Epidemiology of primary brain tumors in dr. Kariadi Hospital Semarang in 2015-2018

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Epidemiology of primary brain tumors in dr. Kariadi Hospital Semarang in 2015-2018

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Abstract. Background: Primary brain tumors are neoplasm originated from brain parenchyma and its surrounding structures. Although primary brain tumors is only 1,4% of all cancers, they causes significant morbidity and mortality. **Objective**: To study the epidemiology of primary brain tumors in Dr. Kariadi General Hospital Semarang between 2015 and 2018. **Methods:** a descriptive epidemiological study taken from medical records of hospitalized patients with primary brain tumors during 2015 - 2018. The data includes demographic characteristics and clinical characteristics. **Results:** There were 175 suspected cases of primary brain tumor, 38.3% occurred in males and 61.7% in females. The peak incidence is in 41-50 years (34.3%). 61.1% live in coastal areas. The frequent symptoms is headache (44.9%), with the most common location was in the frontal lobe (17.7%). The most common type was meningioma (24.5%). Meningioma were more common in females (90.7%), whereas glioma were more common in males (60%). 46.3% patients experienced clinical improvement at the time of discharge. **Conclusions:** The incidence of primary brain tumors are more common in females, the peak incidence are age 41-50 years, and most of them live in coastal areas.

Keywords : **epidemiology; brain tumors; primary brain tumors.**

1 Introduction

Primary brain tumors are a group of neoplasm arising from brain parenchyma and its surrounding structures. These tumors divided into degrees of malignancy from the benign to aggressive. Although primary brain tumors only 1,4% of all cancers, they are including the most aggressive tumors which result in mortality rate of about 60%. Despite these tumors, incidence are a relatively low, brain tumors cause significant health problems in worldwide by their high mortality and morbidity [1, 2]. Benign tumor can be lethal due to their site in the brain, their ability to infiltrate locally and to transform into malignancy [3].

WHO classified central nervous system tumors based on the histological and molecular profile. By the year 2007, WHO classified based on the histopathological characteristic. And by the year of 2016, WHO renewed the diagnosis criteria by adding the molecular parameter [4, 5].

Primary brain tumors etiology is still unsure, but some studies investigated the risk factors such as genetic, ion radiation, viral infection, head trauma, tobacco, and alcohol. Patients with brain tumors' clinical features are based on the volume and location of the tumor, either general from the increased intracranial pressure or focal neurological symptoms [2].

The workup diagnostic for brain tumors including imaging diagnostic by CT-scan, MRI, PET scan of the brain, and cerebrospinal fluid (CSF) analysis. Contrast head MRI is the first imaging modality choice because it produces detail image of the soft tissues, but still, histopathology is the gold standard diagnosis in brain tumors. Treatments for brain tumors are conservative management to reduce intracranial pressure, surgery, radiation, and chemotherapy as indicated [6].

The importance of the brain tumors epidemiology is to know the prevalence and characteristics of brain tumors either the histological or the sociodemography of the patients. There are still limited data about brain tumors epidemiology in Indonesia so that authors study the epidemiology of primary brain tumors in RSUP dr. Kariadi Semarang. It is expected that the presence of epidemiological data can help increase knowledge and early detection of brain tumors patients can be approached.

2 Methods

The research was descriptive epidemiological research with retrospective approach to describe the profile of primary brain tumor patients in RSUP dr. Kariadi Semarang. Data were taken from inpatients' medical records since year 2015 to 2018. The subjects were all inpatients who diagnosed as primary brain tumors. Data

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that were collected were patient's demographic characteristics including gender, age, geographic region, clinical manifestation, tumors location, histopathologic features, and patient's condition at the time of discharge. Data that have been collected then analyzed descriptively to perceive the primary brain tumors' profiles.

3 Results

3.1 Subjects characteristics

There were 175 brain tumor cases suspected as primary brain tumors at RSUP dr. Kariadi Semarang between 2015-2018. All cases that suspected as primary brain tumors included in the research, including cases of unknown imaging results, no surgery, and unknown histopathological results.

