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RELATIONSHIP BETWEEN AGE AND HISTOPATHOLOGICAL TYPE OF MENINGIOMA ACCORDING TO THE WORLD HEALTH ORGANIZATION (WHO)

Meta Zulyati Oktora[*1], Ruhsyahadati[2], Debie Anggraini[3], Alzeri Fajar Sirfa[4]

[1,2,3,4]Universitas Baiturrahmah, Indonesia

***Correspondence Author: metazulyantioktora@fk.unbrah.ac.id**

Abstract:
Background: Meningiomas are the second most common intracranial tumors. The 2016 WHO classification divides the histopathological types of meningiomas into benign (WHO grade I) and malignant (WHO grade II or III). Benign meningiomas are characterized by a well-defined mass adhering to the dura mater and compressing the brain, whereas malignant meningiomas, though rare, are aggressive. Age is a factor that could influence the histopathological type of meningiomas, with incidence increasing with age. Meningiomas commonly occur in middle and old age, peaking in the sixth decade. Age is also a prognostic factor in meningioma occurrences. Method: This was an observational analytic study with a retrospective cross-sectional design on the medical records of meningioma patients at the Anatomical Pathology Laboratory of Dr. M. Djamil Padang Hospital from May 2023 to January 2024. The study included a total of 72 patients. Results: The Chi-Square test showed a p value of 0.330 (p>0.05), indicating no significant relationship between age and the histopathological type of meningiomas. Most meningioma patients were ≥40 years old (76.4%) and female (87.5%). The predominant histopathological type was WHO grade I (88.9%), with tumors ≤5 cm in size (65.3%). Conclusions: There is no significant relationship between age and the histopathological type of meningiomas according to WHO criteria.
***Keywords** : Meningioma, age, histopathological type*

INTRODUCTION

Meningioma is a tumor originating from meningothelial cells in the arachnoid villi, arachnoid membrane, choroid tela, and choroid plexus(1). Meningioma is a type of primary brain tumor characterized by the growth of abnormal and uncontrolled cells that originate from the brain tissue itself. Generally, meningiomas grow very slowly with well-defined lesions.(2)

Meningioma constitutes the second most common type of intracranial tumor, accounting for about 24-30% of all intracranial tumors.(3) According to data from the Central Brain Tumor Registry of the United States (CBTRUS), meningioma is the most frequent tumor in the United States, comprising 39.7% of all primary brain tumors and 55.4% of all non-malignant tumors, with an annual incidence rate of approximately 9.51 patients per 100,000 population.(4) In Indonesia, according to the National Cancer Control Committee, meningiomas account for 13-26% of all primary intracranial tumors.(5)

According to the 2016 WHO classification, the histopathological types of meningiomas are divided into three categories: typical (benign), atypical, and anaplastic (malignant). Typical (benign) meningiomas consist of meningo-thelial,

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fibrous, transitional, psammomatous, angioblastic, mycrocystic, lymphoplasmacyte-rich, metaplastic, and secretory types. Atypical meningiomas are classified as chordoid, clear cell, and atypical. Anaplastic (malignant) meningiomas are composed of papillary, rhabdoid, and anaplastic types.(6) Approximately 80% of meningioma histopathologies are typical, and 20% are atypical.(7)

Meningiomas have a higher prevalence compared to other primary brain tumors, a fact supported by the Health Department which considers meningiomas a local, national, and international issue due to their frequent occurrence and significant impact on public health, thus making meningiomas a case of urgency. The incidence of meningiomas continues to increase with age, with the average age at diagnosis being 66 years. According to a study by Desai and Patel in 2015, meningiomas often occur in the age range of 31-60 years. Meningiomas can also occur at a young age, but they have a low incidence rate.(8)

The research conducted by Damayanti in 2021 found a significant correlation between age and the aggressiveness level of meningioma. However, in 2022, Wahab found that there was no significant relationship between age and the degree of differentiation of meningioma. The study had limitations in sample size, with only 17 patients. An initial survey conducted gathered data from medical records at RSUP M Djamil between 2021-2022, revealing a total of 83 meningioma patients.

METHODS

This study is an analytical observational research with a retrospective cross-sectional design. The sampling technique used was total sampling and utilized secondary data from patient medical records. The sample consisted of 72 meningioma patients at the Pathology Anatomy Laboratory of RSUP Dr. M. Djamil Padang.

The inclusion criteria for the study sample were all meningioma patients at RSUP Dr. M. Djamil, Padang. Exclusion criteria included incomplete medical record data such as age, gender, histopathological type, and tumor size. The research was conducted from May to December 2023 and passed the ethical review by the Faculty of Medicine, Baiturrahmah University No.152/ETIK/-FK-UNBRAH/03/09/2023.

