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The Indonesian Central Nervous System Tumors Registry (Ina-CTR) : 7 years result from single institution of primary brain tumor epidemiology

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ABSTRACT

Background: Primary brain tumor is one of the most cases the neurosurgeon could found, despite good neurosurgery progress, still there is no epidemiologic data that collected from Indonesia as a low middle-income country in Asia.
Objective: The Indonesian central nervous system tumors registry (Ina-CTR) aims to provide epidemiologic data on primary brain tumor in Indonesia and to provoke more wider data collection in Indonesia as a whole nation.
Methods: We collect data from medical records retrospectively from all primary brain tumor patients that we operated in single centre, Dr. Soetomo general academic hospital, from 2012 to 2018. Data collected were gender, age, clinical manifestations, radiographic, operations, and histopathology. All patients underwent surgery for sampling whether biopsy, partial excision or total excision to obtain histopathological data.
Results: A total of 1540 patients were diagnosed with primary brain tumors from 2012-2018. Brain tumors occurred in females more often than in males (female:male, 1.48:1). The most common tumor was meningioma 568 cases (36.9%). Gliomas 553 cases (35.9%), pituitary tumors 195 cases (12.7%), and nerve sheath tumors 92 cases (5.9%) followed in incidence. Glioblastomas accounted for 5.3% of all tumors and 41.8% of all gliomas. In children (<18 years), sellar region tumors (pituitary and craniopharyngioma), embryonal / primitive / medulloblastoma, and germ cell tumors were the most common tumors.
Conclusion: This study should provide valuable information regarding the primary brain tumor epidemiology in Indonesia.

Keywords: ACTH4-10Pro8-Gly9-Pro10, Acute spinal cord injury, IL-1, NF-kB, TNF-α
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INTRODUCTION

Primary brain tumors are a diverse group of neoplasms arising from different cells of the central nervous system (CNS). Although uncommon, there is evidence that the incidence of these tumors has been rising for as much as fifty years.[1] Although brain tumor is a rare disease, the incidence of brain tumors is gradually increasing worldwide due to the development of diagnostic technologies and the increased frequency of imaging tests.[2,3]

Many registries, such as the Korean Central Cancer Registry (KCCR), Central Brain Tumor Registry of the United States (CBTRUS) and surveillance epidemiology and end results program in USA, collect and disseminate the epidemiology of brain tumor.[4]

Due to increase of screening with imaging testing, the incidence of brain tumor is increasing and the frequency of tumor diagnosis is changing in time, even in low middle-income country such as Indonesia, considering as the 4th most populous country in the world thus its epidemiology will certainly impact global epidemiology. Our hospital being the national referral hospital for the eastern part of Indonesia accounted for a major portion of our country's demography profile. There is no published article about structured brain tumors epidemiology from Indonesia, so we aim to provide the pictures of the prevalence and characteristics of brain tumors either the histological or the sociodemographic of the patients in Indonesia. And we dream in the future we could update this article by the population-based system from all around Indonesia.

METHODS

This research is retrospective study for descriptive epidemiological purpose. Data were collected from all brain tumors patients medical records in Dr. Soetomo general academic hospital from 2012 to 2018. Data collected were gender, age, clinical manifestations, radiographic, operations, and histopathology. All patients underwent surgery for sampling whether biopsy, partial excision or total excision to obtain histopathological data.

Clinical manifestation is patient's chief complain when they first diagnosed with brain tumor, whether in emergency installation or in the outpatient clinic.

The radiographic in this study only focus on tumor location and we were using the brain CT scan and conventional brain MRI.

Histology groupings were based on the classification of the CBTRUS (Ostrom et al, 2014). These groupings were broadly based on the World Health Organization categories for brain tumors. Unclassified tumors include unspecified neoplasms and all other tumors. Unspecified neoplasms refer to cases registered based on death certificates only. The tumors which classified into all other tumors were tumors that did not meet the CBTRUS criteria.[5]

Primary brain tumors with the following ICD-O-3 codes were included in the study: brain (C71.0–C71.9), meninges (C70.0–C70.9), cranial nerves and other parts of the CNS (C72.0–C72.9), and pituitary gland, craniopharyngeal duct and pineal gland (C75.1–C75.3).[2,4,6] We exclude all patients which is not Indonesian nationality. Childhood tumors were defined as those diagnosed in patients less than 17 years of age.

RESULTS

A total of 1,540 brain tumor patients were recorded, which undergo surgical procedures, both elective and emergency in our hospital from the period of January 2012 to December 2018. Basic information was collected such as patient demographic characteristics, diagnostic tools, topography, and type of histology according to the international disease classification for oncology, third edition 2007 (ICD-O-3).[2,4,6]

Patients characteristics

From 1,540 patients, female sex was dominated by 920 patients (59.7%) and 620 men (40.3%) with ratio of 3:2. These patients were then grouped into seven age groups, based on the division of the Republic of Indonesia Ministry of Health (2009)[7] using an ordinal scale: 0 - 5 years, 6 - 11 years, 12-16 years, 17 - 25 years, 26 - 35 years, 36 - 45 years, 46 - 55 years, 56 - 65 years and more than 65 years. The largest sample population seen in 36-45 years group, 311 cases (24.2%) and the lowest presentation was found in over 65 years group, 33 cases (2.6%).

Patient's clinical manifestation

From 1540 data on the patient's main complaints were variative. The most common complaints were headaches, 579 cases (37.59%) and the second most was a decrease in consciousness, 308 people (20%). Variations in patient clinical manifestations can be seen in Table 2.

From the table above can be seen several clinical complaints were emergencies so that some surgical measures carried out in emergency setting. A total of 427 patients (27.7%) underwent emergency surgery and 1,113 cases (72.3%) underwent elective surgery.

Incidence according to tumor biological behavior

The overall incidence according to biological behavior is shown in Figure 2. Tumors classified as benign, uncertain, and malignant tumors accounted for 56.1%, 17.8%, and 26,1% of all primary CNS tumors, respectively. The incidence of benign, uncertain and malignant tumors in males was 32.1%, 44.5%, and 54.7% respectively and the incidence of benign, uncertain and malignant tumors in females was 67.9%, 55.5%, and 45.3% respectively. Benign tumors developed nearly twice more frequently in females (587 cases) than in males (278). In contrast,

Table 1. The numbers of total and histologically confirmed cases by histological group, Indonesia, 2012-2018

Histological Group	Total count		Histology (+)	
	N	%	N	%
Tumor of Meninges	568	36,9	521	41,7
Tumor of Neuroepithelial Tissue	553	35,9	414	33,1
Tumor of Cranial and Paraspinal Nerves	92	5,9	51	4,1
Lymphomas and Hematopoietic Neoplasms	11	0,7	10	0,8
Germ Cell Tumors	16	1,0	14	1,1
Tumors of the Sellar Region	195	12,9	156	12,5
Metastatic Tumors	63	4,1	46	3,7
Cyst and Tumor-like Lesions	7	0,4	7	0,6
Local Extension from Regional Tumors	35	2,2	30	2,4
Total	1.540	100	1.249	100