The subjects consisted of 67 men (38.3%) and 108 women (55.1%). Subjects were divided according to age into 11.4 % aged less than 20 years old, 9.1% aged 20-30 years old, 12.6 % aged 31-40 years old, 34.3% aged 41-50 years old, 25.1% aged 51-60%, and 7.4% aged more than 60 years old. The peak incidence is in age 41-50 years, that were 60 subjects (34.3%). Based on the geographic region, 61.1% subjects were from the coast which the altitude is less than 100 meters above sea level, 22.3% subjects were from the low altitude (100-400 m a.s.l), and 12.6% subjects were from the high altitude (>400 m a.s.l)

Table 1. Subjects Characteristics of Primary Brain Tumor

Variable	n	%
Gender		
Female	108	61.7
Male	67	38.3
Age		
Less than 20 years old	20	11.9
20-30 years old	16	11.0
31-40 years old	22	10.2
41-50 years old	60	31.4
51-60 years old	44	25.4
More than 60 years old	13	10.2
Geographic region		
Coast (less than 100 m a.s.l)	107	61.1
Low altitude (100-400 m a.s.l)	39	22.3
High altitude (More than 400 m a.s.l)	22	12.6
Unknown	7	4.0

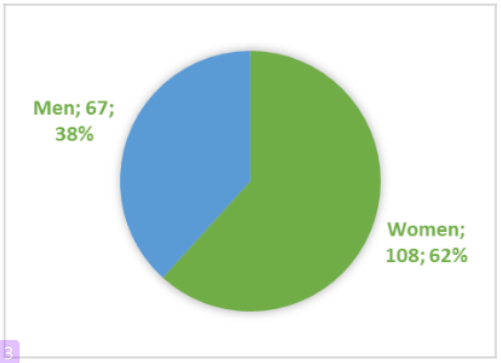

Fig. 1. Distribution of Primary Brain Tumours According to Gender

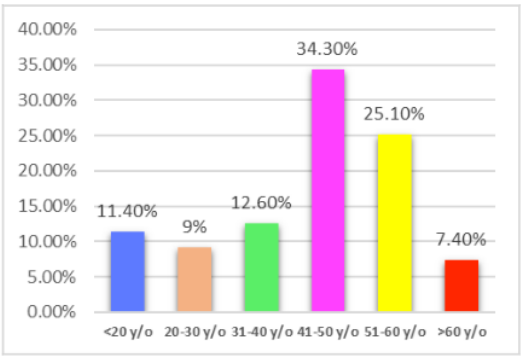

Fig. 2. Distribution of Primary Brain Tumours Based on Age

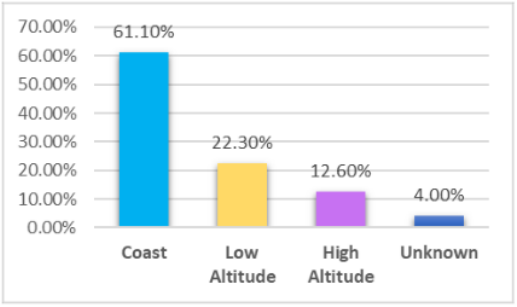

Fig. 3. Distribution of Primary Brain Based on Geographic Region

3.2 Clinical characteristics

The most clinical feature which was gotten from thorough history taking and physical examination was headache which was found in 142 subjects (44,.9%). Based on the imaging of the brain, frontal lobe was the most location. As the result of the biopsy, the most common tumor according to histopathological feature

was meningioma in 35 subjects (20%). From all the subjects, 81 subjects (46.3%) got clinical improvement at the time of discharge, and 36 subjects (20.6%) passed away during hospitalization.