The researchers collected data from the medical records of meningioma patients at the Pathology Anatomy Laboratory of RSUP Dr. M. Djamil Padang. Subsequently, sample selection was performed according to the inclusion and exclusion criteria. Statistical analysis was conducted using SPSS software version 21. Univariate analysis was employed to obtain a description of each independent and dependent variable, while bivariate analysis utilized the Fisher's test to determine the relationship between age and histopathological type. Significance was determined at $p<0.05$. The Mann-Whitney test was used to compare rankings between groups.

RESULTS AND DISCUSSIONS

Frequency Distribution of Meningioma Patients Based on Age

The research results, as shown in Table 1, revealed that 55 (76.4%) meningioma patients were in the middle to old age group ($\geqslant$40 years) and 17

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(23.6%) patients were in the young to middle age group (<40 years). The youngest subject in the study was 20 years old, while the oldest was 76 years old.

Table 1 Frequency Distribution of Meningioma Patients Based on Age

Age (th)	f	%
< 40	17	23,6
≥40	55	76,4

In this study, the majority of participants were over 40 years old. This finding is consistent with the research by Desai and Patel, which noted that the incidence of meningioma tends to be higher in the age range of 31 to 60 years[10]. Additionally, based on a study conducted by Shrilakshmi et al., the incidence of meningioma is also higher in the age group over 40 years old [11].

The phenomenon of increasing incidence rates before the age of 50, especially nearing menopause for women, and the decrease in incidence rates in subsequent age groups can be associated with hormonal instability leading up to menopause and the decline in postmenopausal hormones. The average age of menopause for women is 45.59 ± 5.59 years, which marks the period of estrogen and progesterone hormone decline[12]. This decline is believed to contribute to the decrease in meningioma incidence in postmenopausal women, thus the risk for women in postmenopausal age is considered lower compared to women of reproductive age. This finding aligns with research in Austria that concluded patients over 75 years old tend not to exhibit clinical symptoms[13]. This explains the small number of meningioma cases in this study among participants over 74 years old, with only 1 patient aged 76 years old, who was female.

Frequency Distribution of Meningioma Patients Based on Gender

The research findings, as shown in Table 2, revealed that the majority were female with 63 (87.5%) patients. Meanwhile, male patients numbered only 9 (12.5%)

Table 2 Frequency Distribution of Meningioma Patients Based on Gender

Gander	f	%
Male	9	12,5
Female	63	87,5

This study found that the majority were female, with 63 (87.5%) patients being female. This finding supports the research results of Wiemels, Wrensch, and Claus, which showed that the incidence of meningioma in females has a higher ratio compared to males, namely 8.36:3.61[14]. Data from the WHO in 2016 also confirms that the risk of developing meningioma is higher in females, with an annual incidence rate reaching 10.5 cases per 100,000 females compared to 4.8 cases per 100,000 males[15].

The influence of sex hormones is often associated with the increased incidence of meningioma. Meningioma has been identified to have progesterone and

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estrogen hormone receptors, namely FSH, LH, which are believed to have the ability to suppress tumor cell growth, while in males, high levels of testosterone are believed to provide a protective effect against meningioma[16]. This finding is supported by the research of Blitshteyn, Crook, and Jaeckle, which showed an increased risk in women undergoing hormone replacement therapy[17]. Research by Sun et al. indicates that tumors tend to grow more rapidly during pregnancy and cease growth after childbirth due to the role of hCG hormones. Meanwhile, hPL and prolactin are believed to stimulate tumor cell spread[18].

Frequency Distribution of Meningioma Patients Based on Histopathological Type

The research findings, as shown in Table 3, revealed that Grade I histopathological type accounted for 64 (88.9%) patients. Meanwhile, Grade II or III histopathological types were only found in 8 (11.1%) patients. Additionally, the number of male patients was only 9 (12.5%).

Table 3. Frequency Distribution of Meningioma Patients Based on Histopathological Type

Histopathological Type	f	%
Grade 1	64	88,9
Grade 2-3	8	11,1

This study categorizes meningiomas into two grades, WHO grade I and WHO grade II or III. This division aims to differentiate meningiomas based on the risk of recurrence and their malignancy level. Meningiomas with WHO grade I are generally benign, while those with WHO grade II and III have a higher risk of recurrence and are more aggressive, and can even become malignant.

The study found a predominance of WHO grade I histopathological types, while approximately 11.1% were WHO grade II or III. This finding is supported by the research of Wiemels, Wrensch, and Claus, which showed that around 80% of all meningiomas are benign (WHO grade I). Additionally, the study by Parastuta et al. also indicated that grade I meningiomas are more commonly found, with a percentage of 92%[15].

The expression of progesterone and estrogen receptors is presumed to be more dominant in WHO grade I compared to WHO grade II and III. Considering the majority of meningioma patients in this study are females, differences in receptor expression create dominance in the significant distribution of occurrences in WHO grade I. Stimulation of meningioma growth primarily occurs in WHO grade I through the expression of progesterone, estrogen, and androgen receptors[16].

