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THE QUALITY OF SLEEP IN BRAIN TUMOR PATIENTS

Yunni Diansari[1], Sri Handayani[1], Mukhlisa[1], Selly Marisdina[1], Rizka Aprillia Syahputri[1], Tri Susanty[1], Irfannuddin[2]

[1]Neurology Department of Dr Mohammad Hoesin Hospital Palembang/ Medical Faculty of Universitas Sriwijaya
[2]Physiology Departement of Medical Faculty of Universitas Sriwijaya

ARTICLE INFO

Corresponding author :
Yunni Diansari
Departemen Neurology.
Mohammad Hoesin Hospital.
Medical Faculty. Universitas Sriwijaya

Email:
yunnidiansari@fk.unsri.ac.id

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ABSTRAK

Kualitas tidur yang buruk banyak dijumpai pada penderita tumor otak dengan prevalensi berkisar 53%- 77.7%. Faktor yang berperan terhadap kualitas tidur penderita tumor otak cukup beragam dan jarang diteliti. Enam puluh delapan penderita tumor otak yang berusia ≥ 18 tahun dipilih secara konsekutif dan dilakukan pencatatan data berupa karakteristik sosiodemografis, karakteristik klinis (manifestasi klinis, jenis, lokasi tumor, penyakit komorbid), dan karakteristik pengobatan (tatalaksana dan jenis obat). Kualitas tidur dinilai dengan kuesioner Pittsburgh Sleep Quality Index (PSQI). Data dianalisis secara bivariat dengan chi square dan multivariate dengan regresi logistik. Sekitar 45.6% mengalami kualitas tidur buruk. Usia, jenis kelamin, malignansi sistemik, nyeri, jenis tumor otak primer, lokasi tumor, tatalaksana operatif, radioterapi, steroid memilki hubungan signifikan terhadap kualitas tidur pada penderita tumor otak (p< 0,05). Analisis multivariat menunjukkan usia merupakan faktor yang paling kuat mempengaruhi kualitas tidur pasien tumor otak. Usia, jenis kelamin, keganasan sistemik, nyeri, jenis tumor, lokasi tumor, tatalaksana operatif, radioterapi dan steroid berpengaruh terhadap kualitas tidur pasien tumor otak, namun usia memiliki pengaruh paling kuat.

ABSTRACT

The Quality of Sleep in Brain Tumor Patients. The Quality of Sleep in Brain Tumors Patients. Sleep quality is often compromised in patients with brain tumors. The underlying factors contributing to sleep quality disturbances in this patient population are multifaceted, and investigating these factors remains scarce. Sixty-eight patients with brain tumors, aged ≥ 18 years, were selected consecutively, and data was recorded in the form of sociodemographic characteristics (gender and age), clinical characteristics (clinical manifestations, tumor type, location, comorbid diseases) and therapy characteristics (management and types of drugs). Sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI) questionnaire. Data were analyzed bivariate with chi-square and multivariate with logistic regression. Around 45.6% experienced poor sleep quality. Age, gender, systemic malignancies, pain, type of primary brain tumor, tumor location, operation, radiotherapy, and steroid have a significant relationship with sleep quality in patients with brain tumors (p-value <0.05). Multivariate analysis shows that age is the factor that most strongly influences the sleep quality of patients with brain tumors. Age, gender, systemic malignancies, pain, type of primary brain tumor, tumor location, operative treatment, radiotherapy, and steroids influence the quality of sleep in patients with brain tumors, but age has the most decisive influence.

INTRODUCTION

A brain tumor is defined as a neoplasm-originating brain tissue or a metastatic tumor originating from a primary site elsewhere in the body. Patients with brain tumors frequently report sleep disturbances and rate this problem as one of the most disturbing symptoms. Astri et al. reported that 77.5% of brain tumor patients experienced poor sleep quality. Furthermore, Anindita et al. at Cipto Mangunkusumo Hospital demonstrated that sleep disturbances were experienced by 71.7% of brain tumour patients. Lin et al.[5] reported that 77.7% of brain tumor patients had poor sleep quality. Similarly, Willis et al.[6] found that 61.5% of brain tumor patients had impaired sleep quality. Furthermore, Jeon et al.[7] reported that 53% of brain tumor patients had poor sleep quality.