Table 2. Clinical Characteristics of Primary Brain Tumors

Variable	Freq.	%
Clinical Features		
Headache	142	44.9
Hemiparesis	40	12.7
Visual Impairment	28	8.9
Loss of Consciousness	25	7.9
Seizure	22	7.0
Vomiting	14	4.4
Cranial Nerves Paresis	13	4.1
Aphasia	9	2.8
Dizziness	8	2.5
Cognitive Impairment	7	2.2
Balance Disorder	3	0.9
Tumor Location		
Frontal Lobe	31	17.7
Meninges	24	13.7
Parietal Lobe	22	12.6
Sellar region	21	12.0
Temporal Lobe	14	8.0
Cerebellum	12	6.9
Brainstem	8	4.6
Cerebellopontine Angle	5	2.9
Basis Cranii	3	1.7
Ganglia Basalis	3	1.7
Fossa Posterior	3	1.7
Ventricle	3	1.7
Occipital Lobe	2	1.1
Olfactory Groove	1	0.6
Suprainfra Tentorial	1	0.6
Unidentified	22	12.6
Tumor Histopathology		
Tumors of the Neuroepithelial Tissue		
Astrocytoma WHO Gr. 1 (Plomyxoid, Microcytic, Gesmitocytic, Pilocytic)	13	7.4
Astrocytoma WHO Gr. 2 (Diffuse, Fibrillary, Low-grade, Oligoastrocytoma, Protoplasmic)	11	6.3
Astrocytoma WHO Gr. 3 (Anaplastic Astrocytoma)	5	2.9
Glioblastoma (WHO gr. IV)	18	10.3
Oligodendroglioma	4	2.3
Ependymoma	4	2.3
Tumor of the Meningen		
Meningioma WHO Gr.1 (Microcytic, Fibrous, Transitional, Meningoepithelial, Psammomatous, Secretory)	35	20.0
Meningioma WHO Gr. 2 (Atypical Meningioma)	7	4.0
Meningioma Grade 3 (Anaplastic Meningioma)	1	0.6
Embryonal Tumor		
Medulloblastoma	1	0.6
Germinoma	2	1.1
Primitive Neuroectodermal Tumour	1	0.6
Neuroblastoma	2	1.1
Mesenchymal, non-meningothelial tumours		
Hemangioma	3	1.7
Chordoma	2	1.1
Tumor of the Sellar Region		
Pituitary Adenoma	8	4.6
Tumour of the Cranial Nerve		
Schwannoma	7	4.0
Lymphoma and hemopoietic neoplasm		
High-grade B cell lymphoma	1	0.6
Craniopharyngioma	4	2.3
No Surgery	7	4.0
Unknown Histopathological Result	39	22.3
Condition at the time of Discharged		
Getting Better	81	46.3
Getting Worse (Palliative)	1	0.6
Passed Away	36	20.6
Unknown	57	32.6

Tumors that were more common in males were astrocytoma (55.3%) and pituitary adenoma (62.5%), while the more common in females was meningioma (90.7%), hemangioma (100%), and schwannoma (71.4%).

