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Original Research

Incidence and Clinical Characteristics of Brain Metastases at Wahidin Sudirohusodo and Hasanuddin University Hospitals, Makassar, Indonesia: An 11-Year Retrospective Study

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Introduction: Brain metastases (BM) are the most frequent intracranial tumors in adults, yet epidemiological data remain limited in Indonesia. This study aimed to describe the incidence, clinical presentation, and management patterns of BM over an 11-year period at two tertiary referral hospitals in South Sulawesi, Indonesia.

Materials and Methods: This retrospective multi-center study included patients diagnosed with BM at Dr. Wahidin Sudirohusodo Hospital and Hasanuddin University Hospital in Makassar, Indonesia, from 2013 to 2024. Patients were included if they had radiologically confirmed BM (CT or MRI) and histologically verified primary malignancies. Data on demographics, clinical symptoms, lesion number and location, primary tumor origin, treatment modalities, and mortality outcomes were extracted from medical records. Statistical analyses included descriptive summaries and chi-square test to explore associations between clinical variables and outcomes.

Results: Of 248 patients, most were female (55.2%) and aged 46–65 years (64.5%). Most patients presented with a single lesion (74.6%), predominantly in the parietal lobe (20.6%). Headache was the most common presenting symptom (50.4%). Lung (48.4%) and breast carcinoma (27.0%) were the leading primary malignancies. Conservative management was the predominant treatment (53.6%), followed by chemotherapy (40.7%), while surgical and radiotherapeutic interventions were infrequent. Mortality was higher in patients receiving conservative therapy (59.4%, $p = 0.028$) and those with multiple lesions (66.1%, $p = 0.042$).

Conclusion: BM in our cohort were predominantly associated with lung and breast malignancies and most frequently presented as single lesions in middle-aged adults. The high reliance on conservative management reflects both late-stage presentation and limited access to advanced neuro-oncologic interventions. These findings highlight the need for early detection, expanded therapeutic capacity, and multidisciplinary care to improve outcomes for patients with BM in resource-limited settings.

Introduction

Brain metastases (BM) are the most frequent intracranial tumors in adults, affecting approximately 10–30% of adult cancer patients and 6–10% of pediatric cases [1]. Advances in systemic cancer therapy and neuroimaging have prolonged survival, thereby increasing the incidence of secondary brain involvement. Global estimates suggest that up to 20–40% of patients with systemic malignancy eventually develop BM, most commonly originating from lung, breast, and melanoma primaries [2, 3].

In recent decades, significant advances in BM detection and treatment have reshaped patient outcomes.

High-resolution magnetic resonance imaging (MRI) and positron emission tomography (PET) now enable early detection of smaller or asymptomatic lesions [4-6]. Meanwhile, therapeutic progress including stereotactic radiosurgery (SRS), targeted molecular therapies, and immune checkpoint inhibitors has substantially extended survival for selected patients [7, 8]. Despite these global improvements, data from Indonesia remain limited, underscoring the need for comprehensive local epidemiological studies to inform clinical decision-making and healthcare planning.

However, in Asia particularly in Indonesia data on BM remain scarce. Reports from Malaysia indicate that BM account for approximately 25.2% of intracranial tumors, with lung carcinoma being the predominant primary source, followed by breast and thyroid cancers [9]. A study from the Philippines reported that BM comprised 6.5% of all brain tumors [10]. A single-center study from Indonesia found that the primary tumors most commonly associated with BM were lung (36.5%), breast (34.2%), and gynecological malignancies (9%) [11]. Variability in reported incidence has been noted across Malaysia, the Philippines, and Indonesia, largely reflecting differences in diagnostic resources and cancer screening programs. Overall, most Indonesian studies remain limited to small, single-center case series, lacking systematic analysis and long-term follow-up.

Despite these regional findings, Indonesia lacks comprehensive institutional or population-based data on BM. Most local publications are small, single-center reports focused on clinical case descriptions rather than systematic epidemiological analysis. This scarcity of data hinders accurate estimation of disease burden and limits the development of evidence-based neuro- oncology policies. The present study addresses this gap by examining the incidence and clinical characteristics of patients with BM treated at two major tertiary referral hospitals in Indonesia. By analyzing demographic, radiological, and treatment-related variables over an 11-year period, this study aims to establish foundational local evidence to support future healthcare planning and improve access to multidisciplinary neuro-oncologic care.

Materials and Methods

Study Design and Setting

This retrospective, descriptive study was conducted at Dr. Wahidin Sudirohusodo Hospital and Hasanuddin University Hospital, two tertiary referral centers in Makassar, Indonesia, which function as regional hubs for neuro-oncology and multidisciplinary cancer care.