A complex of factors affects sleep quality among patients with brain tumors. Silva et al.[8] found that demographic variables such as gender and age influence a person's experience of sleep disturbances. In contrast, Astri et al.[4] reported that most of their study subjects were aged ≥ 45 years. Jeon et al. found that demographic variables were not associated with sleep disturbances in patients with brain tumors.[7] Jeon et al. reported that clinical manifestations of motor impairment, lateral weakness, and pain were associated with sleep disturbances.[7] As reported by Astri et al., the frontal lobe, inter-suprasellar, and temporal lobes are the most frequently affected brain tumor sites. These three sites are also the most common locations for sleep disorders, as they influence the sleep-wake cycle[4], as mentioned in Peng, Eban, and Pablo's study. Powell et al. reported that 90% of patients with primary brain tumors undergoing cranial radiation therapy experienced sleep disturbances.[12] Lin et al. reported that steroid use was significantly associated with poor sleep quality[5]. In Wang et al.'s study, steroids caused sleep disturbances in the form of prolongation of sleep latency, shortening of sleep duration, and inhibition of REM sleep[13]**.** Nevertheless, in Indonesia, research investigating these factors remains scarce.

METHODS

This study was conducted as an observational analytic study with a cross-sectional approach at the Neurology Polyclinic of Dr Mohammad Hoesin Hospital in Palembang between August and October 2024. The study population included all patients with brain tumors who received treatment at the Neurology Polyclinic of Dr. Mohammad Hoesin Hospital Palembang between August and October 2024 and met the inclusion criteria. The inclusion criteria for this study were as follows: patients who had been diagnosed with a primary or metastatic brain tumor, aged 18 years or over, and were willing to participate in the study, having signed an informed consent form. Uncooperative patients who had decreased consciousness (GCS < 15) or were diagnosed with a psychiatric disorder by a psychiatrist were excluded from the study. The study assessed independent variables, including sociodemographic characteristics, clinical status, and treatment regimen. The sociodemographic factors were age and gender. The age variables were categorized into two groups: those under 45 and those aged 45 years and above. The clinical factors were clinical manifestations, tumor type, tumor location, and comorbid diseases. The clinical manifestations were classified into the following categories: motor disorders, pain, and seizures. Tumor type was classified as either primary or metastatic. Tumour location was subdivided into six categories: cerebellar hemisphere (CPA), frontal lobe, multiple, parietal lobe, sella-parasella, and temporal lobe. Comorbid diseases were classified into three categories: systemic malignancies, hypertension, and diabetes mellitus. Treatment factors included the management of the tumor and the type of drug used. The tumor

management was categorized into the following groups: conservative, operative, operative, and radiotherapy, and operative, chemotherapy, and radiotherapy. The drug type was categorized as follows: steroids and anti-seizure medications. Sleep quality was assessed using the Pittsburgh Sleep Questionnaire Index (PSQI) questionnaire and categorized as poor sleep quality (PSQI score of >5) and good sleep quality (PSQI score of ≤5). The data analysis included univariate analysis, which was conducted to ascertain the characteristics of the research subjects by presenting the frequency distribution of each variable under study. Bivariate analysis with the chi-square test was conducted to ascertain the relationship between categorical variables and sleep quality. Multivariate analysis with logistic regression identified the most influencing factor in sleep quality. A p-value of <0.05 was regarded as statistically significant

