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ORIGINAL RESEARCH

IMPACT OF BODY MASS INDEX ON PAIN SEVERITY IN LUMBAR FACET ARTHROPATHY: AN OBSERVATIONAL STUDY

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Abstract

Background: Lumbar facet arthropathy is a common cause of chronic low back pain (LBP), with increasing evidence suggesting a link between obesity and pain severity. However, the relationship between body mass index (BMI) and pain intensity in facet-mediated LBP remains underexplored.

Methods: A cross-sectional study was conducted on 50 patients aged 40–70 with clinically diagnosed lumbar facet arthropathy at Siloam General Hospital Lippo Village between February and June 2022. BMI was calculated and categorised per the WHO Asia-Pacific criteria. Pain severity was measured using the Numerical Rating Scale (NRS). Associations between BMI and pain severity were analysed using Chi-square or Fisher's exact tests.

Results: Most patients were female (52%) and aged 51–60 years (42%). Obesity was prevalent (46%), and 54% of participants experienced severe pain. A significant association was found between higher BMI and pain severity ($p = 0.004$), with overweight or obese patients having 8.73 times higher odds (95% CI: 2.04–37.30) of reporting severe pain compared to those with normal or underweight BMI.

Discussion: These findings suggest a strong relationship between elevated BMI and increased pain severity in lumbar facet arthropathy. Potential mechanisms include increased mechanical loading and systemic inflammation mediated by adipokines.

Conclusion: Higher BMI is significantly associated with greater pain severity in patients with lumbar facet arthropathy.

Keywords: Lumbar facet arthropathy, low back pain, BMI, obesity, pain severity, facet joint degeneration, numeric rating scale.

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Introduction

Low back pain (LBP) is one of the most prevalent musculoskeletal disorders globally, with epidemiological studies indicating that approximately 80% of individuals will experience at least one episode of LBP during their lifetime. [1,2]. It stands as a leading cause of disability worldwide and imposes a substantial

socioeconomic burden due to increased healthcare utilisation, work absenteeism, and decreased productivity[3–5].

Low back pain (LBP) is one of the most prevalent musculoskeletal disorders globally, with epidemiological studies indicating that approximately 80% of individuals will experience at least one episode of LBP during their lifetime. [1,2]. It stands as a leading cause of disability worldwide and imposes a substantial socioeconomic burden due to increased healthcare utilisation, work absenteeism, and decreased productivity[3–5].

Facet joint arthropathy accounts for approximately 15% to 41% of chronic low back pain cases [6]. Lumbar facet joints, also known as zygapophysial joints, are paired synovial articulations between one vertebra's inferior articular process and the vertebra's superior articular process below. These joints are critical in maintaining segmental spinal stability, limiting excessive motion, and supporting controlled flexion, extension, and axial rotation. Facet-mediated pain arises when the facet joints undergo degenerative changes or inflammation, a condition clinically termed lumbar facet arthropathy [7,8]. Structural deterioration typically begins with cartilage degradation and progresses to joint space narrowing, subchondral bone sclerosis, osteophyte formation, and synovial hypertrophy [9]. Clinically, lumbar facet arthropathy presents as localised paraspinal pain typically worsened by lumbar extension and rotation, but usually occurs without significant neurological deficits. Radiological findings may support diagnosis through evidence of joint degeneration, although confirmation is optimally achieved via intra-articular injections [10,11].

Obesity, commonly assessed using body mass index (BMI), is a well-established risk factor for various musculoskeletal disorders, including osteoarthritis, intervertebral disc disease, sacroiliac joint dysfunction, piriformis syndrome, and other forms of non-specific low back pain[12–17]. BMI, a commonly used proxy for body fat composition, is classified by the World Health Organization (WHO) into underweight, normal, overweight, and obese[18]. Numerous studies have established a correlation between elevated BMI and increased mechanical loading on spinal structures, contributing to accelerated wear of the facet joints[19]. Additionally, adipose tissue functions as an active endocrine organ, producing pro-inflammatory cytokines such as interleukin-6 (IL-6), tumour necrosis factor-alpha (TNF-α), and leptin, which may further exacerbate joint inflammation and pain sensitivity [20,21].

While previous studies have shown a positive correlation between elevated BMI and low back pain severity [22,23], the specific link between BMI and pain intensity in patients with lumbar facet arthropathy remains insufficiently explored. Although low back pain is a multifactorial condition influenced by various factors, including physical activity, metabolic status, and fat distribution, this study focuses explicitly on BMI for several reasons. First, BMI remains the most widely used and accessible anthropometric indicator in clinical and epidemiological settings, offering a simple, reproducible, and cost-effective measure of obesity[24]. Second, while factors such as

visceral fat or metabolic conditions (e.g., insulin resistance) are known to influence systemic inflammation and pain modulation [25–27], these factors require advanced imaging techniques or laboratory evaluations, which are not routinely available in observational studies or resource-limited settings. Given the pathophysiological plausibility and increasing prevalence of obesity, understanding this relationship is critical for optimising clinical management and informing preventive strategies.