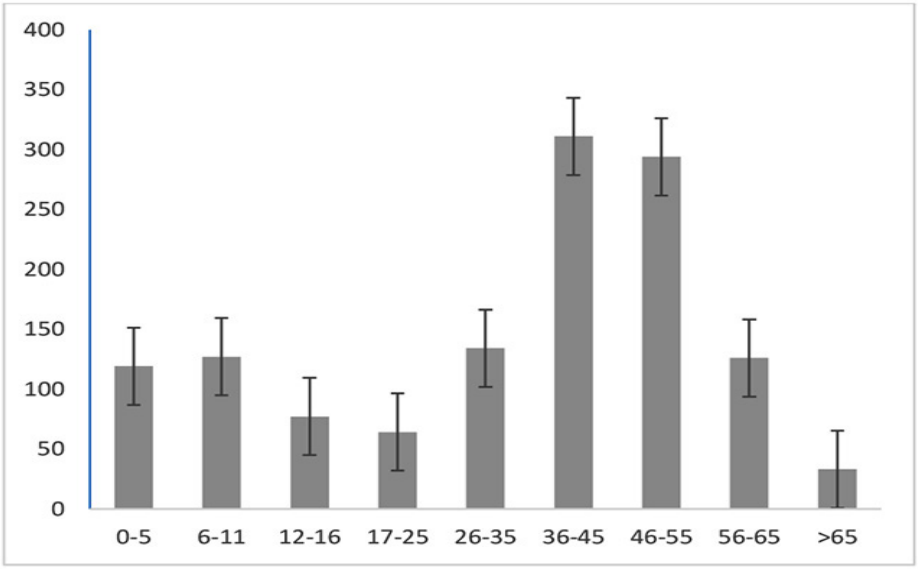

Figure 1. Patients characteristics. Among them in the age group 0-5 years, 119 cases (9.3%); the age group 6-11 years, 127 cases (9.9%); the age group 12-16 years, 77 cases (6.0%); the age group of 17-25 years were 64 cases (4.9%), the age group 26-35 years were 134 cases (10.4%); the age group 46-55 years were 294 cases (22.9%) and the age group 56-55 years as many as 126 cases (9.8%).

the incidences of borderline tumors were noted to be similar.

Distribution of tumors according to originating site

The incidence according to the originating site is shown in Figure 3. Brain parenchyma (44,5%) were the most common site of primary brain tumors, followed by the meninges (36,9%), sellar region (12,7%), and cranial nerves (5,9%). Tumors of the meninges developed more than 4 times frequently in females (Figure 3). The sellar region tumors showed 1.3 times incidence of males than females. The other sites seems similar in incidence according to sex.

The incidence of each site specific tumor according to age is shown in Figure 4. Tumors of the brain parenchyma increase rapidly and reached the peak in the first decade, and then gradually decrease until sixth decade. Tumors of the meninges seldom occurred in childhood, the incidence of which increased from the second decade and peaked in the fourth decade. Sellar tumors increased rapidly in late adolescents and peaked in the fifth decade, which decreased thereafter.

Table 2. Patient's clinical manifestation

Clinical manifestations	n	(%)
Headache	579	37,59
Decrease of consciousness	308	20,00
Seizure	121	7,85
Paralysis	78	5,06
Aphasia	32	2,07
Cranial nerve palsy	96	6,23
Visual disturbance	174	11,29
Balance disorder	152	9,87

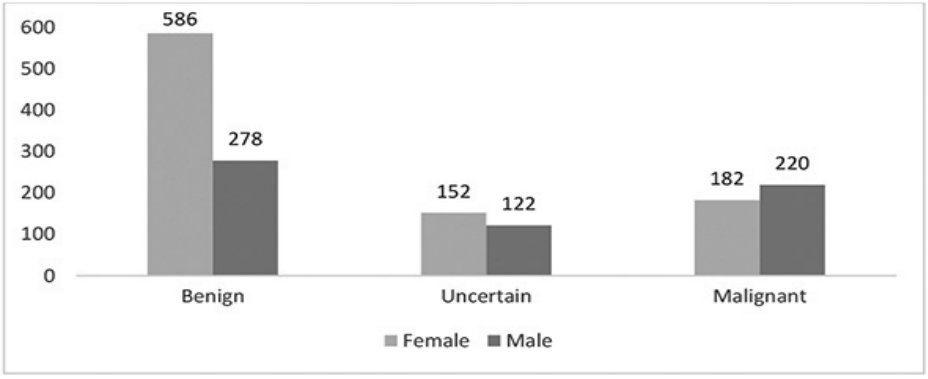

Figure 2. Distribution of primary Brain and CNS tumors according to sex and behavior, Indonesia, 2012-2018. CNS: central nervous system

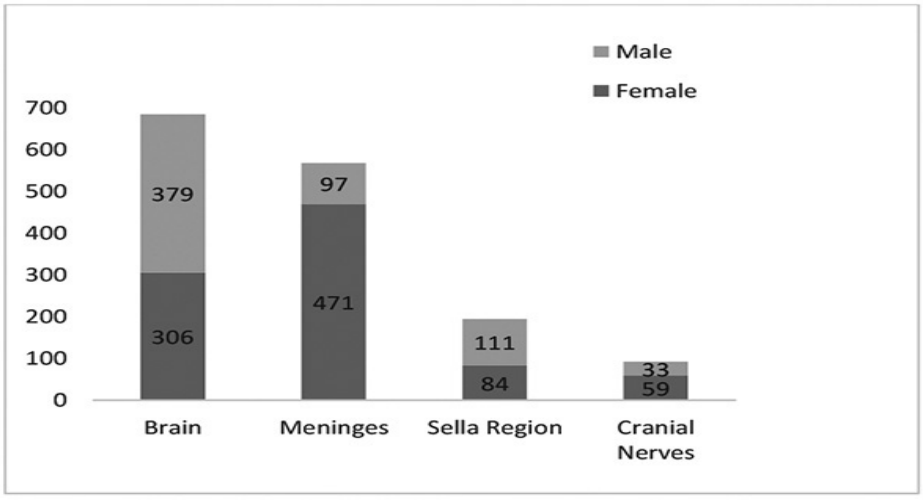

Figure 3. Distribution of all Brain and CNS tumors according to the topography, Indonesia, 2012-2018. CNS: central nervous system.