RESULT

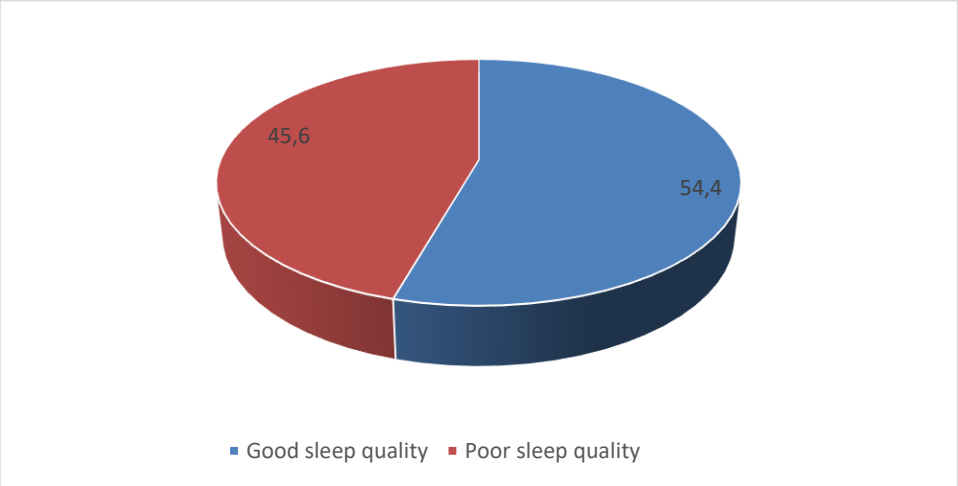
Table 1. Distribution of Sociodemographic and Clinical Factors in Brain Tumour Patients

Variable	Total	Percentage (%)
Age		
< 45 years old	25	36,8
≥ 45 years old	43	63,2
Sex		
Man	26	38,2
Woman	42	61,8
Comorbids		
Systemic malignancy		
Yes	18	26,5
No	50	73,5
Hypertension		
Yes	12	17,6
No	56	82,4
Diabetes Mellitus		
Yes	2	2,9
No	66	97,1
Clinical manifestation		
Motoric deficit		
Yes	63	92,6
No	5	7,4
Pain		
Yes	35	51,5
No	33	48,5
Seizure		
Yes	45	66.2
No	23	33.8
Types of Brain Tumours		
Primary tumor	50	73,5
- Meningioma	34	68,0
- Astrocytoma	13	26,0
- Glioblastoma Multiforme	2	4,0
- Ependymoma	1	2,0
Metastatic tumor	18	26,5
Tumour Location		
CPA	2	2,9
Frontal lobe	18	26,5
Multipel	18	26,5
Parietal lobe	9	13,2
Sella-Parasella	3	4,4
Temporal lobe	18	26,5

Table 2. Distribution of Treatment Factors in Brain Tumor Patients

Variabel	Total	Percentage (%)
Treament		
Surgery	52	76,5
Radiotherapy	42	61,8
Surgery + Radiotherapy	20	29,4
Surgery + Radiotherapy +	6	8,8
Drug		
Steroid		
Yes	24	35,3
No	44	64,7
Anti-seizure		
Yes	45	66,2
No	23	33,8
Painkiller		
Yes	34	50,0
No	34	50,0

Sixty-eight patients with brain tumors, aged ≥ 18 years, were selected consecutively. As shown in Table 1, the majority of subjects in this study were female (61.8%), with the highest age being ≥45 years (63.2%). In terms of clinical characteristics, the majority of subjects had primary brain tumors (73.5%), with the most common type being meningioma (68%). 26.5% of the study subjects had brain tumors located in the frontal, temporal, and multiple lobes. The majority of patients with brain tumors had clinical manifestations of motor dysfunction (92.6%). Most subjects had no comorbidities (55.9%) based on comorbidity characteristics. As shown in Table 2, most subjects in this study were treated surgically (76.5%). Overall, 66.2% of subjects received antiepileptic medication.



Graphics 1. Distribution of Sleep Quality Disorders In Brain Tumor Patients

Most subjects had good sleep quality (54.4%), and approximately 45.6% had poor sleep quality, as shown in Graphics 1.

