

Adults brain tumor in Cipto Mangunkusumo General Hospital: A descriptive epidemiology

Tiara Aninditha¹, Putra Yudhistira Pratama¹, Henry Riyanto Sofyan¹, Darma Imran¹,
Riwanti Estiasari¹, Fitri Octaviana¹, Mirna Marhami Iskandar², Jonathan Odilo³, Retno Asti Werdhani⁴,
Renindra A. Aman⁵, Teguh AS Ranakusuma¹

¹ Department of Neurology, Faculty of Medicine, Universitas Indonesia/Rumah Sakit Cipto Mangunkusumo, Jakarta, Indonesia

² Department of Neurology, Faculty of Medicine and Health Sciences, Universitas Jambi, Jambi, Indonesia

³ Faculty of Medicine, Universitas Indonesia/Rumah Sakit Cipto Mangunkusumo, Jakarta, Indonesia

⁴ Department of Community Medicine, Faculty of Medicine, Universitas Indonesia/Rumah Sakit Cipto Mangunkusumo, Jakarta, Indonesia

⁵ Department of Neurosurgery, Faculty of Medicine, Universitas Indonesia/Rumah Sakit Cipto Mangunkusumo, Jakarta, Indonesia

ABSTRACT

Background. Brain tumor is a rare tumor with low incidence. Although it is a rare tumor, the mortality of brain tumor is disproportionately high. Many countries have already published epidemiology of brain tumor. However, the epidemiology of brain tumor in Indonesia remains to be investigated. This article aimed to provide descriptive epidemiology of brain tumor.

Methods. The data of brain tumor acquired from Department of Neurology and Neurosurgery Cipto Mangunkusumo General Hospital from 2014 to 2016. The histopathology classification of primary intracranial tumors was based on WHO classification of CNS tumors 2016 while brain metastasis was classified based on other histopathological types. The variables were analyzed and presented descriptively.

Results. There were 316 subjects acquired in this study. Most of the subjects (68%) were women. The mean age of this study was 43.8 (11.7). Most of the subjects (86.1%) had primary histopathology. Lung cancer was the most commonly found brain metastasis in this study (34.1%).

Conclusions. This is a pilot study of brain tumor epidemiology in Indonesia. Collaboration with other centers in Indonesia is needed to give a more representative insight of brain tumor in Indonesia.

Keywords: brain tumor, cancer, epidemiology, descriptive study

INTRODUCTION

Brain tumor is a rare tumor with worldwide incidence of 296,851 cases worldwide. Those numbers accounted for 1.6% of cancer incidence. The mortality caused by CNS tumor were 241,037 or 2.5% of cancer mortality cases (1). The worldwide incidence of primary malignant brain tumor was 5.57 per 100,000 populations while brain metastasis prevalence was estimated to be 8.4-14.3 per 100,000 populations (2,3). Although rare, intracranial tumor is a

devastating disease due to disability and high mortality rate. The histology of primary brain tumor was mostly benign (69.8%) with most of the tumor consisted of meningioma and tumor of the pituitary (4). Meanwhile, glioblastoma and astrocytoma were 2 most common primary malignant brain tumor (4).

Efforts to publish intracranial tumor epidemiology were done continuously. The incidence and mortality rate of CNS tumor have been described along with the histopathologic type. Despite the

Corresponding author:

Tiara Aninditha

E-mail: t.aninditha@ui.ac.id

Article history:

Received: 15 September 2021

Accepted: 20 December 2021

abundance of published epidemiology of intracranial tumor, there is a lack of publication of intracranial tumor epidemiology in Indonesia. The estimation of incidence and mortality of CNS tumor in Indonesia in 2016 were 6,337 and 5,405 cases (5). However, there was a lack of histopathological data of intracranial tumor in Indonesian population. The authors of this research studied the epidemiology of intracranial tumor in Cipto Mangunkusumo Hospital. This article is expected to provide insight into the demography and histopathology of intracranial tumor in Indonesia.

METHODS

This is a cross-sectional retrospective study of intracranial tumor in Cipto Mangunkusumo General Hospital. All adult intracranial tumor patients admitted to Cipto Mangunkusumo General Hospital from 2014 to 2016 were included in this study. Age, gender, tumor location, and histopathology type of the tumor acquired from the Department of Neurology and Department of Neurosurgery registry along with medical records. The histopathology classification of primary intracranial tumors was based on WHO classification of CNS tumors 2016 while brain metastasis was classified based on other histopathological types. The variables were analyzed and presented descriptively. Collected data were analyzed using descriptive statistics in SPSS version 22.0 (IBM SPSS, Somers, N.Y., USA).