Incidence according to tumor location in the brain

The tumor sites treated were located in 13 locations namely (i) meningen, (ii) frontal lobes, (iii) temporal lobes, (iv) parietal lobes, (v) occipital lobes, (vi) cerebellum, (vii) intercellular regions, (viii) cerebellopontine angle (CPA), (ix) pineal, (x) ventricles, (xi) basal ganglia, (xii) thalamus and (xiii) brainstem. Of the 1,285 tumor data, the most common location is meningen, with 496 cases (38.6%) followed by interlaced regional locations with 199 cases (15.4%) and cerebellar with 182 cases (14.2%). The fewest locations were in the basal ganglia which were 8 cases (0.6%). (Figure 5)

The location of the meningen tumor was then spread over 14 locations namely (i) frontal, (ii) temporal, (iii) parietal, (iv) occipital, (v) olfactory groove, (vi) interrupted tubercle, (vii) cavernous, (viii) sphenoorbita, (ix) clinoids, (x) foramen magnum, (xi) CPA, (xii) petroclival, (xiii) falx and (xiv) parasagital. Of the 496 tumor data located in meningen, the majority were located in sphenoorbita in 101 cases (20.4%) followed by convection in frontal in 83 cases (16.7%) and convection in parietal in 80 cases (16.1%) while the location that was most rarely found was the foramen magnum in 5 cases (1.01%). (Figure 6)

Incidence according to specific histology

Histologically, tumors of meninges were the most common (36.9%), followed by neuroepithelial tumors (35.9%) and tumors of the sellar region (12.7%) as shown in in Figure 5 and Figure 6. Neuroepithelial tumors of neuroepithelial tissue were composed of astrocytic tumors, oligodendroglial tumors, ependymal tumors, choroid plexus tumors, pineal region tumors, and embryonal tumors.

Most of the neuroectodermal tumors were gliomas (93.4%), which accounted for 12.7% of all primary brain tumors. Glioblastomas accounted for 5.3% of all tumors and 41.8% of all gliomas. Among histologically confirmed cases, glioblastomas accounted for 46.2% of all gliomas (Table 3).

Tumors of neuroepithelial tissue

From 1,540 data of patients with brain tumors undergoing surgery at Dr. Soetomo from the 2012-2018 period obtained tumors of neuroepithelial tissue (tumors of neuroepithelial tissue) as many as 553 cases (35.9%). In this group the dominant results were obtained in the male sex as many as 310 people (56.1%), the age group of 6-11 years as many as 152 people (27.5%). Tumor sites were more supratentorial (280 cases, 50.6%) than infratentorial (274 cases, 49.4%) with 1 patient suffered from multiple tumor lesions.

Of the 553 entries for surgery for neuroepithelial tissue tumors, 217 emergency cases (39.2%) and elective surgery were 336 cases (60.8%). Extent of resection in neuroepithelial tissue brain tumor cases that were recorded were gross total resections of 122 cases, subtotal resections of 134 cases, partial resections of 47 cases and biopsy of 17 cases. tumor size was more in the group less than 60 mm in 313 cases (74.7%) with an average size of 47.5 mm.

From the results of histopathological examination of brain tumors that were successfully obtained, medulloblastoma (WHO grade IV) was the most histopathological results in 97 cases, followed by astrocytoma (WHO grade I) as many as 81 cases, then glioblastoma (WHO grade IV) as many as 65 cases.

Tumors of meninges

From 1,540 data of patients with brain tumors undergoing surgery at Dr. Soetomo General Academic Hospital from the 2012-2018 period obtained tumors of meninges (tumors of meninges) as many as 568 data in the tumor type group of meningeal tissue. In this group the dominant results were found in the female sex, with 471 people (82.9%) with the most age group being in the 36-45 years age group (237 cases, 41.7%). The

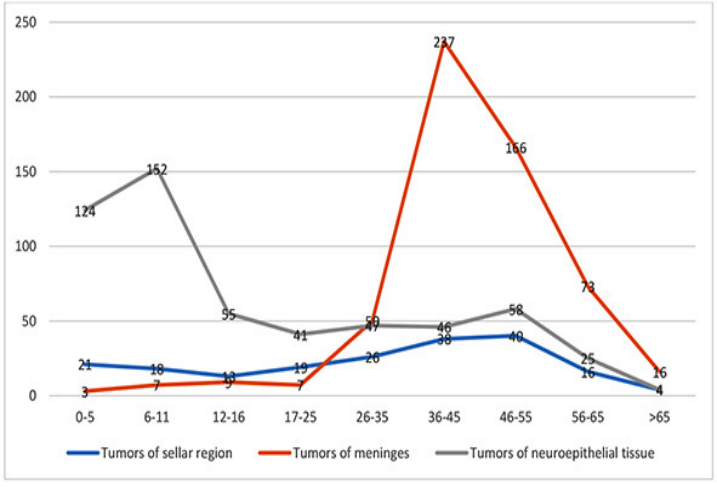

Figure 4. Distribution of primary brain and CNS tumors according to age for selected histology, Indonesia, 2012-2018. CNS: central nervous system.

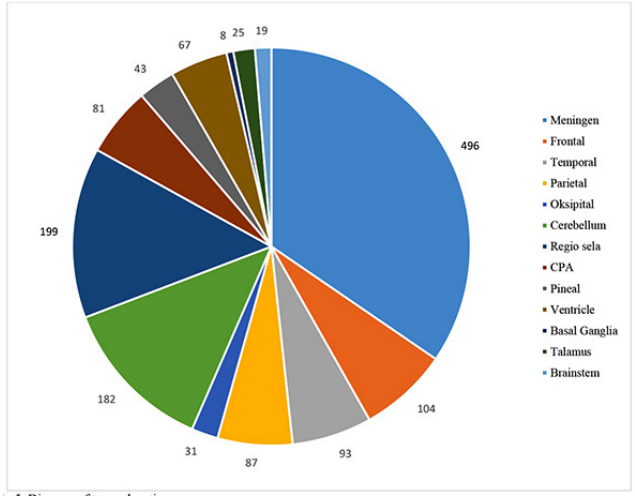

Figure 5. Diagram of tumor location

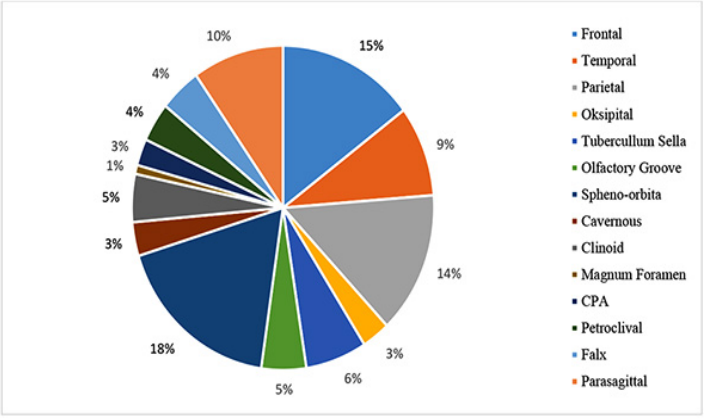

Figure 6. Diagram of meninges tumor location

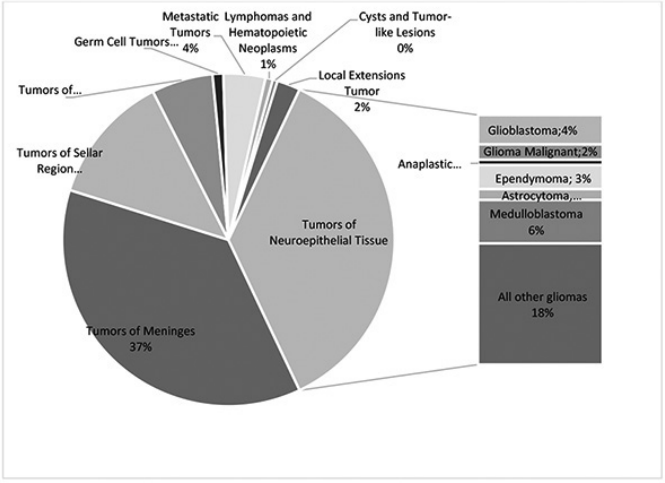

Figure 7. Distribution Of brain tumors classification.