Materials and Methods

Fifty patients from the outpatient department at Siloam General Hospital Lippo Village were enrolled in this cross-sectional study between February and June 2022. The sample recruitment was done using a non-probability purposive sampling technique. All participants were aged between 40 and 70 years and were clinically diagnosed with lumbar facet arthropathy based on history, physical examination, and clinical judgment by a neurologist. The diagnostic criteria required the presence of at least three out of four clinical features suggestive of facet-mediated pain: (1) localized pain over the lumbar vertebral region, (2) tenderness upon palpation, (3) referred pain to the thigh or lower extremity, and (4) pain exacerbated by lumbar extension and rotation but relieved by flexion. We excluded patients with a history of spinal trauma, spinal deformities, or those who did not consent to participate in the study.

After obtaining informed consent, participants were asked to complete a structured form, which included demographic information such as age, sex, height, weight, and BMI calculation. Pain severity, as the primary dependent variable, was measured using the Numerical Rating Scale (NRS), with pain levels categorised as mild (1–3), moderate (4–6), and severe (7–10)[28,29]. The independent variable in this study was BMI derived from self-reported height and weight, and classified based on the World Health Organization (WHO) Asia-Pacific guidelines, with the following cutoffs: underweight (<18.5 kg/m²), normal (18.5–22.9 kg/m²), overweight (23.0–24.9 kg/m²), obese I (25.0–29.9 kg/m²), and obese II (≥30.0 kg/m²)[18].

The collected data were entered and tabulated using Microsoft Excel 2013 and analysed with IBM SPSS Statistics version 24. The association between pain severity and BMI was examined using Chi-square or Fisher's exact test, depending on the distribution of expected values. Statistical significance was considered at $p < 0.05$. Descriptive statistics were used to summarise the demographic data.

This study adhered to established ethical principles and received approval from the Faculty of Medicine Ethics Committee, Pelita Harapan University. All participants were fully informed about the study's objectives, procedures, and potential benefits prior to enrollment. Written informed consent was obtained from each participant, confirming their voluntary agreement to participate in the study.

Results

This study included 50 participants with lumbar facet atrophy, most of whom were female (Table 1). The majority of

patients (42%) were in the 51–60 age group, followed by the 61–70 age group (32%) and the 40–50 age group (26%). The highest proportion of participants was categorised as obese (46%), while 24% were overweight, 28% had normal BMI, and only one patient (2%) was underweight. Pain severity was dominated by the severe category, with 27 patients (54%) experiencing severe pain, while 20 patients (40%) reported moderate pain, and only three patients (6%) had mild pain.

A strong association was observed between BMI and pain severity. Among patients with severe pain, the majority (89%) were overweight or obese, while only 11% had a normal or underweight BMI. Conversely, in the mild to moderate pain group, 52% had normal or underweight BMI, and 48% were overweight or obese. This association was statistically significant (p = 0.004), with overweight or obese patients having 8.73 times higher odds (95% CI: 2.04–37.30) of experiencing severe pain compared to those with normal or underweight BMI (Table 2).

Discussion

This study aimed to examine the association between BMI and pain severity in patients diagnosed with lumbar facet arthropathy. Among 50 patients, the majority were in the 51–60 age group (42%) with a near-equal gender distribution. Most notably, 46% of patients were classified as obese, and 54% experienced severe pain. A significant association was found between higher BMI (overweight/obese) and severe pain (p = 0.004), with an odds ratio of 8.73 (95% CI: 2.04–37.30), indicating that individuals with elevated BMI were over eight times more likely to report severe pain than those with normal or underweight BMI. These findings are consistent with prior research demonstrating that obesity and elevated BMI are strongly associated with increased prevalence and severity of low back pain, including facet-mediated pain[15,19,23,30].

Table 1. Demographic Characteristics of Patients with Lumbar Facet Arthropathy

Subject characteristics	N (50 patients)
Age Group (years)	
40-50	13 (26 %)
51-60	21 (42 %)
61-70	16 (32 %)
Gender	
Male	24 (48 %)
Female	26 (52 %)
BMI Category	
Underweight	1 (2 %)
Normal	14 (28 %)
Overweight	12 (24 %)
Obese	23 (46 %)
Pain Severity	
Mild (NRS 1-3)	3 (6 %)
Moderate (NRS 4-6)	20 (40 %)
Severe (NRS 7-10)	27 (54 %)

Table 2. Association Between BMI Categories and Pain Severity in Patients with Lumbar Facet Arthropathy

Subject characteristics	Pain Severity		p-value	OR [95 % CI]
	Mild/ Moderate (n=23)	Severe (n=27)		
BMI Category				
Under-weight/ Normal	12 (52%)	3 (11%)	0.004	8.73 [2.04 - 37.30]
Overweight/ Obese	11 (48%)	24 (89%)		

Supporting this, a study by Suri et al. showed that higher BMI is significantly associated with a greater risk of developing

moderate facet joint osteoarthritis, particularly among individuals classified as overweight or obese.

Moreover, Suri et al. also reported that each 1-unit increase in BMI (kg/m²) was associated with an 8% increase in the risk of moderate facet joint osteoarthritis, suggesting that even small BMI increments can meaningfully contribute to progressive facet joint degeneration[31]. A prior study conducted by Kalichman et al. demonstrated that among 187 randomly selected individuals, those classified as obese based on BMI had a significantly higher prevalence of facet joint arthritis (odds ratio 2.8 [1.1–7.2])[32]. A similar finding was reported by Higgins et al., who analysed data from 1,759,338 individuals with musculoskeletal disorders and found that higher BMI (particularly >27 kg/m²) was significantly associated with increased odds of musculoskeletal pain severity, including low back pain cases[33].