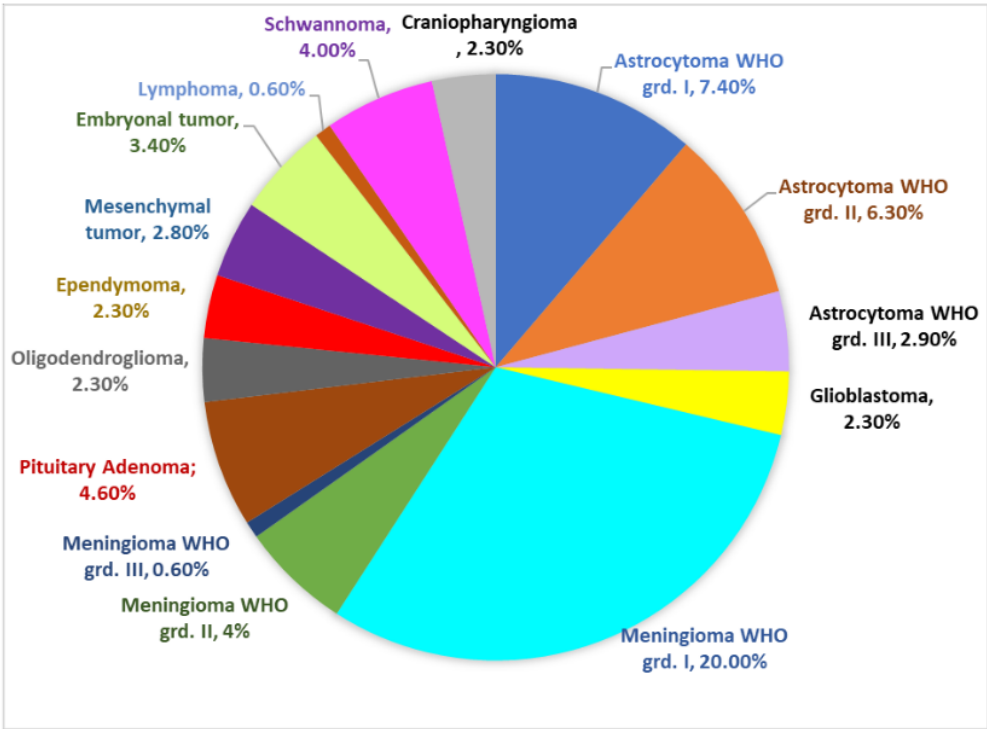

Fig. 4. Distribution of Primary Brain Tumors Based on Histopathological Features

Table 3. Tumor Histology Based on Gender

Type	n	Gender	
		Men	Women
Astrocytoma WHO gr. I (Gesmitocytic, Microcytic, Pilocytic, Pilomyxoid)	13	6 (46.2%)	7 (53.8%)
Astrocytoma WHO gr. II (Diffuse, Fibrillary, Low-grade, Oligoastrocytoma, Protoplasmic)	11	9 (81.8%)	2 (18.2%)
Astrocytoma WHO gr. III (Anaplastic)	5	1 (20%)	4 (80%)
Glioblastoma (WHO gr. IV)	14	8 (57.1%)	6 (42.9%)
Oligodendroglioma	5	4 (80%)	1 (20%)
Ependymoma	3	2 (66.7%)	1 (33.3%)
Meningioma WHO grd. I (Meningothelial, Microcytic, Psammomatous, Secretory, Transitional)	10	1 (10%)	9 (90%)
Medulloblastoma	1	1 (100%)	
Germinoma	2	1 (50%)	1 (50%)
Primitive Neuroectodermal Tumour (PNET)	1		1 (100%)
Neuroblastoma	1		1 (100%)

Hemangioma	3		3 (100%)
Chordoma	2	1 (50%)	1 (50%)
Pituitary Adenoma	6	3 (50%)	3 (50%)
Schwannoma	1		1 (100%)
Primary CNS lymphoma	1	1 (100%)	
No Surgery	6	2 (33.3%)	4 (66.7%)
Unknown Histopathological Result	33	13 (39.4%)	20 (60.6%)
TOTAL		53	65

The incidence of Grade I Astrocytoma was highest at age 41-50 years old, grade II was at age 51-60 years old. Glioblastoma more common in 51-60 years (44.4%). Meningioma more common in 41-50 years (55.8%). Embryonal tumors, ependymoma, and craniopharyngioma more common in less than 20 years old.