The research already had ethical approval from the Medical Ethic Committee Faculty of Medicine Universitas Indonesia No. 1105/UN2.F1/ETIK/2018.

RESULTS

There were 316 subjects acquired in this study. Majority of subjects were women (68 %) aged ≤ 45

years old (59.5 %) and had supratentorial tumor (89.9 %). Meningioma was found in 145 (45.1 %) patients and is the most common histopathology in this study. Pituitary adenoma found in 44 (13.9%) subjects. Meanwhile, glioma was found in 37 (11.7%) subjects. The characteristics of subjects could be seen in Table 1.

The average age of grade I meningioma was 44.6 (7.5). There were 105 (87.5%) women subjects in grade I meningioma. There were 13 (72.2%) subjects of low-grade glioma were men. The location of low-grade glioma among subjects were mainly supratentorial (88.9%). Meanwhile, all subjects with high-grade glioma were supratentorial. The demographic characteristics of each histopathology were described in Table 2.

In this study, there were 44 subjects with intracranial metastasis. Lung cancer histopathology was most prevalent in intracranial metastasis found in 15 (34.1%) subjects. Breast cancer was second most prevalent in 11 (25%) subjects. The histopathology of intracranial metastases could be seen in Table 3.

DISCUSSION

This is descriptive epidemiological research of intracranial tumor conducted in Cipto Mangunkusumo General Hospital from 2014 to 2016 with retrospective approach. In this study, the majority of subjects (68%) were women. This finding is consistent with several epidemiological studies of brain tumor that shown 50.8-61.4% of subjects were women (4,6-8). However, a report by Salehpour et al. shown that 50.4% of primary brain tumor patients were men (9). The difference of gender proportion maybe due to different population of study.

The average age of subjects in this study is 43.8 (11.7) years old. Brain Tumor Registry of Japan reported 52% of patients aged 50-74 (6). The average

TABLE 1. Subjects' characteristics

Variables	Classification	N	%
Gender	Women	215	68
	Men	101	32
Age	Mean (SD)	43.8 (11.7)	
Location	Supratentorial	284	89.9
	Infratentorial	32	10.1
Histopathology	Meningioma	145	45.9
	Pituitary adenoma	44	13.9
	Glioma	38	12
	Lymphoma	13	4.1
	Schwannoma	9	2.8
	Craniopharyngioma	3	0.9
	Medulloblastoma	1	0.3
	Neuroblastoma	1	0.3
	Metastasis	44	13.9
	Other primary (unspecified)	18	5.7

TABLE 2. Demographic characteristics by histopathology (N=316)

Histopathology		Age Mean (SD)	Gender		Location	
			Male N(%)	Female N(%)	Supratentorial N(%)	Infratentorial N(%)
Meningioma	WHO gr. I	44.6 (7.5)	15 (12.5)	105 (87.5)	115 (95.8)	5 (4.2)
	WHO gr. II	44.9 (11.3)	5 (20)	20 (80)	22 (88)	3 (12)
Pituitary adenoma		41 (11.9)	19 (43.2)	25 (56.8)	N/A	
Glioma	Low-grade glioma	44.2 (13.2)	13 (72.2)	5 (27.8)	16 (88.9)	2 (11.1)
	High-grade glioma	39.1 (14.2)	12 (60)	8 (40)	20 (100)	0 (0)
Lymphoma		46.3 (18.1)	3 (23.1)	10 (76.9)	12 (92.3)	1 (7.7)
Schwannoma		41.9 (13.8)	2 (22.2)	7 (77.8)	N/A	
Craniopharyngioma		37 (4.6)	2 (66.7)	1 (33.3)	N/A	
Medulloblastoma		18 (N/A)	1 (100)	0 (0)	0 (0)	1 (100)
Neuroblastoma		24 (N/A)	0 (0)	1 (100)	1 (100)	0 (0)
Metastasis		49.6 (11.7)	18 (40.9)	26 (59.1)	37 (84.1)	7 (15.9)
Others unclassified primary tumor		37.1 (16.2)	11 (61.1)	7 (38.9)	14 (77.8)	4 (22.2)

TABLE 3. The histopathology of brain metastasis (N=44)