The pathophysiological mechanisms underlying this association are multifactorial. From a biomechanical perspective, excess body weight imposes greater axial loading on the lumbar spine, particularly on the facet joints, accelerating joint degeneration through repetitive stress and microtrauma[7,19,31]. Over time, this stress induces cartilage wear, osteophyte formation, and joint space narrowing, all contributing to pain generation. Beyond mechanical loading, obesity is also associated with systemic inflammation due to the increased secretion of pro-inflammatory cytokines such as TNF-α and IL-6 from adipose tissue [20,21]. These cytokines not only exacerbate local inflammation within the facet joints but also promote central and peripheral sensitisation, which amplifies pain perception and lowers the pain threshold.

These findings highlight the importance of incorporating weight management into the treatment paradigm for lumbar facet arthropathy. Interventions targeting BMI reduction may result in pain reduction, particularly when combined with other conservative or interventional treatments. Addressing obesity targets the mechanical load on the facet joints and may also reduce systemic inflammation that contributes to pain sensitisation.

Several limitations of this study should be acknowledged. First, the cross-sectional design precludes the ability to establish causal relationships between BMI and pain severity; longitudinal studies are needed to clarify this temporal association. Second, the study was conducted during the COVID-19 pandemic, limiting in-person data collection opportunities. Consequently, some patient information had to be obtained indirectly through clinicians, potentially introducing reporting bias and reducing the accuracy of clinical assessments. Third, this study did not analyse the relationship between pain severity and potential confounding variables such as psychosocial stressors, physical activity levels, or comorbid conditions like diabetes or depression, all of which may influence pain perception or interact with BMI. Future research with larger sample sizes should incorporate these variables into multivariate models to better adjust for potential confounding factors.

Conclusion

This study demonstrates a significant association between elevated body mass index and increased pain severity in patients with lumbar facet arthropathy. Individuals classified as overweight or obese were over eight times more likely to report severe pain compared to those with normal or low BMI, reinforcing the role of excess weight in exacerbating facet joint pathology. The underlying mechanisms likely involve biomechanical stress on spinal structures and systemic inflammation mediated by adipose-derived cytokines. These findings highlight the clinical relevance of incorporating weight management strategies into the multidisciplinary care of patients with lumbar facet arthropathy.

Conflict of Interest

The authors declared no conflict of interest.

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ORIGINAL RESEARCH

THE RELATIONSHIP BETWEEN STROKE SUBTYPES AND COGNITIVE FUNCTION IN ISCHEMIC STROKE PATIENTS AT SILOAM HOSPITAL LIPPO VILLAGE

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Abstract

Introduction: Stroke is the second leading cause of death and a major cause of disability worldwide, including in Indonesia, and has an impact on cognitive function. Stroke can be classified based on the Bamford system into: Lacunar Infarct (LACI), Partial Anterior Circulation Infarct (PACI), Posterior Circulation Infarct (POCI), and Total Anterior Circulation Infarct (TACI), each with distinct clinical characteristics and lesion locations. This study aims to analyze the relationship between stroke subtypes and cognitive function in ischemic stroke patients using the MoCA- Ina questionnaire, to understand the clinical symptom differences and predict anatomical lesion sites in ischemic stroke subtypes based on the Bamford classification.

Methods: This was a cross-sectional analytical study involving 40 ischemic stroke patients. Data were collected using the MoCA-Ina questionnaire to assess the cognitive function of ischemic stroke patients.

Results: There was a significant relationship between stroke subtypes (anterior vs. posterior circulation) and cognitive function in ischemic stroke patients (P-value = 0.000), where patients with anterior circulation involvement showed greater cognitive impairment than those with posterior involvement.

Conclusions: There is an association between stroke subtype and cognitive function in ischemic stroke patients at Siloam Hospital Lippo Village, particularly affecting the cognitive domains of language, delayed recall, abstraction, and attention.

Keywords: stroke subtype, cognitive function, ischemic stroke

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Introduction

Stroke is one of the leading causes of death and disability worldwide. The World Stroke Organization reports that approximately 13.7 million new cases of stroke occur each year, with 5.5 million resulting in death. Stroke can be categorized into ischemic and hemorrhagic types, with ischemic stroke accounting for approximately 80% of all cases. Ischemic stroke occurs due to obstruction of blood flow to the brain caused by an embolus,

thrombus, or hypoxia, leading to neurological dysfunction. The prevalence of stroke in Indonesia remains high, with regions such as North Sulawesi (10.8%), Yogyakarta Special Region (10.3%), and Jakarta (9.7%) reporting significant incidence rates. Stroke not only causes motor impairment but also cognitive deficits that impact patients' quality of life. Cognitive function encompasses various aspects such as memory, attention, language, and orientation, all of which may be affected depending on the location of the brain infarct.

Bamford classifies ischemic stroke into four subtypes based on lesion location and clinical symptoms: Lacunar Infarct (LACI), Partial Anterior Circulation Infarct (PACI), Posterior Circulation Infarct (POCI), and Total Anterior Circulation Infarct (TACI). Several studies have indicated that different stroke subtypes may affect cognitive function differently. Research by Malik and Maulina found that patients with LACI, PACI, and TACI experienced cognitive impairment, while POCI showed no significant association. However, another study by Bozdoğan et al. reported a correlation between POCI and cognitive dysfunction.