Table 3. The numbers of incidence, crude rate and age-standardized rate in the most common histologically confirmed cases by histological group, Indonesia, 2012-2018

Pathological Anatomy	Female			Male			Total		
	N	CR	ASR	N	CR	ASR	N	CR	ASR
Tumor of Meninges									
Meningioma	8	0.06	0.06	0	0.000	0.000	8	0.030	0.059
Meningioma Anaplastic Type	19	0.14	0.14	12	0.089	0.089	31	0.116	0.228
Meningioma Angiomatous and Fibroblastic Type	1	0.01	0.01	0	0.000	0.000	1	0.004	0.007
Meningioma Angiomatous and Microcystic Type	4	0.03	0.03	2	0.015	0.015	6	0.022	0.044
Meningioma Angiomatous Type	6	0.05	0.04	3	0.022	0.022	9	0.034	0.066
Meningioma Atypical Type	22	0.17	0.16	10	0.074	0.074	32	0.120	0.235
Meningioma Atypical with Glia Infiltration	0	0.00	0.00	1	0.007	0.007	1	0.004	0.007
Meningioma Chordoid Type	17	0.13	0.12	6	0.045	0.045	23	0.086	0.169
Meningioma Fibroblastic and Microcystic Type	10	0.08	0.07	1	0.007	0.007	11	0.041	0.081
Meningioma Fibroblastic Type	35	0.26	0.25	3	0.022	0.022	38	0.142	0.279
Meningioma Meningothelial and Microcystic Type	1	0.01	0.01	0	0.000	0.000	1	0.004	0.007
Meningioma Meningothelial Type	18	0.14	0.13	0	0.000	0.000	18	0.067	0.132
Meningioma Meningothelial, Microcystic and Fibrola	1	0.01	0.01	0	0.000	0.000	1	0.004	0.007
Meningioma Meningotheliomatous Type	3	0.02	0.02	1	0.007	0.007	4	0.015	0.029
Meningioma Metaplastic Type	2	0.02	0.01	0	0.000	0.000	2	0.007	0.015
Meningioma Microcystic Type	25	0.19	0.18	5	0.037	0.037	30	0.112	0.220
Meningioma Psammomatous Type	9	0.07	0.06	3	0.022	0.022	12	0.045	0.088
Meningioma Rhabdoid Type	2	0.02	0.01	0	0.000	0.000	2	0.007	0.015
Meningioma Secretoric Type	1	0.01	0.01	0	0.000	0.000	1	0.004	0.007
Meningioma Transtitional and Angiomatous Type	3	0.02	0.02	0	0.000	0.000	3	0.011	0.022
Meningioma Transtitional and Fibroblastic Type	0	0.00	0.00	1	0.007	0.007	1	0.004	0.007
Meningioma Transtitional and Metaplastic Type	0	0.00	0.00	1	0.007	0.007	1	0.004	0.007
Meningioma Transtitional and Microcystic Type	10	0.08	0.07	0	0.000	0.000	10	0.037	0.073
Meningioma Transtitional and Secretoric Type	1	0.01	0.01	0	0.000	0.000	1	0.004	0.007
Meningioma Transtitional dan Angiomatous Type	1	0.01	0.01	0	0.000	0.000	1	0.004	0.007
Meningioma Transtitional Type	184	1.39	1.32	29	0.216	0.215	213	0.798	1.564
Meningioma Transtitional with Bone Infiltration	1	0.01	0.01	0	0.000	0.000	1	0.004	0.007
Meningioma Transtitional with Duramater Infiltrati	1	0.01	0.01	0	0.000	0.000	1	0.004	0.007
Meningioma Transtitional with Myxomatic Degenerati	1	0.01	0.01	0	0.000	0.000	1	0.004	0.007
Meningioma with Bone Infiltration	1	0.01	0.01	0	0.000	0.000	1	0.004	0.007
Meningioma with Glial Infiltration	2	0.02	0.01	0	0.000	0.000	2	0.007	0.015
Meningioma with Myxoid Change	1	0.01	0.01	0	0.000	0.000	1	0.004	0.007
Meningioma with Myxomatic Degeneration	1	0.01	0.01	0	0.000	0.000	1	0.004	0.007
Meningioma with Parenchyme Infiltration	0	0.00	0.00	1	0.007	0.007	1	0.004	0.007
Meningoma Fibroblastic and Microcystic Type	1	0.01	0.01	0	0.000	0.000	1	0.004	0.007
Meningotheliomatous	3	0.02	0.02	0	0.000	0.000	3	0.011	0.022
Olfactory Groove Meningioma	1	0.01	0.01	0	0.000	0.000	1	0.004	0.007
Atypical Teratoid Rhabdoid Tumor	5	0.04	0.04	4	0.030	0.030	9	0.034	0.066
Primitive Neuroectodermal Tumor	6	0.05	0.04	7	0.052	0.052	13	0.049	0.095
Ewing Sarcoma	4	0.03	0.03	2	0.015	0.015	6	0.022	0.044
Hemangioblastoma	6	0.05	0.04	4	0.030	0.030	10	0.037	0.073
Hemangioma	6	0.05	0.04	0	0.000	0.000	6	0.022	0.044
Hemangioma Cavernosa	0	0.00	0.00	1	0.007	0.007	1	0.004	0.007
Hemangioma Choroidal	1	0.01	0.01	0	0.000	0.000	1	0.004	0.007
Chordoid	6	0.05	0.04	0	0.000	0.000	6	0.022	0.044
Fibrosarcoma	3	0.02	0.02	1	0.007	0.007	4	0.015	0.029