Table 3. Bivariate Analysis of Sociodemographic and Clinical Factors on Sleep Quality in Brain Tumour Patients
*[a]Chi Square Test, *p < 0,05*

Variable	Poor Sleep Quality (≥5)		Good Sleep Quality (<5)		*p*	OR
	n	%	n	%		
Age						
< 45 years old	5	20,0	20	80,0		0.163
≥ 45 years old	26	60,5	17	39,5	0,001[a]*	
Sex					0,038[a]*	2,880
Man	16	61,5	10	38,5		
Woman	15	35,7	27	64,3		
Penyakit Komorbid						
Hypertension						
Yes	8	66,7	4	33,3	0,106[a]	2,870
No	23	41,1	33	58,9		
Diabetes Melitus						
Yes	1	50,0	1	50,0	0,117[a]	2,522
No	29	43,9	37	56,1		
Systemic malignancy						
Yes	13	72,2	5	27,8	0,008[a]*	4,622
No	18	36,0	32	64,0		
Clinical manifestation						
Motoric deficit						
Yes	30	47,6	33	52,4	0,233[a]	3,636
No	1	20,0	4	80,0		
Pain						
Yes	20	57,1	15	42,9	0,049[a]*	2,667
No	11	33,3	22	66,7		
Seizure						
Yes	21	46,7	24	53,3	0,803[a]	1,138
No	10	43,5	13	56,5		
Types of Brain Tumors						
Primary tumor	18	36,0	32	64,0	0,008[a]*	0,216
Metastatic tumor	13	72,2	5	27,8		
Tumor Location						
CPA	1	3,2	1	2,7	0,035[a]*	0,029
Frontal lobe	4	12,9	14	37,8		
Multiple	13	41,9	5	13,5		
Parietal lobe	6	19,4	3	8,1		
Sella-Parasella	1	3,2	2	5,4		
Temporal lobe	6	19,4	12	32,4		

Tables 3 and 4 show the bivariate analysis between sociodemographic, clinical, and treatment factors on sleep quality in brain tumor patients. The table shows that age, gender, comorbidities of cytological malignancy, clinical manifestations of pain, type of brain tumor, tumor location, surgical management, radiotherapy management, and steroid drugs have a significant relationship with sleep quality in brain tumor patients with *p*-value <0.05.

All variables with p< 0.25 A multivariate analysis was performed to determine which variables significantly influenced sleep quality in patients with brain tumors. Age, sex, hypertension, diabetes mellitus, systemic malignancy, motor symptoms, pain, type and location of brain tumor, surgical management, radiotherapy management, combined surgical management, radiotherapy and chemotherapy, steroids, and analgesics were variables that qualified for multivariate logistic regression analysis. The variables significantly associated with poor sleep quality in brain tumor

patients were age and radiotherapy management. Age had the strongest association with poor sleep quality in brain tumor patient

Table 4. Bivariate Analysis of Treatment Factors on Sleep Quality in Brain Tumour Patients

Variable	Poor Sleep Quality (>5)		Good Sleep Quality (<5)		*p*	OR
	n	%	n	%		
Treatment						
Surgery	19	36,5	33	63,5	0,007[a]*	0,192
No surgery	12	75,0	4	25,0		
Radiotherapy	26	61,9	16	38,1		
No Radiotherapy	5	19,2	21	80,8	0,001[a]*	6,825
Surgery + Radiotherapy	9	45,0	11	55,0	0,950[a]	0,967
None	22	45,8	26	54,2		
Surgery + Radiotherapy + chemotherapy	5	83,3	1	16,7	0,052[a]	6,923
None	26	41,9	36	58,1		
Drugs						
Steroid						
Yes	16	66,7	8	33,3	0,010[a]*	3,867
No	15	34,1	29	65,9		
Anti-seizure						
Yes	21	46,7	24	53,3	0,803[a]	1,138
No	10	43,5	13	56,5		
Pain killer						
Yes	19	55,9	15	44,1	0,088[a]	2,322
No	12	35,3	22	64,7		

*Chi-Square Test, *p < 0,05*

DISCUSSION

This analytical observational study aims to determine the factors that affect sleep quality in patients with brain tumors. About 45.6% of subjects in this study experienced poor sleep quality. Astri et al., Lin et al., and Wilis et al. reported that most brain tumor patients experienced poor sleep quality.[1,5,6] Most subjects in this study were ≥ 45 years old and female. Astri et al. reported that most study subjects were ≥ 45 years old and female (65%).[1] This study showed a significant relationship between age and gender on the sleep quality of brain tumor patients. Silva et al.'s study reported similar findings that female gender and advanced age were associated with poor sleep quality in tumor patients.[8] This is not in line with Jeon et al., who reported that age and gender were not related to the sleep quality of brain tumor patients.[7] In women, there are fluctuations in estrogen and progesterone, which affect changes in sleep architecture.