To date, research findings on the relationship between ischemic stroke subtypes and cognitive function remain inconsistent. In Indonesia, studies using the Indonesian version of the Montreal Cognitive Assessment (MoCA-Ina) are still limited. Therefore, this study aims to analyze the relationship between ischemic stroke subtypes based on Bamford's classification and cognitive function using MoCA-Ina, in order to provide further insight into clinical manifestations and predict the anatomical site of stroke lesions.

Materials and Methods

This study is a numerical comparative analytical study with a cross-sectional design aimed at analyzing the relationship between ischemic stroke subtypes and cognitive function using the MoCA-Ina assessment tool. Samples were selected through purposive sampling from outpatient ischemic stroke patients at Siloam Hospital Karawaci. Inclusion criteria included patients aged 18–65 years with a history of ischemic stroke for more than one month. Exclusion criteria consisted of a history of severe head injury, brain tumor or inflammation, dementia, depression, education level of ≤12 years, and aphasia. Data were collected through interviews and MoCA-Ina assessments. Statistical analysis was conducted using IBM SPSS version 27.0. The Kolmogorov- Smirnov test showed that the data were normally distributed ($p = 0.129$), and the independent samples t-test was subsequently applied, with p-values < 0.05 considered statistically significant. This study was approved by the Ethics Committee of the Faculty of Medicine, Pelita Harapan University (040/K-LKJ/ETIK/I/2023), and written informed consent was obtained from all participants.

Results

This study aims to analyze the relationship between ischemic stroke subtypes and patients' cognitive function using the MoCA-Ina. The results are presented objectively in the form of tables and statistical analyses.

Subject Characteristics

This study involved 60 ischemic stroke patients, of whom 40 met the

inclusion criteria, while 20 were excluded due to dementia, depression, or having an education level of ≤12 years.

Table 1. Subject Characteristic (N=40)

Characteristic	N (%)
Gender	
Female	6 (15)
Male	34 (85)
Age	
Minimum	43
Maximum	65
Mean	58,28
BMI (Body Mass Index)	
Normal	13 (32,5)
Overweight	10 (25)
Obesity	17 (42,5)
Comorbidities	
Hypertension	26 (65)
Cholesterol	24 (60)
Heart disease	16 (40)
Diabetic	20 (50)
Stroke Subtypes	
Anterior system	32 (80)
- LACI (lacunar stroke)	9
- TACI (Total Anterior Cerebral Infarction)	0
- PACI (Partial Anterior Circulation Infarct)	23
Posterior System	8 (20)
- POCI (Posterior Cerebral Infarction)	
MoCA-Ina Score	
- Minimal	14
- Maximal	29
- Median	20,5
- Mean	20
Cognitive Function	
- Affected <26	33(82,5)
- Not affected ≥26	7(17,5)

Of the 40 respondents, the majority were male (85.0%), with an age range of 43–65 years (mean age 58.28 years). Based on the Body Mass Index (BMI), 32.5% had normal weight, 25% were overweight, and 42.5% were obese. Hypertension (65%) was the most common comorbidity, followed by high cholesterol (60%), diabetes (50%), and heart disease (40%).

The Relationship Between Stroke Subtypes and Cognitive Function

Table 2. The mean MoCA-Ina score based on stroke subtypes (N = 40)

Stroke Subtype	N	Mean	Std. Deviation	Std. Mean
Anterior	32	18,625	3,03	0,536
Posterior	8	26,125	4,61	1,63

Table 3. Statistical test results of stroke subtypes and cognitive function.

No	Variabel	MoCA-Ina		
		Mean ± SD	Min/Max	*P-value*
1.	Anterior	18,625 ± 3,03	14/25	0,000
2.	Posterior	26,125 ± 4,6	15/29	

Table 4. Bivariate analysis results between stroke subtypes and cognitive function.

	Anterior		Posterior		*P value*
	Mean ± SD	Min/max	Mean ± SD	Min/max	
Visuospatial	3,37 ± 1,62	0/5	4,5 ± 0,756	3/5	0,067
Naming	2,4 ± 0,665	1/3	2,8 ± 0,35	2/3	0,056
Orientation	5,25 ± 0,84	3/6	5,75 ± 0,7	4/6	0,077
Language	1,75 ± 0,718	0/3	2,76 ± 0,7	1/3	0,001
Delayed Recall	0,8 ± 1,28	0/4	2,37 ± 1,06	0/3	0,003
Abstraction	1,37 ± 0,6	0/3	2,37 ± 0,74	1/3	0,002
Attention	3,68 ± 1,53	1/6	5,5 ± 1,06	3/6	0,003

Statistical Analysis

The Kolmogorov-Smirnov test showed that the data were normally distributed (p = 0.129). Levene's test indicated a p-value of 0.813 (>0.05), suggesting homogeneity of the data. The independent samples t-test revealed a significant difference in MoCA-Ina scores between the anterior and posterior stroke subtypes (p = 0.000). These results indicate that patients with posterior system stroke have better cognitive function compared to patients with anterior system stroke.