Tumor of Neuroepithelial Tissue									
Medullobalstoma, NOS	23	0.17	0.16	19	0.142	0.141	42	0.157	0.308
Medulloblastoma	9	0.07	0.06	20	0.149	0.148	29	0.109	0.213
Medulloblastoma Anaplastic Type	1	0.01	0.01	3	0.022	0.022	4	0.015	0.029
Medulloblastoma Classic Type	2	0.02	0.01	4	0.030	0.030	6	0.022	0.044
Medulloblastoma Desmoplastik/Nodular Type	2	0.02	0.01	6	0.045	0.045	8	0.030	0.059
Medulloblastoma Large Cell Type	0	0.00	0.00	2	0.015	0.015	2	0.007	0.015
Medulloblastoma Nodular	1	0.01	0.01	4	0.029	0.029	5	0.019	0.036
Pilocytic Astrocytoma	40	0.30	0.29	38	0.283	0.282	78	0.292	0.573
Astrocytoma	1	0.01	0.01	2	0.015	0.015	3	0.011	0.022
Astrocytoma Anaplastic	0	0.00	0.00	1	0.007	0.007	1	0.004	0.007
Astrocytoma High Grade	7	0.05	0.05	4	0.030	0.030	11	0.041	0.081
Astrocytoma Low Grade	1	0.01	0.01	1	0.007	0.007	2	0.007	0.015
Anaplastic Astrocytoma	5	0.04	0.04	5	0.037	0.037	10	0.038	0.073
Anaplastic Astrocytoma, NOS	1	0.01	0.01	0	0.000	0.000	1	0.004	0.007
Malignant Astrocytoma	0	0.00	0.00	2	0.015	0.015	2	0.007	0.015
Diffuse Astrocytoma	1	0.01	0.01	3	0.022	0.022	4	0.015	0.029
Diffuse Fibrilary Astrocytoma	0	0.00	0.00	2	0.015	0.015	2	0.007	0.015
Fibrillary Astrocytoma	5	0.04	0.04	3	0.022	0.022	8	0.030	0.059
Pleomorphic Xanthoastrocytoma	1	0.01	0.01	2	0.015	0.015	3	0.011	0.022
Anaplastic Oligoastrocytoma	4	0.03	0.03	3	0.022	0.022	7	0.026	0.051
Anaplastic Oligodendroglioma	2	0.02	0.01	5	0.037	0.037	7	0.026	0.051
Oligoastrocytoma	0	0.00	0.00	4	0.030	0.030	4	0.015	0.029
Oligodendroglioma	7	0.05	0.05	1	0.007	0.007	8	0.030	0.059
Glioblastoma	22	0.17	0.16	37	0.276	0.274	59	0.221	0.433
Glioblastoma with Oligodendroglioma Component	0	0.00	0.00	1	0.007	0.007	1	0.004	0.007
Glioblastoma, NOS	2	0.02	0.01	3	0.022	0.022	5	0.019	0.037
Diffuse Midline Glioma	1	0.01	0.01	0	0.000	0.000	1	0.004	0.007
Gliosarcoma	1	0.01	0.01	0	0.000	0.000	1	0.004	0.007
Ganglioglioma	0	0.00	0.00	3	0.022	0.022	3	0.011	0.022
Pineoblastoma	0	0.00	0.00	1	0.007	0.007	1	0.004	0.007
Central Neurocytoma	0	0.00	0.00	3	0.022	0.022	3	0.011	0.022
Neurinoma	1	0.01	0.01	1	0.007	0.007	2	0.007	0.015
Neurofibroma	7	0.05	0.05	5	0.037	0.037	12	0.045	0.088
Neurofibroma Plexiform	1	0.01	0.01	0	0.000	0.000	1	0.004	0.007
Choroid Plexus Carcinoma	1	0.01	0.01	0	0.000	0.000	1	0.004	0.007
Choroid Plexus Papilloma	3	0.02	0.02	2	0.015	0.015	5	0.019	0.037
Ependymoma	9	0.07	0.06	16	0.119	0.119	25	0.094	0.184
Clear Cell Ependymoma	3	0.02	0.02	0	0.000	0.000	3	0.011	0.022
Cellular Ependymoma	4	0.03	0.03	0	0.000	0.000	4	0.015	0.029
Anaplastic Ependymoma	9	0.07	0.06	11	0.082	0.082	20	0.075	0.147
Benign Ependymal Cyst	2	0.02	0.01	0	0.000	0.000	2	0.007	0.015
Papillary Ependymoma	1	0.01	0.01	0	0.000	0.000	1	0.004	0.007
Tumors of Sellar Region									
Adamantinomatous Craniopharyngioma	11	0.08	0.08	22	0.164	0.163	33	0.124	0.242
Papillary Craniopharyngioma	4	0.03	0.03	8	0.060	0.059	12	0.045	0.088
Adenoma Hypophysis	43	0.32	0.31	63	0.469	0.467	106	0.397	0.778
Adenoma Hypophysis Atypical	3	0.02	0.02	0	0.000	0.000	3	0.011	0.022
Adenoma Hypophysis with Papillary Carcinoma Metastasis	0	0.00	0.00	1	0.007	0.007	1	0.004	0.007

N: incidence, CNS: central nervous system, CR: crude rate, ASR: age-standardized rate, NOS: not otherwise specified

location of tumors were mostly found in supratentorial in 505 cases (88.9%) and infratentorial location in 70 cases (12.3%) with 7 cases were found with multiple lesions. From 568 surgical action data, it was found 94 cases underwent emergency surgery (16.6%) while 474 cases had elective surgery (83.4%). From the total excision and / or biopsy procedure, it was found that the highest grade of Simpson grade I resection was 208 cases. Tumor size was found most in the size group of less than 60 mm in 366 cases (72.6%) with an average size of 50.9 mm.

From the results of histopathological examination of brain tumors in 568 data on the surgery of brain tumors with a group of tumors diagnosed as tumors originating from meningeal tissue, the data obtained were tumor of meninges as the most group with 383 cases followed by WHO Grade classification Meningiomas II as many as 58 cases and WHO grade III meningioma classification were 33 cases.

Tumors of cranial, spinal and peripheral nerves

From 1,540 data of patients with brain tumors undergoing surgery at Dr. Soetomo General Academic Hospital from the period 2012-2018 found 92 patients (5.9%) of whom are types of tumors originating from cranial nerves, spinal nerves and peripheral nerves (tumors of cranial, spinal and peripheral nerves). Of the 92 patients the highest distribution was found in the group of women with a total of 59 cases (64.1%) with the most age group being in the 46-55 years group with 34 cases (36.9%) with 84.8% (78 cases) of tumors were infratentorial. From 92 data of surgical actions, there were 38 emergency surgery actions (41.3%) with 37 of them being shunt installation, while elective surgical actions were obtained as many as 54 cases (58.7%).

From the results of histopathological examination of brain tumors in 92 surgical action data of tumor groups diagnosed as tumors originating from cranial, spinal and peripheral nerve tissue, schwannomas were the largest group, with 38 cases followed by 13 cases of neuroblastomas.

Tumors of sellar region

From 1,540 data of patients with brain tumors undergoing surgery at Dr. Soetomo General Academic Hospital from the period 2012-2018 obtained tumors from the interlaced region (tumors of sellar region) as many as 195 (12.7%) data in the tumor type group from the interposed region. In this group the dominant results were found in the male gender, as many as 111 people (56.9%) and most were in the age group of 46-55 years, as many as 40 people (20.5%). From the surgical action data, 49 cases (25.1%) of shunts were obtained while surgical excision of 141 cases (72.3%) where the most technique used EETH (endoscopic endonasal transphenoidal hypophysectomy) technique, which was followed by excision craniotomy in 47 cases, while excision with SLTH (sublabial transphenoidal hypophysectomy) technique in seven cases. Extent of resection in the regional brain tumor cases that have been recorded are GTR (gross total resection) of 84 cases, STR (subtotal resection) of 28 cases, PR (partial resection) of 27 cases and B (biopsy) of one case. The average tumor size was 39.3 mm.

From the results of histopathological examination of brain tumors in 195 data on the surgical action of a group of tumors that were diagnosed as intercellular tumors, the majority were hypophysis adenomas with 101 cases followed by craniopharyngiomas (WHO grade I) of 45 cases.