Histopathology	N(%)
Lung cancer	15 (34.1)
Breast cancer	11 (25)
Cervical cancer	3 (6.8)
Melanoma	2 (4.5)
Nasopharyngeal carcinoma	1 (2.3)
Adenoid cystic carcinoma	1 (2.3)
Squamous cell carcinoma	1 (2.3)
Colon cancer	1 (2.3)
Endometroid adenocarcinoma	1 (2.3)
Adenocarcinoma unspecified	1 (2.3)
Metastasis unspecified	7 (15.9)

age of brain tumor patients in South Korean patients were 54.4 (8). Meanwhile, the average age of brain tumor patients in Iran were 52.6 (9). A CBTRUS report also shown that median age of brain tumor diagnosis were 60 years old (4). The average age of patients in this study was relatively younger than most of published article. Brain tumor epidemiology study published by Ardhini et al. in Indonesia showed that peak incidence of brain tumor was in 41-50 years old (10). This showed that Indonesian people had younger onset of brain tumor compared to other countries. After the brain tumor classified histopathologically, the average age of each histopathology ranged from 39.1-49.6 years old. We concluded the onset of brain tumors is generally younger than widely published research. This is an interesting finding since although the incidence rate of brain tumor is the lowest in Southeast-Asian region (2), the onset of brain tumor is youngest in Indonesia. The cause of younger onset of brain tumor remains to be investigated.

Tumor location in this study was found 89.9% in supratentorial. Several articles also showed that su-

pratatentorial tumors are found in most patients. CBTRUS reported that more than 84% of brain tumor found in supratentorial location (4). In Jordan, 22.6% of brain tumor were infratentorial. Ardhini et al. described 16% of brain tumor were infratentorial (10).

In this study, there were 272 patients with primary brain tumor. Most of the patients with primary brain tumor had meningioma which comprised 53.3% of patients with primary brain tumor. Meningioma is the most common primary brain tumor. Various epidemiological studies showed that meningioma prevalence was 22-37.6% of patients (4,7-10). The finding of this study was exceedingly high compared to other studies. Another study in Indonesia only showed 24.6% prevalence of meningioma (10). This is probably due to Cipto Mangunkusumo General Hospital being a national referral and difficult cases of meningioma were sent to the highest referral level. The ratio of women to men in meningioma patients was 6.25:1. It has been known that female sex hormone influenced the female predominance in meningioma. Nevertheless, the published epidemiology of meningioma shown that the ratio of women to men was 2-3:1 (11). Ardhini et al. also reported women to men ratio of 9:1 in grade I meningioma (10). The disproportionately high number of women to men in meningioma patients along with its risk factors in Indonesia should be investigated.

Pituitary adenoma placed second among primary brain tumors in this study which comprised 16.2% of primary brain tumor patients. As much as 56.8% of pituitary adenoma were women. The prevalence of pituitary adenoma among epidemiological studies were 4.6-19.3% with majority of patients were female (7-10).

Glioma accounted for 14% of primary brain tumor patients in this study classified into 20 patients

with high-grade glioma and 18 with low-grade glioma. Various epidemiological studies showed the prevalence of glioma patients among primary brain tumors were 15.1-42.7% (6-8,10). Male comprised 66% of glioma patients. The predominance of male in glioma patients is due to gender-specific response to P53 loss of function that act as tumor suppressor gene (12). The proportion of glioma in this study was lower, maybe due to population differences.

The population study of brain metastasis is limited. Up to 40% of cancer patients developed brain metastasis with 60-75% were symptomatic. It is estimated that the number of brain metastases was 3-10 times of primary malignant brain tumors (13). The average age of brain metastasis in this study was 49.6 years old. Again, the finding is younger than the epidemiological study that stated the peak incidence of brain metastasis was 60 years old (3). Brain metastasis from lung cancer was found in 34.1% of patients and the most common cancer metastasized to the brain. Metastasis from breast cancer found in 25% patients. The finding is consistent with finding of Sperduto et al. and Giordana et al. that shown lung cancer is the most common cancer that metastasize to brain along with breast cancer (14,15). Brain metastasis found in 23-36% of non-small cell lung carcinoma (NSCLC) patients by autopsy study. Meanwhile, 45% of Small Cell Lung Carcinoma (SCLC) patients developed brain metastasis by autopsy study (3). This showed that brain metastasis is common from brain metastasis making it the most common cancer that metastasizes to the brain. Meanwhile, breast cancer is the second most common cancer that metastasizes to the brain with 18-30% breast cancer patients developing metastasis to brain by autopsy study (3). However, due to limited subjects, brain metastasis profile couldn't be precisely represented in this study.