Study Population

All patients diagnosed with BM between January 2013 and December 2024 were eligible. Inclusion criteria were:

1. Radiologically confirmed BM by computed tomography (CT) or MRI.

2. Histopathological confirmation of the primary tumor.

3. Complete medical records containing demographic

data, clinical presentation, imaging findings, treatment,and outcomes.

Patients with incomplete records, unconfirmed primary tumors, or primary brain tumors were excluded.

Data Collection

Data were collected using a consecutive sampling method from hospital medical record databases. Extracted variables included age, sex, clinical symptoms, number and location of brain lesions, primary tumor origin, treatment modality (conservative, chemotherapy, radiotherapy, surgery, or combined therapy), and mortality status.

Diagnostic Confirmation

BM were diagnosed based on neuroimaging findings obtained through CT or MRI. MRI was preferred when available, particularly for cases with inconclusive CT results or small suspected lesions. Each diagnosis was confirmed by at least two board-certified radiologists experienced in neuro-oncology imaging. Typical diagnostic features included ring-enhancing lesions with perilesional edema, mass effect, and location consistent with metastatic distribution patterns.

Primary tumors were verified by histopathological examination of biopsy or surgical specimens from extracranial sites. For cases where biopsy was not feasible, diagnosis was supported by characteristic radiological findings and strong clinical correlation with a known systemic malignancy.

Definition of Lesion Categories

BM were categorized based on the number of discrete metastatic foci observed on neuroimaging. A single lesion was defined as one distinct intracranial metastatic focus detected on contrast-enhanced CT or MRI, regardless of its size or anatomical location. In contrast, multiple lesions referred to the presence of two or more anatomically separate metastatic deposits within the brain parenchyma identified during the same imaging session. Lesions separated by sulci or located in different cerebral lobes were considered distinct foci, ensuring consistency with established neuro-oncological imaging criteria.

Clinical Variable Definitions

Neurological symptoms including headache, motor weakness, altered consciousness, seizures, and visual disturbances were defined as presenting complaints occurring concurrently with radiologically confirmed BM. Conservative management encompassed symptomatic and palliative measures administered without surgical or radiotherapeutic intervention, such as corticosteroid therapy, anticonvulsant medication, and general supportive care. Mortality outcomes were classified as in-hospital death (occurring during active inpatient treatment) or outpatient death

(recorded after discharge during follow-up).

Diagnostic Approach and Standardization

Diagnostic imaging was performed using institutional protocols aligned with the American College of Radiology (ACR) and European Association of Neuro- Oncology (EANO) recommendations. MRI sequences typically included T1-weighted pre- and post-contrast, T2-weighted, and FLAIR images. CT scans were obtained with intravenous contrast and 5-mm slice thickness. Imaging data were cross-validated between Wahidin Sudirohusodo and Hasanuddin University Hospitals to ensure consistency.

Data Integrity and Missing Data Management

All extracted data were verified by two independent reviewers. Missing variables were cross-checked using both electronic and archived paper records. When essential information (e.g., primary tumor confirmation, imaging findings) remained unavailable after verification, the case was excluded from final analysis.

Minor missing demographic or treatment data were handled through pairwise deletion to preserve statistical validity. Potential misclassification bias particularly regarding lesion number and tumor origin was minimized by requiring dual verification from both radiology and pathology reports.

Data Analysis

All data were coded, cleaned, and organized using Microsoft Excel (version 2019; Microsoft Corp., Redmond, WA, USA) before being exported for statistical analysis in IBM SPSS Statistics (version 26; IBM Corp., Armonk, NY, USA). Descriptive statistics were used to summarize demographic, clinical, imaging, and treatment variables. Categorical data were expressed as frequencies and percentages.

Although the study was primarily descriptive, exploratory comparative analyses were performed to identify potential associations between key subgroups. Chi-square tests were applied to examine relationships between categorical variables such as sex, age group, primary tumor origin, number of lesions, and treatment modality. Independent-sample t-tests were used for continuous variables when assumptions of normality were met. A two-tailed p value of <0.05 was considered statistically significant.

Results

A total of 248 patients with BM were included in this study (Table 1).

Variables		n (%)	Missing data (n, %)
Sex			0 (0.0)
	Male	111 (44.8)	
	Female	137 (55.2)	
Age groups (years)			0 (0.0)
	12–25	3 (1.2)	
	26–45	51 (20.6)	
	46-65	160 (64.5)	

