process and one example that has an important role in ageing is hormone regulation by IGF, (3) immunological theory states that the immune system will decrease its function over time, thereby increasing a person's risk for infectious disease or the body's inability to protect itself from external stressors¹⁷.

Another theory that can explain why old age has a risk of malignancy is the theory of damage and error. Damage and error theory consists of several theories, (1) wear and tear theory states that ageing in

cells and tissues occurs because the cells or tissues are used continuously, (2) the rate of living theory states that the greater the metabolism of a basal oxygen cell or tissue, the shorter the age of the cell or tissue, (3) cross-linking theory states that accumulation of cross-link proteins will damage cells and tissues, (4) free radical theory states that superoxide and free radicals will damage the macromolecular components of cells such as nucleic acids, lipids, sugars, and proteins. This damage will accumulate and cause reduced cell and tissue function. The somatic DNA damage theory (5) states that DNA damage occurs at any time, but this damage will be repaired by the DNA repair process. When a genetic mutation occurs and accumulates, it will cause dysregulation at the cellular level and initiate neoplasms¹⁷.

In this study, headache is found to be the most common symptoms, can be caused by a delay in the diagnosis of primary brain tumours. Headache complaints have a relationship with the greater size of the tumour so that with increasing tumour stage, headache complaints will be more frequently found^{18,19}.

In this study, primary brain tumour in the frontal lobe is more common than other lobes. The growth of primary brain tumours in certain lobes associated with gene anomalies. One genetic anomaly in brain tumours is an anomaly in the IDH gene. IDH is an enzyme that plays a role in glucose metabolism and if a mutation occurs in this gene will cause changes in DNA methylation. Paldor et al found that mutations in IDH would be more frequently found in GBM that occur in lobes other than frontal or multilobes, whereas IDH without anomalies were more frequently found in GBM that occurred in the frontal area. Based on this, differences in the location of brain tumors have a relationship with



genetic anomalies that occur. In this study, genetic anomaly data was not obtained²⁰.

Based on the results obtained, primary brain tumours are more likely to occur on one side. The asymmetric primary brain tumour has not been much studied, but this can be related to early tumour detection and its correlation with certain neurological deficits. Structurally and functionally, the brain has differences between the two sides. The size of the right hemisphere is 1.3% greater than that of the left hemisphere, the amount of substantia grisea is relatively more found in the left hemisphere than the right hemisphere. The right hemisphere generally has a role in visual-spatial perception, while the left hemisphere has a role in language, speech and verbal memory²¹. In addition, based on research Salo et al found that brain tumors that occur in the right hemisphere are associated with a worse quality of life²². Lateralization of the tumour also has an association with cell phone use. This is because when using a cellphone when calling, an individual will put the cellphone on the side of his dominant ear so as to allow the occurrence of primary brain tumours unilaterally^{9,11}.

Stage 4 is more likely to be found in this study because RSUP Dr. Kariadi is one of the national referral hospitals, so the stadium found is an advanced stage.

CONCLUSION

Frequency of primary brain tumour events in RSUP Dr. Kariadi Semarang The period of January 2017 - December 2018 found 71 patients, but there were 38 cases with complete data so that the rest of the study subjects were not included in the study. Patients with primary male brain tumours are more commonly found aged 50-59 years. The most common symptoms and signs in brain tumour patients are headaches,

limb disorders, and disturbance of consciousness.

Histopathological examination showed that the type of astrocytic tumour is the type most often found, especially in male patients. Stage 4 and stage 3 are the most common stages in astrocytic tumours in male patients.

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