Discussion

The results of this study show a significant difference in cognitive function between anterior and posterior ischemic stroke subtypes. Patients with posterior stroke had higher MoCA-Ina scores compared to those with anterior stroke (p = 0.000), indicating better-preserved cognitive function in this group. This study is consistent with the findings of Malik and Maulina (2005), who reported cognitive impairment in patients with LACI, PACI, and TACI subtypes, but not in POCI. However, these results contradict the study by Bozdoğan et al., which found that POCI can also lead to cognitive decline. This discrepancy may be due to variations in measurement methods and sample characteristics. The majority of patients in this study had hypertension (65%), which is a major risk factor for stroke. Additionally, obesity (42.5%) is also associated with cognitive impairment, as shown in the study by Zolla Natallian (2022). These findings highlight the importance of early detection of risk factors to prevent post-stroke cognitive impairment. The clinical implication of this study is the importance of classifying stroke subtypes to determine the appropriate rehabilitation approach. MoCA-Ina has been shown to have higher sensitivity than MMSE in detecting cognitive impairments in stroke patients. This study has limitations in the sample size, which is not fully homogeneous, and did not control for sociodemographic and lifestyle factors. Future research is recommended to increase the sample size, consider confounding factors, and conduct longitudinal studies to understand long-term changes in cognitive function.

Conclusion

This study shows a significant difference in cognitive function between anterior and posterior ischemic stroke subtypes. Patients with posterior stroke have better cognitive function compared to those with anterior stroke, as evidenced by higher MoCA-Ina scores (p = 0.000). These results emphasize that the classification of ischemic stroke subtypes plays a role in determining the level of cognitive impairment.The implication of this finding is the importance of cognitive screening in stroke patients based on subtypes, which can help in planning more optimal rehabilitation. Further research with a longitudinal design and larger sample size is needed to strengthen these findings and explore other factors contributing to cognitive decline in ischemic stroke patients.

Conflict of Interest

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ORIGINAL RESEARCH

ISCHEMIC STROKE RISK FACTORS IN SILOAM LIPPO VILLAGE TEACHING HOSPITAL

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Abstract

Introduction: Acute ischemic stroke is the second leading cause of death worldwide and considered a major health problem leading to significant disability and mortality. Stroke Risk factors epidemiology various among population. This study conducted to identify stroke risk factors in Siloam Lippo Village, a secondary teaching hospital in Banten Province, Indonesia.

Methods: This is a cross sectional study of acute ischemic stroke in the Stroke Unit of Siloam Lippo Village Teaching Hospital over a period of 3 months from January 2020 to March 2020. Data regarding the patients' clinical profile, medical history and diagnostic test results were collected then analyzed using spreadsheet and SPSS version 21.0 software.

Results: Forty-eight subjects met inclusion criteria in this study, 25 (52.08%) were male and 23 (47.92%) were female with a mean age of 58.16 ±12.02 years old. The most common risk factor for ischemic stroke in this study is hypertension (83,33%), followed by cigarettes smoking (45,83%), dyslipidemia (51,67%), diabetes mellitus (37,5%), previous stroke (37,5%) and history of heart disease (31,25%). More than 90% of subjects with hypertension and diabetes were uncontrolled.

Conclusions: The most common risk factor for ischemic stroke in this study is hypertension and cigarettes smoking, while dyslipidemia, diabetes mellitus, previous stroke and history of heart disease found in more than one-third of the subjects. Uncontrolled status for hypertension and diabetes were more than 90%.

Keywords: Hypertension, ischemic stroke, risk factors

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Introduction

Acute ischemic stroke is the second leading cause of death worldwide and considered a major health problem leading to significant disability and mortality. Global Burden of Disease 2021 showed that stroke caused about seven million deaths and over 160 million DALYs (Disability-adjusted life-years lost). Indonesia recorded an increase in the prevalence stroke in Indonesia, from 7 % in 2013 to 10.9 % in 2018. Stroke also caused high disability rate and dependency in the elderly population and increased health care cost to 2.57 trillion rupiah in 2018.[2]

Stroke Risk factors epidemiology various among population. In one Asia

study, hypertension is the most frequent risk factor, followed by diabetes mellitus and cigarettes smoking.[3] This study conducted to identify stroke risk factors in Siloam Lippo Village, a secondary teaching hospital in Banten Province, Indonesia

Materials and Methods

This is a cross sectional study of acute ischemic stroke in the Stroke Unit of Siloam Lippo Village Teaching Hospital over a period of 3 months from January 2020 to March 2020. Data regarding the patients' stroke risk factors based on medical history and diagnostic test results were collected then analyzed using spreadsheet and SPSS version 21.0 software.

Results

Forty-eight subjects met inclusion criteria in this study, 25 (52.08%) were male and 23 (47.92%) were female with a mean age of 58.16 ±12.02 years old. The average age for female population was 61.17 ±13.19 years old, which is more than 5 years older than average age of the male population (55.40 ±10.32 years old). Most of the subjects (87,5%) were under 75 years old, and one-third of the subjects were under 55 years old.

Hypertension was the most prevalent risk factors in this study, followed by smoking, dyslipidemia and diabetes mellitus, previous stroke and heart disease. Almost all of hypertensive and diabetic patients are uncontrolled based on medical history and blood parameters. Nineteen subjects in this study are still active smokers with average 20-40 cigarettes daily.