Lymphomas and hematopoietic neoplasms

From 1,540 data of patients with brain tumors undergoing surgery at Dr. Soetomo general academic hospital from the period 2012-2018 obtained tumors which are lymphoma and neoplasms of hematopoietic (lymphomas and hematopoietic neoplasms) as many as 11 cases (0.7%) in the lymphoma and neoplasm types group of hematopoietic. In this group the dominant results were obtained in the male sex, namely as many as eight people (72.7%) with the most age groups in the age group 26-35 years, namely as many as three people (27.3%). The highest location in this tumor group is supratentorial, in nine cases (81.8%). Of the 11 surgical action data that were successfully recorded, it was found that the most types of actions performed on lymphoma and neoplasms of hematopoietic were excision as many as seven cases and four others were biopsy.

From the results of histopathological examination of brain tumors on 11 surgical action data of tumor groups diagnosed as lymphoma and neoplasms from hematopoietic, most obtained were malignant lymphoma as many as six cases followed by granulocytic sarcomas many as three case.

Germ Cells Tumors

From 1,540 data of patients with brain tumors undergoing surgery at Dr. Soetomo General Academic Hospital from the period 2012-2018 obtained tumors which are tumors of germ cells (germ cells tumors) as many as 16 cases (1.03%) in the tumor type group of germ cells. In this group the dominant results were obtained in the male sex, namely 13 people (81.25%) with the most age group being in the age group of 12-16 years i.e. as many as 6 people (46.2%). The most frequent location of this tumor group was infratentorial in nine cases (56.25%) and tumors in supratentorial locations in seven cases (43.75%). From the 16 surgical action data that was successfully recorded, it was found that the most types of actions performed on germ cell tumors were excision as many as seven cases.

From the results of histopathological examination of brain tumors in 16 surgical action data of tumor groups that were diagnosed as germ cell tumors, the highest number was germinoma (WHO grade II) as many as nine cases followed by malignant germ cell tumor (WHO type IV) as many as three cases.

Cysts and tumor-like lesions

From 1,540 data of patients with brain tumors undergoing surgery at Dr. Soetomo General Academic Hospital from the 2012-2018 period found seven cases (0.54%) were cysts and tumor-like lesions according to the data entry of surgical actions in brain tumors. In this group the dominant results were found in the female sex, namely as many as five people (71.4%) with the most age groups in the age group 26-35 years, as many as four people (57.1%). The most frequent location of this tumor group is infratentorial, which

is four cases (57.1%) of which three are in the CPA region (cerebellopontine angle) and one case is in the cerebellum. Three cases were supratentorial, all of which were at the base of the skull (skull base). Seven surgical action data performed electively. The most type of surgery performed was the excision of the lesion in six cases (85.7%) and one case was biopsy. The smallest lesion size is 19 mm with the largest size being 61 mm. The mean size of the lesion was 42.6 mm with a standard deviation of approximately 13.9 mm.

From the results of histopathological examination of brain tumors on seven surgical action data of tumor groups that were diagnosed as cysts and tumor-like lesions were found to be the most epidermoid cyst in five cases followed by benign ependymal cyst in two case.

DISCUSSION

Basic principles of national cancer register and WHO ICD-O code

The cancer register consists of collecting standard information relevant to the disease in the affected individual. Important information includes personal identity, tumor characteristics, basis and date of diagnosis, and date of death.[4] Information about tumor characteristics with respect to morphology, topographic location, and behaviour is very important to individualize each tumor. To guarantee an equal direct comparison of all registrants, the cancer register standard that has been used is the international classification of diseases for oncology (ICD-O).[4]

The gold standard for recording morphology of tumors still uses histopathological diagnosis (basis of diagnosis: microscopically verified). The classification is mainly based on the morphological characteristics of the tumor such as cytology, degree of differentiation, and proliferative activity. The WHO classification[5,8] provides diagnostic criteria for individual tumor entities, which serve as references for global pathologists. According to the level of malignancy and associated prognosis of the patient, the tumor is divided into WHO grade I-IV.[9]

The Indonesian central nervous system tumors registry (Ina-CTR) register is a preliminary study in making systems and methods that can be used later in prospective research on a larger scale. From January 2012 to December 2018, 1,285 patients were obtained.

This tumor register data can be used as a basis for: (1) collecting comprehensive incidence data on all primary brain tumors in Indonesia, (2) conduction of descriptive epidemiological studies on tumor entities, (3) maintaining high data quality through a high degree of certainty of cases , (4) direct relationship between case registers with medical practice and research.[4]

Indonesian brain tumor register data for 2012-2018 by age group

The average age at diagnosis according to data obtained from the CBTRUS / central nervous system (CNS) tumor in the United States (US), for all primary CNS tumors was 60 years, with an incidence of 23.03 per 100,000 population. The highest incidence in the age group of more than 85 is 83.75 per 100,000 population.[4] This is seen contrary to the data that has been obtained, where the highest incidence in the productive age group is age 36-45 years with 311 cases (24.2%), followed by the age group 46-55 years with 294 cases (22, 9%) and the age group 26-35 years of 134 cases (10.4%). This difference can be due to the low life expectancy in Indonesia[7] and is accompanied by a new BPJS system policy set in 2015. Grouping the incidence of tumor types can be linked to age and is useful in determining the initial diagnosis and calculating the life expectancy of patients suffering from brain tumors (Figure 8).[2,4,6,8,10]

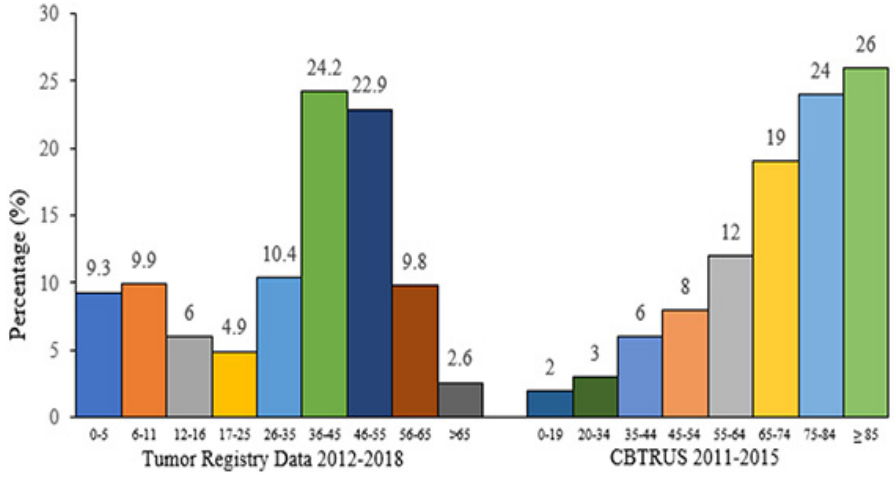

Figure 8. Comparison of age distribution in 2012-2018 tumor data with CBTRUS 2011-2015.[4,6]

Indonesian brain tumor register data for 2012-2018 by sex

Meningiomas are the most frequent intracranial tumors. The number of meningiomas prevalence in our centre reaches one third of all central nervous system tumors. The global incidence of cerebral meningioma itself varies, ranging from 1.3 / 100,000 to 7.8 / 100,000.[11] The prevalence of meningiomas alone can reach 50.4 / 100,000 to 70.7 / 100,000.[12,13]