Frequency Distribution Of Meningioma Patients Based On Tumor Size

The research findings, as presented in Table 4, revealed that 47 (65.3%) meningioma patients had tumor sizes ⩽5 cm. Meanwhile, 25 (34.7%) meningioma patients had tumor sizes >5 cm.

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Table 4 Frequency Distribution Of Meningioma Patients Based On Tumor Size

Tumor Size	f	%
≤ 5 cm	47	65,3
>5 cm	25	34,7

This study found that many patients had tumor sizes ≤5 cm (65.3%), while 34.7% of meningioma patients had tumor sizes >5 cm. This finding is consistent with a study conducted by Ishaq, Ibrahim, and Iskandar, which found that the percentage of meningioma tumor sizes was also higher in the group with tumor sizes ≤6 cm compared to tumor sizes >6 cm[19].

Meningiomas with small sizes often do not show symptoms, while those with larger sizes tend to cause clinical manifestations. Meningioma symptoms can be general due to tumor pressure on the brain and spinal cord, or they can be specific due to disruption of normal function in specific parts of the brain or pressure on nerves or blood vessels[20].

The Relationship Between Age and Histopathological Type of Meningioma Patients

Based on Table 5, it was found that 55 (76.4%) meningioma patients were in the age group of ⩾40 years, with 50 (90.9%) patients classified as WHO grade I histopathological type and 5 (9.1%) patients classified as WHO grade II or III histopathological type. Meanwhile, there were 17 (23.6%) meningioma patients in the age group of ⩾40 years, with 14 (82.4%) patients classified as WHO grade I histopathological type and 3 (17.6%) patients classified as WHO II or III histopathological type.

A Fisher's test was conducted, yielding non-significant results indicating no significant relationship between age and histopathological type of meningioma patients, with a significance value of 0.330 (p> 0.05). Additionally, the Mann-Whitney test results showed that the <40 years age group tended to have more severe histopathological types of meningioma (WHO grade II or III) compared to the ⩾40 years age group.

Table 5 The Relationship Between Age and Histopathological Type of Meningioma Patients

	Histopathological Type			
	Grade 1	**Grade 2-3**	**f (%)**	**p***
Age (th)				0,330
< 40	14 (82,4%)	3 (17,6%)	17 (23,6%)	
≥40	50 (90,9%)	5 (9,1%)	55 (76,4%)	
f (%)	64 (88,9%)	8 (11,1%)	72 (100%)	

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p*< 0,05 significant
Mann-Whitney Test; Mean rank of age groups <40 years age group 38.85; ⩾40 years age group 35.77

The research results show that 55 (76.4%) patients were in the age group ≥40 years. Out of these, 50 (90.9%) patients were classified as WHO grade I, while 5 (9.1%) patients were classified as WHO grade II or III. In the <40 years age group, there were 17 (24.4%) patients, with 14 (82.4%) of them classified as WHO grade I and 3 (17.6%) patients classified as WHO grade II or III.

The research by Motebejene, Kaminsky and Choi which states that individuals in the middle to old age range tend to have more benign characteristics of meningioma (grade I), originating from clonal expansion of a mutated single cell that arises sporadically. Meanwhile, in the young to middle age group, meningioma is more commonly associated with histopathological types of higher differentiation, namely WHO grade II or III. This contradicts the findings of this study, which indicate that only 3 patients in the young to middle age group were classified as WHO grade II or III.

The Fisher's test result yielded a value of p = 0.330 (p> 0.05), indicating no significant relationship between age and histopathological type of meningioma. This finding is consistent with the research by Stephen et al., which stated that there is no relationship between age and histopathological type of meningioma with a p-value of 0.61[(20)].

The Mann-Whitney test results showed that the <40 years age group (38.85) tended to have more severe histopathological types of meningioma (WHO grade II or III) compared to the ≥40 years age group (35.77). This finding aligns with the research by Motebejane, Kaminsky, and Choi, which associates it with specific genetic disorders such as neurofibromatosis, Gorlin syndrome, meningiomatosis, and rare cases like Castleman syndrome. Additionally, radiation exposure in children with a history of previous malignancy, such as medulloblastoma, is also considered a risk factor that can increase the degree of differentiation of meningioma in children to young adults [(20)].

CONCLUSIONS

The majority of meningioma patients were aged ⩾40 years, female, had WHO grade I histopathological type, tumor size ⩽5 cm, and there was no relationship between age and the histopathological type of meningioma according to the World Health Organization (WHO).

Suggestions for future research include investigating other risk factors associated with the histopathological type of meningioma, such as Body Mass Index (BMI), as well as the role of hormonal receptors and other biological markers associated with the age of meningioma patients.

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