Table 4. Tumor Histology According to Age

Type	**n**	**Age (years old)**					
		< 20	**21-30**	**31-40**	**41-50**	**51-60**	**>60**
Astrocytoma WHO gr. I (Gesmitocytic, Microcytic, Pilocytic, Pilomyxoid)	13	1 (7.7%)	3 (23.1%)		6 (46.2%)	1 (7.7%)	2 (15.4%)
Astrocytoma WHO gr. II (Diffuse, Fibrillary, Low-grade, Oligoastrocytoma, Protoplasmic)	11	1 (9.1%)	2 (18.2%)	2 (18.2%)	1 (9.1%)	5 (45.5%)	
Astrocytoma WHO gr. III (Anaplastic)	5				2 (40%)	2 (40%)	1 (20%)
Glioblastoma (WHO gr. IV)	18	1 (5.6%)	2 (11.1%)		6 (33.3%)	8 (44.4%)	1 (5.6%)
Oligodendroglioma	4				3 (75%)	1 (25%)	
Ependymoma	4	3 (75%)	1 (25%)				
Meningioma WHO grd. I (Meningothelial, Microcytic, Psammomatous, Secretory, Transitional)	35		1 (2.9%)	3 (8.6%)	21 (60%)	8 (22.9%)	2 (5.7%)
Meningioma WHO grd. II (Atypical)	7		1 (14.3%)	2 (28.6%)	3 (42.9%)	1 (14.3%)	
Meningioma WHO grd. III (Anaplastic)	1			1 (100%)			
Medulloblastoma	1	1 (100%)					
Germinoma	2	2 (100%)					
Primitive Neuroectodermal Tumour (PNET)	1	1 (100%)					
Neuroblastoma	2	1 (50%)			1 (50%)		
Hemangioma	3	1 (33.3%)	1 (33.3%)				1 (33.3%)
Chordoma	2		1 (50%)		1 (50%)		
Pituitary Adenoma	8			2	3	3	

				(25%)	(37.5%)	(37.5%)	
Schwannoma	7	1 (14.3%)		3 (42.9%)	1 (14.3%)	2 (28.6%)	
Primary CNS lymphoma	1					1 (100%)	
Craniopharyngioma	4	3 (75%)			1 (25%)		
No Surgery	7		1 (14.3%)	1 (14.3%)	1 (14.3%)	2 (28.6%)	2 (28.6%)
Unknown Histopathological Result	39	4 (10.3%)	3 (7.7%)	8 (20.5%)	10 (25.6%)	10 (25.6%)	4 (10.3%)
TOTAL		20	16	22	60	44	13

Subjects with primary brain tumors mostly lived in coastal area, i.e. astrocytoma (57.4%), meningioma (60.4%), schwannoma (71.4%), and craniopharyngioma (50%). While all subjects with ependymoma, hemangioma, germinoma, and pituitary adenoma lived in coastal area. One subject with primary CNS lymphoma and medulloblastoma lived in the low altitude region. None of the tumors were from high altitude regions.

Table 5. Tumor Types Frequency According to The Altitude of Residence

Type	**n**	**Altitude of Residence**			
		Coast	**Low Altitude**	**High Altitude**	**Unknown**
Astrocytoma WHO gr. I (Gesmitocytic, Microcytic, Pilocytic, Pilomyxoid)	13	8 (61.5%)	3 (23.1%)	2 (15.4%)	
Astrocytoma WHO gr. II (Diffuse, Fibrillary, Low-grade, Oligoastrocytoma, Protoplasmic)	11	8 (72.7%)	1 (9.1%)	2 (18.2%)	
Astrocytoma WHO gr. III (Anaplastic)	5	3 (60%)	1 (20%)	1 (20%)	
Glioblastoma (WHO gr. IV)	18	8 (44.4%)	6 (33.3%)	3 (16.7%)	1 (5.6%)
Oligodendroglioma	4	2 (50%)	1 (25%)	1 (25%)	
Ependymoma	4	3 (75%)			1 (25%)
Meningioma WHO grd. I (Meningothelial, Microcytic, Psammomatous, Secretory, Transitional)	35	22 (62.9%)	8 (22.9%)	4 (11.4%)	1 (2.9%)
Meningioma WHO grd. II (Atypical)	7	3 (42.9%)	1 (14.3%)	2 (28.6%)	1 (14.3%)
Meningioma WHO grd. III (Anaplastic)	1	1 (100%)			
Medulloblastoma	1		1 (100%)		
Germinoma	2	2 (100%)			
Primitive Neuroectodermal Tumour (PNET)	1	1 (100%)			
Neuroblastoma	2	1 (50%)			1 (50%)
Hemangioma	3	3 (100%)			
Chordoma	2	1 (50%)	1 (50%)		
Pituitary Adenoma	8	8 (100%)			
Schwannoma	7	5		1	1