Table 1. Stroke Risk Factors (n=48)

Risk Factors		N	Percentage
Hypertension		40	83,33
Sex	Male	20	50
	Female	20	50
Duration	<1 year	1	2.5
	1-5 years	13	32.5
	5-10 years	17	42.5
	10-20 years	8	20
	>20 years	1	2.5
Status	Uncontrolled	39	97.5
	Controlled	1	2.5
Smoking		22	45,83
Sex	Male	20	90.91
	Female	2	9.09
Duration	10 - 20 years	2	9.09
	20 - 30 years	7	31.82
	30 - 40 years	3	13.64
	40 – 50 years	8	36.36
	>50 years	2	9.09
Dyslipidemia		20	41,67
Sex	Male	11	55
	Female	9	45
Diabetes Mellitus		18	37,5
Sex	Male	7	38.89
	Female	11	61.11
Duration	< 1 year	2	11.11
	1 – 5 years	3	16.67
	5 – 10 years	9	50
	10 – 20 years	4	22.22
Status	Uncontrolled	17	94.44
	Controlled	1	5.56
Previous Stroke		18	37.5
Sex	Male	10	55.55
	Female	8	44.45
Events	One-time	17	94.44
	Two-time	1	5.56
Heart Disease		15	31,25
Sex	Male	8	53.33
	Female	7	46.67
Type	Hypertensive Heart Disease	9	60
	Atrial Fibrillation	7	46.67
	Congestive Heart Failure	1	6.67
	Coronary Artery Disease	2	13.33

Discussion

Age has been known as one of stroke risk factors, with the risk increasing considerably after the age of 55, but in recent years, more data showed that stroke also occur in younger people. World Stroke Oraganization in 2022 showed that over 62% of all stroke occur in people under 70 years of age.[4] In this study, 87,5% of subjects were under 75 years old, and one-third of the subjects were under 55 years old. Stroke rise in younger people has been linked to sedentary life style which caused increased hypertension, diabetes and obesity, so as cigarettes smoking and heart disease.[5]

Women also known to have higher risk to stroke, due to longer life expectancy, higher prevalence of hypertension and obesity compared to men. In this study, female subjects were slightly lower than male, this might be due to younger age of subjects where esterogen in premenopausal women has beneficial effects on the cardiovascular system and reduce atherosclerotic risk through its impact on lipids.[6,7]

In this study hypertension was the most common risk factor which found in 83,3% of the subjects. This data is consistent with a study in Cipto Mangunkusumo Hospital on 2016 which found that 83.4% of patients had hypertension.[8] A study in Korean population showed that one-year increase of hypertension duration continuously increased the adjusted risk of ischaemic stroke. This is also consistent with our findings where most patients had history of hypertension for 5–10 years.[9] Another alarming finding is that 39 (97.50%) out of 40 patients with hypertension were uncontrolled which could have greatly contributed to acute ischemic stroke.

Cigarettes smoking is also a major health issue and must be regarded as a significant risk factor that contributes to acute stroke. A large case-control study involving 32 countries showed an 8-fold risk increase of large vessel stroke for age group of 50–59 who smoked more than 20 cigarettes/day. [10] In our study, 22 (45.83%) subjects had history of cigarettes smoking, out of which 19 are still active smokers who smoke 20-40 cigarettes/day.

In this study, dyslipidemia and diabetes are the fisk factors found in more than one-third of subjects. Previous studies showed that in people with diabetes, the risk of stroke is increased approximately two-fold and have worse post-stroke outcomes and a greater risk for stroke recurrence as compared with those without diabetes. Dyslipidemia's role in the pathogenesis of ischemic stroke, on the other hand, is less clear. Elevated LDL-C and low HDL-C levels appear to increase the risk of ischemic stroke, whereas the importance of high triglyceride levels is less clear. [11,12]

Atherosclerosis process plays a great role both in ischemic stroke and coronary heart disease, and strong corelation between acute coronary syndrome and ischemic stroke has been well established. Studies also showed that previous stroke, atrial fibrillation or flutter, and heart failure are substantial risk factors for ischemic stroke after an acute coronary syndrome. In this study, both previous stroke and heart disease found more than

one-third of subjects, which shows consistency with previous studies.

Conclusion

Ischemic stroke is a huge burden and full recovery still faces great challenges in Indonesia, therefore risk factors identification and management are crucial in primary and secondary prevention. The most common risk factor for ischemic stroke in this study is hypertension and cigarettes smoking, while dyslipidemia, diabetes mellitus, previous stroke and history of heart disease found in more than one-third of the subjects. Most of these risk factors can be managed with medication and lifestyle modification, but we still found large proportion of uncontrolled status.

Conflict of Interest

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CASE REPORT

STRESS-INDUCED BELLY DANCER'S DYSKINESIA IN A YOUNG WOMAN: A RARE CASE REPORT

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Abstract

Background: Belly dancer's dyskinesia (BDD) is a movement disorder characterized by involuntary and slow writhing, rhythmic contractions of the abdomen. This rarely encountered phenomenon has not been sufficiently explored, with limited evidence regarding its exact pathophysiology, etiology, and treatment. We present a rare case of stress-induced BDD in a 30-year-old female.