The age and gender pattern of meningioma events from the Central Nervous System Registry in Gironde, France for the period 2000-2011 gives a picture of the incidence of meningiomas in women by about three times more frequent compared with the incidence in men, with the biggest difference observed between ages 30 and 59 years up to 3.6 times.[11] Other studies showed the dominance of women prevalence in meningioma for about two times higher than men.[4,6,10,14] The tendency of meningiomas in this female gender group can be considered in seeing the results of the tumor data collection. Two to three times the number of women with meningiomas and meningioma considerations as the most central nervous system tumors can contribute to the tendency to have more central nervous system tumors in the female sex.[4,6,10,14] Besides sex, age also increases progressively until the age of

89 years and reaches a peak incidence of 22.2 / 100,000 in the age group 75 and 89 years.[11]

Gender differences give similar results to the literature review where in this study the authors found female sex group dominance of 782 patients (60.8%) and 503 men (39.2%). This is in line with data on CBTRUS where overall 42.0% of all tumors diagnosed between 2011 and 2015 occurred in men (165,148 tumors) and 58.0% in women (227,834 tumors).[4] This is also in line with the results obtained from data with the Korean Central Cancer Registry (KCCR) the incidence of men is 37.1% and the incidence of women is 62.9% (Figure 9).[6]

Results of epidemiological studies conducted in several flashlights in Indonesia also showed similar results, namely in Dr. dr. Kariadi Hospital in Semarang where the percentage of women was 61.7% and men were 38.3%. In other hospitals in Bandar Lampung City with the percentage of women equal to 65% and males by 35%, and studies in the pediatric population at Adam Malik Hospital Medan with a percentage of 67% women and 33% men, while different results were reported from epidemiological studies in 10 hospitals in North Sumatra Province , a smaller percentage of women is 49.3% and men with a percentage of 50.7%.[15–18] This difference can be attributed to the time of observation carried out for 4 months while other studies conducted over a period of 12 months.

Indonesian brain tumor register data for 2012-2018 is based on histopathology

The most common type of tumor histopathology is the meninges tumor group with a percentage of 39.2% which is almost similar to the data obtained in KCCR of 37.9% and in CBTRUS of 37.1%.[4,6] The next most frequent tumor was neuroepithelial by 32.6% while in the second most KCCR was the tumor of sellar region with 19.3%. Neuroepithelial tumors also rank second in CBTRUS 2011-2015 with 28.2%. Sellar region tumors in this study was ranked third with a percentage of 12.4%, as in CBTRUS 2011-2015 with 16.5%. Subsequently followed by peripheral nervous system tumors, metastases, local extension tumors, germ cell tumors, lymphoma and neoplastic tumors and cystic tumors (Figure 9).[4,6] While in Indonesia itself, there have been several studies that have tried to provide a holistic distribution of histology cases of brain tumors in several neurosurgery education centres, both adults and children. However, most of these reports do not use ICD-O and of all these are not uniform and cannot be compared with international brain tumor registrations. (Figure 10).[15–18]

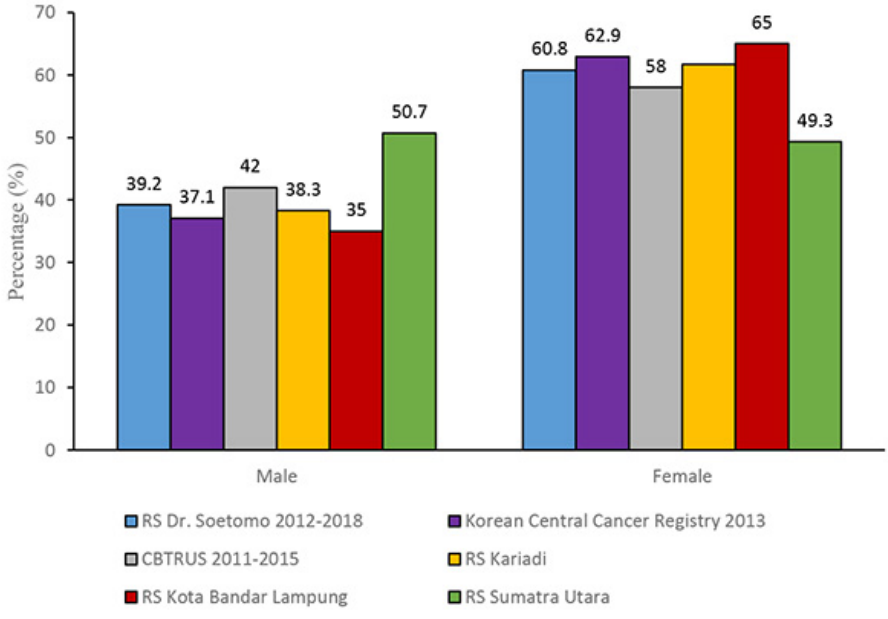

Figure 9. Comparison of sex distribution in tumor data 2012-2018. Data from the Korean central cancer registry 2013, CBTRUS 2011-2015, Dr. Kariadi Hospital Semarang, Hospital in Bandar Lampung City, and hospitals in North Sumatra Province.

One of the highlights is the number of glioblastomas in the author's data is quite low (4.2%) and almost similar to the data in Korea (5.3%), but the rate of glioblastoma is very high in the US, where based on CBTRUS 2011-2015, the prevalence rate of glioblastoma reaches 14.7%. Need to be further studied what factors cause the prevalence of glioblastoma prevalence in Asia and America.[4,6]

Primary brain tumors consist of a large spectrum of clinically and genetically heterogeneous disorders. According to the latest WHO classification, more than 120 different brain tumor entities have been recognized. Based on biological behaviour, brain tumors fall into three broad categories: (1) benign tumors [ICD-O0], (2) tumors with moderate or uncertain behaviour [ICD-O1], and (3) malignant tumors [ICD-O3]. Individuals in the pediatric and adult patient categories can be affected. In childhood, brain tumors are the most common group of neoplasms and are the most frequent cause of cancer-related deaths in this age group. Most brain tumors occur sporadically. So far, only a few environmental risk factors have been established, for example the long-term sequel of ionizing radiation. Low frequency electromagnetic fields (eg cell phone use) have also been proposed as potential risks and are currently under debate. However, in most brain tumors, the underlying etiological risk factors remain unclear.[19,20]

Differences in tumor register data

Not many striking differences were found between brain tumor registers from author data and data in other countries compared, apart from the age of the operated patients who were much younger in the author's data. This is most likely due to differences in life expectancy between Indonesia and other countries whose authors compare the data (Korea, America). Resection rates in almost all tumor cases in the author's data are quite

good, reaching more than 60% of total excision, even in cases of emergency surgery. This shows that the readiness of the writer as a tertiary reference in Indonesia is quite good in handling cases of brain tumors and is not much different from other health centres in other countries.[4,6,21,22]

Based on the findings this time, the researcher can conclude that there is a need to produce more accurate and comparable estimates of the incidence and prevalence of primary brain tumors in Indonesia. A standard approach to the study of epidemiology of tumors is needed to better understand the burden of disease and possible geographical variations in the incidence rate. Future studies can be carried out to investigate the incidence or prevalence of brain tumors that adopt the same methodology and use a standardized approach to ascertain cases of brain tumors, as example population-based method.