Limitations

This article is among the first articles to study brain tumor in Indonesia after Ardhini et al. (10) that describe primary brain tumor in Kariadi Hospital, Semarang. This study is expected to give insight into brain tumor in Indonesia. However, there were several limitations of this study. Other variables such as performance status, specific location of tumor, and size of tumor had not yet been described. The pediatric patients not included in this study could affect the proportion of each tumor histopathology because brain tumor in children and adults have different histopathological trends. This study is only describing tumor from a single institution even though Cipto Mangunkusumo General Hospital is a national referral hospital. To better represent brain tumor epidemiology in Indonesia, a collaboration among institutions should be done. Those collaborations could produce rate of brain tumor in population from each histopathology and answer several questions left in this study such as age onset of brain tumor age onset in Indonesia, other histopathology that had not yet represented in this study, brain tumor metastasis rate in Indonesian populations, and so on. Further study of Indonesian brain tumor epidemiology warrants a better insight of those clinical entities.

CONCLUSIONS

This is a pilot study of brain tumor epidemiology in Indonesia. Collaboration with other centers in Indonesia is needed to give a more representative insight of brain tumor in Indonesia.

REFERENCES

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2018;68(6):394-424.
2. Leece R, Xu J, Ostrom QT, Chen Y, Kruchko C, Barnholtz-Sloan JS. Global incidence of malignant brain and other central nervous system tumors by histology, 2003-2007. *Neuro Oncol.* 2017;19(11):1553-64.
3. Ostrom QT, Wright CH, Barnholtz-Sloan JS. Brain metastases: epidemiology. *Handb Clin Neurol.* 2018; 149:27-42.
4. Ostrom QT, Cioffi G, Gittleman H, Patil N, Waite K, Kruchko C, et al. CBTRUS Statistical Report: Primary Brain and Other Central Nervous System Tumors Diagnosed in the United States in 2012-2016. *Neuro Oncol.* 2019;21(Suppl 5):v1-v100.
5. Brain GBD, Other CNSCC. Global, regional, and national burden of brain and other CNS cancer, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol.* 2019; 18(4):376-93.
6. Brain tumor registry of Japan (2001-2004). *Neurol Med Chir (Tokyo).* 2014; v.54(Suppl):1-102.
7. Tamimi AF, Tamimi I, Abdelaziz M, Saleh Q, Obeidat F, Al-Husseini M, et al. Epidemiology of Malignant and Non-Malignant Primary Brain Tumors in Jordan. *Neuroepidemiology.* 2015;45(2):100-8.
8. Jung KW, Ha J, Lee SH, Won YJ, Yoo H. An updated nationwide epidemiology of primary brain tumors in republic of Korea. *Brain Tumor Res Treat.* 2013;1(1):16-23.
9. Salehpour F, Mirzaei F, Meshkini A, Parsay S, Salehi S, Asl MMB. Trends in Primary Brain Tumors: A 5-Year Retrospective Histologically Confirmed Study in Tabriz, Iran, 2011-2016. *Asian J Neurosurg.* 2019;14(2):427-31.
10. Ardhini R, Tugasworo D. Epidemiology of primary brain tumors in dr. Kariadi Hospital Semarang in 2015-2018. *E3S Web of Conference.* 2019;125(16004).
11. Baldi I, Engelhardt J, Bonnet C, Bauchet L, Berteaud E, Gruber A, et al. Epidemiology of meningiomas. *Neurochirurgie.* 2018;64(1):5-14.

12. Sun T, Warrington NM, Luo J, Brooks MD, Dahiya S, Snyder SC, et al. Sexually dimorphic RB inactivation underlies mesenchymal glioblastoma prevalence in males. *J Clin Invest.* 2014;124(9):4123-33.
13. Soffietti R, Franchino F, Ruda R. Brain metastasis as complication of systemic cancers. In: Schiff D, Arrilaga I, Wen PY, editors. *Cancer Neurology in Clinical Practice.* 3rd ed. Boston: Springer; 2018.
14. Sperduto PW, Chao ST, Sneed PK, Luo X, Suh J, Roberge D, et al. Diagnosis-specific prognostic factors, indexes, and treatment outcomes for patients with newly diagnosed brain metastases: a multi-institutional analysis of 4,259 patients. *Int J Radiat Oncol Biol Phys.* 2010;77(3):655-61.
15. Giordana MT, Cordera S, Boghi A. Cerebral metastases as first symptom of cancer: a clinico-pathologic study. *J Neurooncol.* 2000;50(3):265-73.