In this study, over half of the participants reported experiencing pain. The bivariate analysis revealed a statistically significant correlation between pain and sleep quality. Similarly, Jeon et al. reported a significant relationship between the clinical manifestations of pain. Tumors in the brain increase intracranial pressure, which causes pain that can affect sleep quality. The majority of subjects in this study had primary brain tumors located in the frontal lobe, temporal lobe, or multiple brain tumors. The bivariate analysis demonstrated a statistically significant correlation between tumor type and tumor location and the incidence of sleep quality disorders. This result is consistent with the findings of the Day et al. study, which reported that sleep disturbances were prevalent among primary brain tumor patients.[1]. Similarly, Astri et al. observed that frontal lobe,

inter-suprasellar, and temporal lobe tumors were associated with sleep quality due to their role in regulating the sleep-wake cycle.[9–11]

Furthermore, the majority of brain tumor patients who underwent operative treatment or radiotherapy experienced poor sleep quality. Bivariate analysis demonstrated a statistically significant correlation between tumour management, specifically surgical and/or radiotherapeutic procedures, and the prevalence of sleep disturbances. Huang et al. reported that in patients with brain tumors, sleep quality declined after two years postoperatively in 73% of cases. As reported by Powell et al., over 90% of patients with primary brain tumours undergoing cranial radiation therapy experienced poor sleep quality. Operative procedures can result complications such as damage to brain parenchyma, which may lead to the release of inflammatory mediators and other substances that can impact sleep quality.[16] Radiotherapy to the brain can also cause inflammation, potentially triggering an immunomodulatory response that results in abnormal melatonin production. Abnormal melatonin secretion has been associated with excessive daytime sleepiness.[17]

Steroids have been found to have a significant relationship with sleep quality. Lin et al. [5] reported similar results, indicating that steroid use significantly correlates with sleep quality. Wang et al. [17] observed that repeated cortisone injections lengthened sleep latency, reduced sleep duration, and inhibited REM sleep in mice. Glucocorticoids that have receptors in the HPA axis will suppress ventrolateral preoptic nuclei (VLPO), so that it will interfere with the initiation of the NREM phase.[13]

Multivariate analysis shows that age has the most substantial relationship to the incidence of sleep quality disorders in patients with brain tumors. In the general population, Ohayon et al found that sleep disorders were experienced by 50% of subjects over the age of 65. [18] Mainio et al's research, which also conducted a study on brain tumour patients, found The mean age of patients experiencing sleep disorders was found to be 46.9 + 12.1 years.[19] Sleep architecture also changes with age. Up to the age of 60 years, the percentage of N3 sleep decreases linearly at 2% per decade. The percentage of REM sleep also diminishes, although the decline is more subtle. As with N3, the percentage of REM sleep appears to plateau after age 60. The net result of these changes is an increase in N1 and N2. In addition, sleep efficiency continues to decline due to increased sleep latency, arousals from sleep and time awake after sleep onset; however, the mechanisms responsible for these changes in sleep architecture are unclear. Although it has been postulated that these changes reflect age-related reduction in EEG amplitude produced by the increase in electrical impedance of the skull and scalp, they are more likely a reflection of age-related neural degeneration and changes in hormonal systems.[20]

CONCLUSION

Age, gender, systemic malignancies, pain, type of primary brain tumor, tumor location, operative treatment, radiotherapy, and steroids influence the quality of sleep in patients with brain tumors. However, age has the most decisive influence on sleep quality.

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