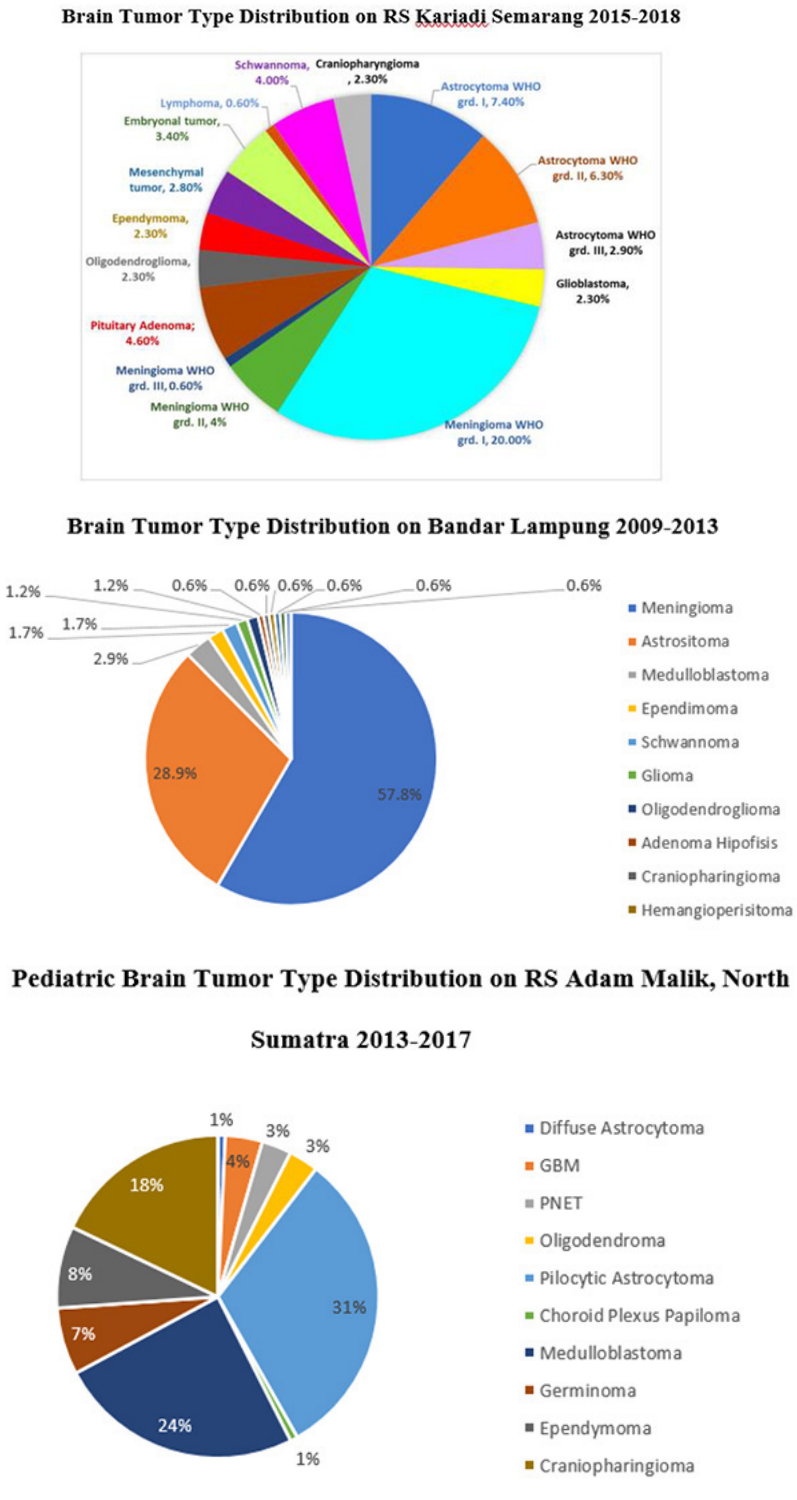

Figure 10. Distribution of tumor types in several centres in Indonesia.[15–18]

Research Limitation

This study has a weakness in the form of differences in the completeness of the patient's medical record data for tumor data 2012-2018 in which patients who have sufficiently complete and registered data are patients who undergo hospitalization and surgery at the author's health centre. This shows the need for follow-up for more complete data collection and recording so as to be able to obtain a more representative and better validated distribution of brain tumor epidemiology in Indonesia.[4,6,23]

1. Data is not complete and records are not standardized.
2. Written medical records and other radiological and diagnostic data which are still in conventional form thereby reducing the overall speed, accuracy and completeness of the data.
3. Conventional medical record systems and electronic medical records that are not yet equivalent to the quality of electronic medical records in the comparative developed health system (United States and South Korea) and the absence of a national data registration system (for example: institutional and national medical data collection systems in developed countries) so the possibility of data collection errors is still high.
4. Incomplete follow-up output so that it cannot carry out prognostic analysis in the form of survival analysis.

CONCLUSIONS

Tumor registry data of Dr. Soetomo General Academic Hospital 2012-2018 period can be used as a basis for further data collection, conduction of further descriptive epidemiological studies, and for future medical practice and research. Age distribution of patients in the brain tumor registry data Dr. Soetomo General Academic Hospital for the 2012-2018

period was younger than the brain tumor data from other countries with the highest incidence group at the age of 36-45 years (24.2%). No significant differences were found between the sex groups in the brain tumor register data of Dr. Soetomo General Academic Hospital period of 2012-2018 with other countries or similar research in Indonesia. The most common type of tumor histopathology in brain tumor register data is Dr. Soetomo General Academic Hospital in the 2012-2018 period was a meninges tumor (39.2%), followed by a neuroepithelial tumor (32.6%) then a tumor in the regional region (19.3%). The glioblastoma rate in our data ranges from 4.2%, not much different from the glioblastoma number in the Korean tumor register data (5.3%) but only nearly a quarter of the glioblastoma number in CBTRUS 2011-2015 (14.7%).

The main clinical complaint in patients in the brain tumor registry data Dr. Soetomo General Academic Hospital period of 2012-2018 is a headache followed by a decrease in consciousness and focal neurological symptoms. This shows that the average brain tumor patient in Indonesia comes with an emergency brain tumor. The location of the most common brain tumors in this data is meninges, followed by the sellar region, as in CBTRUS 2011-2015, but the number of tumors in the cerebellum area in our data ranges from 12.7%, double that of the 2011-2015 CBTRUS data (around 6%). We conclude this is related to the age distribution of our patients who are much younger.

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DECLARATIONS

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Conflict of interest

Authors have no conflict of interest.

Ethical approval

This research had been approved by Ethical Committee

Authors' contributions

Authors took part in design of the study and contributed to data collection. MFRP and RTZW did literature review and drafted the manuscript. JW and HBN made critical revisions to the manuscript and all authors agreed to accept equal responsibility for accuracy of the contents of this article.

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