	>65	33 (13.3)	
Number of lesions			0 (0.0)
	Single	185 (74.6)	
	Multiple	63 (25.4)	
Clinical symptoms			0 (0.0)
	Headache	125 (50.4)	
	Decreased consciousness	45 (18.1)	
	Neurological deficit	37 (14.9)	
	Dyspnea	7 (2.8)	
	Seizures	7 (2.8)	
	Visual disturbance	3 (1.2)	
	Others	24 (9.6)	
Tumor Location			0 (0.0)
	Parietal lobe	51 (20.6)	
	Occipital lobe	31 (12.5)	
	Frontal lobe	29 (11.7)	
	Temporal lobe	28 (11.3)	
	Cerebellum	19 (7.7)	
	>2 regions	90 (36.2)	
Primary tumor origin			0 (0.0)
	Lung	120 (48.4)	
	Breast	67 (27)	
	Head and neck	10 (4)	
	Intestinal	10 (4)	
	Lymphoma	5 (2)	
	Others	36 (21.7)	
Treatment Modality			0 (0.0)
	Conservative management	133 (53.6)	
	Chemotherapy	101 (40.7)	
	Chemoradiation	4 (1.6)	
	Surgery	9 (3.6)	
	Radiotherapy only	1 (0.4)	
Mortality rate			3 (1.2)*
	Outpatient death	134 (54.0)	
	In-hospital death	111 (44.8)	

Table 1. Characteristics of Patients with Brain Metastases (n = 248).

Note: * Missing due to unrecorded outpatient outcome.

Females constituted a slight majority (55.2%), and the predominant age group was 46–65 years (64.5%), consistent with the typical onset period for solid- organ malignancies. Most patients presented with a single metastatic lesion (74.6%), and the parietal lobe (20.6%) was the most common site of intracranial involvement.

Headache was the leading clinical presentation (50.4%), followed by decreased consciousness (18.1%) and focal neurological deficits (14.9%). Less frequent symptoms included seizures, dyspnea, and visual disturbances. Lung carcinoma (48.4%) and breast carcinoma (27.0%) were the predominant primary tumor origins, mirroring global trends in BM etiology.

Regarding management, conservative treatment primarily corticosteroids, anticonvulsants, and supportive care was administered to more than half of the cohort (53.6%), while chemotherapy was

used in 40.7% of cases. Surgical and radiotherapeutic interventions were infrequently performed.

Mortality analysis (Table 2) revealed that patients receiving conservative management had the highest death rate (59.4%, p = 0.028), followed by those treated with chemotherapy (49.5%).

Variable		Deaths (n)	Mortality Rate (%)	p-value*
Treatment Modality				0.028
	Conservative management	79	59.4	
	Chemotherapy	50	49.5	
	Chemoradiation	2	50	
	Surgery	3	33.3	
	Radiotherapy only	0	0	
Primary Tumor Origin				0.067
	Lung	69	57.5	
	Breast	30	44.8	
	Head and neck	6	60	
	Intestinal	6	60	
	Lymphoma	2	40	
	Others	18	54.5	
Number of Lesions				0.042
	Single	92	50.3	
	Multiple	41	66.1	

Table 2. Mortality Stratified by Treatment Modality, Primary Tumor Site, and Lesion Number (n = 245).

Note, *Chi-square test

Mortality was also higher in patients with multiple lesions (66.1%, p = 0.042) compared with those with single lesions (50.3%). Although mortality varied by primary tumor origin, the difference was not statistically significant (p = 0.067).

Discussion

This study provides an overview of the demographic, clinical, and pathological characteristics of patients with BM treated at two tertiary referral hospitals in Indonesia over an 11-year period. The findings highlight several similarities and differences compared with global trends in BM epidemiology.

BM were most frequently observed in females aged 46–65 years. These results align with previous reports that indicate BM are most common in individuals aged 50–70 years, coinciding with peak incidence of primary malignancies such as lung and breast cancer [12]. Although some literature reports male predominance due to higher smoking rates and lung cancer incidence [13, 14], our findings suggest that gender distribution may vary depending on the primary cancer profile of the population.

Headache was the predominant clinical presentation, consistent with global data indicating that increased intracranial pressure is a frequent early manifestation of BM. Other neurological symptoms, including decreased consciousness, paralysis, and seizures, were also observed but at lower frequencies. Interestingly, single brain lesions were more prevalent than multiple lesions in this cohort, differing from MRI-based studies that report multiple metastases in up to two-thirds of patients [15]. This discrepancy may reflect limited MRI availability, late-stage presentation, or

under-detection of micrometastases on CT imaging, which was the predominant diagnostic tool during earlier study years. The parietal lobe was the most frequent metastatic site, consistent with reports of preferential metastasis to regions of high cerebral blood flow [16, 17]. Lung carcinoma remained the leading primary source of BM, followed by breast carcinoma, in agreement with global trends [16].

To ensure reproducibility, our study explicitly defined diagnostic and clinical parameters. The operational definitions of “single” and “multiple” lesions adhered to conventional neuro-oncology imaging standards, improving comparability with other regional and international studies [7, 18]. The diagnostic protocol requiring both radiologic confirmation and histopathologic verification of primary malignancy minimized misclassification bias and strengthened the internal validity of the findings.