		(71.4%)		(14.3%)	(14.3%)
Primary CNS lymphoma	1		1 (100%)		
Craniopharyngioma	4	2 (50%)	1 (25%)		1 (25%)
No Surgery	7	4 (57.1%)	1 (14.3%)	2 (28.6%)	
Unknown Histopathological Result	39	22 (56.4%)	13 (33.3%)	4 (10.3%)	
TOTAL		107	39	22	7

5 Discussion

This research was descriptive epidemiological research with primary brain tumors patients who were treated in RSUP dr. Kariadi Semarang year 2015 – 2018 as the subjects by retrospective approach from patients' medical records. In this research, female incidence was more common than male, i.e. 38.3% male and 61.7% female, concordant to the older references from the study in Spain and Korea which the frequency of women was higher than men, i.e. 57.25% and 61.4%, while the database from CBTRUS and meta-analysis study in America claimed that the incidence of female was more than men which were 24.77 vs 20.34 per 100.000 populations and 15.8 vs 14.33 per 100.000 populations. However, Pineros et al. claimed from the recent study that the incidence of male was equal to female [1, 7, 10, 13, 14].

Primary brain tumor patients were mostly at the age of 41-50 years old, which was different from other recent studies that primary brain tumor's incidence increased by the age, especially high-grade glioma which often found at the age of more than 60 years old [7-9].

The most common symptoms were headache concordant to the recent studies in which headache was the most common symptom of either primary or metastatic brain tumors as the result of increased intracranial pressure. Adams et al. claimed that the incidence of headache was 48-56% [11, 12].

In this research, brain tumors most were in frontal lobe, while some recent studies claimed meninges as the most location of brain tumors wherefor in this research, the incidence of axial tumors e.g. astrocytoma was more than the tumors of meninges [7].

The most histopathological feature in this research was meningioma (24.5%). There were various results of the recent studies, the studies from RSCM, Pineros et al. from America, and Fuentes-Raspall et al. from Spain claimed that the most histopathological feature was glioma, while CBTRUS claimed that the most common primary brain tumor was meningioma. Some studies showed that the incidence of meningioma was higher in western than in Asia [7,10,15,16].

Most patients got better at the time of discharged, but because of the data limitations, factors affecting the outcomes were not analyzed.

Most common primary brain tumors in this study are meningioma (24.5%), similar to the literature that showed the ratio of male: female were 1:1.4-2.6 [16]. Glioma was found more in men than women (55.8% vs 44.2%) which concordant to the recent references and studies. Sun et al. claimed that there was oncogenic and genetic mutation mechanism which is higher in men so that the prevalence of glioma is higher in men than women [7, 17, 18].

Data on environmental exposure to primary brain tumors remain unknown and controversial. In this research, the geographic region was categorized based on Samodra et al. Most patients with primary brain tumors lived in the coastal areas (< 100 m a.s.l). There were no studies that analyzed the altitude of residence to primary brain tumors. In this research, 61.14% patients lived in the coastal areas, but there was no data about the environmental and occupational exposures. In Indonesia which is an agrarian country, almost all residents work as a farmer. According to Badan Pusat Statistik (BPS), populations aged >15 years old who work in agricultural is about 38.35%. This fact proves that there is high exposure to agricultural chemicals such as pesticides that are believed to be neurotoxic and carcinogenic. A meta-analysis study in 1998 by Kuder et al showed a moderately increased risk that was statistically significant for primary brain tumors among farmworkers. Otherwise, coastal area also has more pollution from industry and vehicles than the highland [2, 19-21] .

6 Conclusion

There were 175 cases of brain tumors suspected as primary brain tumors in RSUP dr. Kariadi Semarang between 2015-2018. The incidence more common in females than males, which most in the age of 41-50 years old, and almost all lived in the coastal areas. The most common clinical feature is headache caused by space-occupying effect and increased intracranial pressure. The most type of tumor according to histopathological feature is meningioma, which found more common in female. Patients mostly live on the coast where there is agricultural chemicals exposure as one of the brain tumor risk factors.

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