Case summary: A 30-year-old female presented with a 2-month history of involuntary abdominal movements that were sudden in onset, approximately lasting 5-10 minutes, with preserved consciousness. Her symptoms were initially precipitated by stress. However, they worsened within the past week during her menstrual period. Past medical history was significant for long-standing anxiety disorder and depression, for which she took vortioxetine 10mg/day, clonazepam 0.75mg/day, and lorazepam 0.5mg/day routinely. Upon examination, undulating and continuous movements of the abdominal wall were observed. A diagnosis of BDD was made and the patient was treated with an increased dose of clonazepam 1mg/day. Her symptoms significantly improved within three days.

Discussion: Aside from an underlying psychogenic factor, our patient did not have other risk factors for BDD, such as exposure to neuroleptics or history of abdominal trauma. Although certain drugs have been reported to induce BDD, the medications she took have never been reported to cause this condition. Thus, it is most likely that her dyskinesia was stress-induced.

Conclusion: Clinicians may not be familiar with BDD due to its infrequency, and the lack of standardized diagnostic and management strategies makes it challenging to diagnose and treat. Therefore, further research and exposure to BDD are imperative.

Keywords: dyskinesia, belly dancer's dyskinesia, movement disorder.

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Introduction

Belly dancer's dyskinesia (BDD) is a rare movement disorder which manifests as dyskinetic, involuntary, and frequently rhythmic contractions of the anterior abdominal muscles, resembling a belly dance. These contractions may present variably but have been described as mostly bilateral with slow writhing patterns similar to athetosis, often causing abdominal and/or chest pain and dyspnea.[1,2] BDD involves the contraction of multiple

muscles of the abdomen, including the rectus abdominis, internal and external obliques, transverse abdominis, pectoralis major, and perineum muscles.[3]

Numerous etiologies may cause this condition, including abdominal trauma and several known medications. Although the underlying mechanism remains unclear, it is thought to result from the dysfunction of inhibitory spinal interneurons or from structural changes in local neuronal circuits.[4] Studies have shown an association between the effect of hormonal changes during the menstrual period on patients with movement disorders, such as Parkinson's disease and dystonia.[5] However, this possible association remains inadequately explored, especially in BDD patients. We report a rare case of menstrual-related exacerbation of BDD in a 30-year-old female.

Case Presentation

A 30-year-old female presented with a 2-month history of episodic, involuntary abdominal movements. The movements were sudden in onset and generalized, but mainly involved her abdomen. They were painless and lasted approximately 5-10 minutes with preserved consciousness. Her symptoms were initially precipitated by stress and subsided during sleep. However, she noticed these movements worsened in the past week during her menstrual period. She did not have a previous history of pregnancy, trauma nor surgical procedures of the abdomen. The patient had a history of anxiety disorder and depression, and routinely took vortioxetine 10 mg/day, clonazepam 0.75 mg/day, and lorazepam 0.5 mg/day.

Vital signs were stable. Upon examination, there were involuntary, continuous, and undulating abdominal movements. On supine position, these movements were more visible, with notable suppression observed during breath-holding. Neurological examination did not reveal any deficits. An electroencephalogram (EEG) was conducted to rule out seizures, which revealed unremarkable results. Other diagnostics such as MRI of the brain and spine, abdominal fluoroscopy, and electromyography (EMG) were not conducted. She was diagnosed with belly dancer's dyskinesia (BDD) and was put on an increased dose of clonazepam 1mg/day. She was also advised to halt the consumption of vortioxetine. Upon the next follow-up after one week, she reported improvement of symptoms within three days. She was provided with clonazepam 2mg/day only to be taken in case of recurrence.

Discussion

The diagnosis of BDD is primarily clinical but may be supported by diagnostic modalities, such as fluoroscopy and electromyography (EMG) of the diaphragm.[1,9] Further investigation with brain and spinal cord imaging may also be conducted to exclude any underlying structural abnormalities.[3,6] However, there are currently no standardized testing protocols for BDD. Thus, despite the variety of proposed diagnostic approaches available, its diagnosis remains highly

complex and challenging. It is essential to obtain comprehensive history and perform thorough examination in order to accurately diagnose this condition, as diagnostic tools are only supplementary and may not always provide evidence that could account for such movements.[2,7,8] In this patient, there were no neurological deficits that would suggest an underlying structural abnormality. Additionally, the presence of her long-standing psychiatric condition points to a stress-induced etiology. Therefore, we did not conduct extensive diagnostics on this patient.

These involuntary movements of the abdomen may present variably, but commonly consist of repetitive, writhing movements of gradual onset which often subside during sleep. Shortness of breath and abdominal and/or chest pain may also be experienced by patients with BDD.[1] In approximately 50% of cases, a previous history of local trauma or surgical procedures of the abdomen is present.[8] Although the majority of cases are idiopathic, a range of etiologic factors have been suggested, including abdominal surgery, diaphragmatic flutter, intramedullary thoracic cord tumor, levodopa-induced movements, and basal ganglia lesions.[9] Through thorough history, the aforementioned etiologies were excluded based on clinical grounds. Contractions of the abdomen may frequently be mistaken for convulsions. In our patient, ictal etiology has been ruled out with an EEG.

Certain medications have been reported to induce BDD, including levodopa,[10] clebopride,[8] and galantamine.[11] A notable association between BDD and the dopaminergic system is highlighted in these cases. Studies have proposed that serotonin may exert an indirect inhibitory effect on the dopaminergic system, leading to a reduction in dopaminergic activity.[12,13] Our patient's medication history was significant for long-term use of vortioxetine, a selective serotonin reuptake inhibitor (SSRI). Although SSRIs have been associated with the development of movement disorders, there are currently no reported cases of SSRI-induced BDD.[14] In addition, our patient has been on medication with SSRI for many years prior to the onset of her dyskinesia, with no history of consuming the aforementioned drugs that may induce BDD, further confirming that her BDD is not drug-induced.