The predominance of conservative management in this cohort requires contextual interpretation within the framework of Indonesia’s oncology practice and healthcare system. International guidelines, including those from the European Association of Neuro-Oncology (EANO) and the National Comprehensive Cancer Network (NCCN), recommend surgical resection or SRS for patients with limited BM and good performance status [19-21]. However, these modalities were not consistently available in either institution during the study period. Many patients presented with advanced disease, multiple metastases, or poor performance status, precluding aggressive local interventions. Furthermore, comorbidities such as cardiopulmonary compromise and late neurological deterioration limited surgical eligibility. Systemic factors including radiotherapy infrastructure constraints, limited neurosurgical capacity, and financial barriers further contributed to the high reliance on conservative treatment. Comparable trends have been reported in other low- and middle-income countries, where treatment decisions often prioritize palliative intent over curative approaches.

Financial and logistical barriers also influenced therapeutic choices. Under Indonesia’s universal health coverage scheme (JKN), advanced neuro-oncologic procedures remain centralized in urban tertiary hospitals, resulting in referral delays and unequal access to specialized care. Consequently, many patients presented in late stages or with comorbidities that precluded surgical or radiosurgical intervention, making conservative therapy the most feasible option within existing infrastructure. These findings underscore how both clinical and systemic constraints shape treatment outcomes, reflecting the broader challenges of neuro-oncology care in middle-income settings.

Potential confounding factors must also be acknowledged. Variations in primary tumor biology, comorbidities, and treatment accessibility likely affected both clinical presentation and survival outcomes. Lung cancer–related BM generally progress more aggressively and carry poorer prognoses than breast cancer–derived lesions, which may explain differences in mortality rates across subgroups. As a retrospective study, reliance on medical records introduces the risk of information bias due to incomplete documentation of symptoms, treatments, or follow-up data. Misclassification of lesion type or cause of death may have occurred in cases with limited imaging or unavailable histopathologic verification. Although such limitations are inherent to retrospective designs, systematic data checking and standardized variable definitions were applied to minimize bias and enhance validity.

Despite its contributions, this study has several methodological limitations. Restricted MRI access, especially in earlier years, may have led to underdiagnosis of small or asymptomatic metastases. Contrast-enhanced CT, though more accessible, provides lower sensitivity for detecting micrometastases and posterior fossa involvement. Additionally, the absence of molecular profiling prevented the analysis of subtype-specific metastatic patterns particularly relevant for lung and breast cancers, where mutations such as EGFR, ALK, and HER2 significantly influence disease behavior and treatment response. As a hospital-based retrospective cohort, selection bias is also possible, as patients referred to tertiary centers typically present with advanced or symptomatic

disease, limiting generalizability to the broader Indonesian cancer population.

Future research should prioritize prospective multicenter studies with standardized imaging protocols and molecular profiling to provide a more comprehensive understanding of BM in Indonesia. Expanding MRI and biomarker testing access across regional hospitals would facilitate earlier detection and enable personalized treatment strategies. Integrating neuroimaging data with national cancer registries would also reduce selection bias and improve the accuracy of epidemiological surveillance, supporting evidence-based policy development and equitable neuro-oncology care nationwide.

In conclusion, BM remain a substantial clinical challenge in low- and middle-income healthcare settings. The predominance of conservative management in this cohort underscores both limited access to advanced neuro-oncologic interventions and the frequent late-stage presentation at diagnosis. To improve patient outcomes, national strategies should prioritize early detection, expansion of radiotherapy and neurosurgical capacity, and integration of multidisciplinary tumor boards into routine oncology care. Incorporating molecular diagnostics and survival analyses into future prospective studies will further elucidate prognostic determinants and inform the development of evidence-based management guidelines for BM in Indonesia.

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Declarations

Clinical trial registration

Not applicable

Conflicts of interest/Competing interests

Authors declare that they have no conflicts of interest.

Availability of data and material

The data sets used and/or analyzed during the current study are available from the corresponding authors per reasonable request.

Authors' contributions

DW contributed to the conception, design, and final drafting of the manuscript. KJS, NH and JO contributed to data collection. DW, KJS, NH, JO, and MF contributed to the primary drafting of the manuscript. DW supervised the study. All authors approved the final version for submission.

Ethics approval

This study was approved by the Ethics Committees of Dr. Wahidin Sudirohusodo Hospital and Hasanuddin University Hospital, South Sulawesi, Makassar, Indonesia, in accordance with

institutional guidelines and the Declaration of Helsinki.

Consent to participate

Written informed consent was obtained from all participants, and the trial was conducted in accordance with the Declaration of Helsinki.

Consent for publication

Written informed consent was obtained from all participants, and the trial was conducted in accordance with the Declaration of Helsinki.

Declaration on generative AI and AI-assisted technologies in the writing process

None.

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