Psychogenic factors are known to provoke BDD, including anxiety and hysteria.[15] Stress is known to directly affect the motor system function due to the presence of glucocorticoid receptors in certain motor regions, thus making these areas vulnerable to the effects of cortisol, a hormone produced by stress. Our patient's past medical history was significant for long-standing anxiety disorder and depression. She reported that her abdominal contractions were especially prominent in the presence of stress. Therefore, her underlying psychogenic condition may have been the precipitating factor for her BDD.

Exacerbation of dyskinesia during our patient's menstrual period remains a matter of intrigue. Albeit there is currently no data addressing the impact of hormonal changes during menstruation on motoric

symptoms of BDD, several studies have reported worsening of motor symptoms during the menstrual period in other movement disorders, namely Parkinson's disease (PD) and dystonia.[16,17] Evidence suggests that estrogen plays a role in the dopaminergic system, although the precise mechanisms by which it acts on basal ganglia circuits and contributes to the worsening of movement disorders remain largely unclear and unexplored. The absence of hormonal-related BDD cases warrants further research on the matter.

The primary approach in the management of BDD is symptomatic treatment, as the efficacy of previously reported therapeutic options remains a matter of debate. These drugs include benzodiazepines, beta-blockers, vitamin B12 supplements, antipsychotics, anti-seizure medications, and antidepressants.[6] Clonazepam is a benzodiazepine that has been found to decrease the frequency and intensity of abdominal contractions in BDD. Comparable to our case, Gupta *et al.* reported successful alleviation of dyskinesia with clonazepam. In contrast, Kono *et al.* reported relapse and progressive worsening of BDD after cessation of clonazepam.[18] Tamaya *et al.* reported the successful treatment of BDD with haloperidol.[19] However, antipsychotics are often associated with a significant number of adverse effects, and on occasion may exacerbate dyskinetic symptoms in patients with BDD induced by medications affecting the dopaminergic pathway.[20] In drug-induced cases, the offending medication should be discontinued.[6] In this patient, we used clonazepam to manage her BDD. In addition, her underlying psychiatric condition was addressed through education regarding its possible impact on her BDD.

Several invasive techniques have been suggested in the treatment of BDD. A case series by Alshubaili *et al.* reported full recovery of BDD with botulinum toxin injections, although further evidence is still required to assess their effectiveness.[21,22] The successful use of transcutaneous electrical nerve stimulation (TENS) in BDD has also been reported.[8] In individuals with refractory BDD despite treatment with oral medications and botulinum toxin injections, deep brain stimulation (DBS) may be considered. Schrader *et al.* and Valálik *et al.* reported significant improvement of dyskinesia with DBS targeting the internal globus pallidus.[23,24] However, evidence-based recommendations for the management of BDD are still unavailable to date, making its treatment largely based on case reports and expert opinions. In our case, the patient's contractions resolved with oral medication, therefore invasive therapeutic strategies were not required.

Conclusion

BDD continues to present significant diagnostic and therapeutic challenges, primarily due to the lack of standardized diagnostic and treatment guidelines. Given that BDD is a clinical diagnosis, it is imperative for clinicians to maintain a high index of suspicion and to be well-versed in its manifestations and diverse etiologies to ensure accurate diagnosis and appropriate management. This case demonstrates a previously

unreported association between BDD and the menstrual period.

Conflict of Interest

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CASE REPORT

POSTICTAL FUGUE IN TEMPORAL LOBE EPILEPSY: A CASE REPORT

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Abstract

Introduction: Temporal lobe epilepsy (TLE) is the most prevalent form of epilepsy. Postictal fugue, a state of altered consciousness and amnesia that can lead to unusual behaviors, is an unusual type of postictal phase in TLE. This case report describes a rare case of postictal fugue in adult-onset TLE.

Case Report: A 27-year-old man with complaints of recurrent seizures over the past six years, described as blank staring accompanied by purposeless action with each episode lasting 5-10 minutes on average. During the episodes, he can perform various activities without the ability to recall the events after regaining consciousness. There were neither aura nor specific triggers preceding the episodes. Some long-term memories are impaired. No other cognitive impairment is found. There was a long-standing history of substance use. Electroencephalogram examinations revealed abnormal spikes wave in bilateral temporal region.

Discussion: The patient's symptoms resemble dissociative fugue but is attributed to an organic etiology, which is mesial/limbic TLE. The postictal phase which manifests as postictal fugue is caused by the abnormal electrical activity in the hippocampus leading to disruption in memory formation and spatial navigation. The underlying mechanism causing epilepsy is thought to be related to the prolonged history of substance abuse.

Conclusion: The postictal phase in TLE can present in various forms and may be challenging to diagnose. Therefore, it is crucial to thoroughly investigate the causes of organic dissociative disorder, including postictal fugue in TLE.

Keywords: Postictal fugue, temporal lobe epilepsy, organic dissociative disorder

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Introduction

Temporal lobe epilepsy (TLE) is the most prevalent form of focal epilepsy. It is usually diagnosed in the first two decades of life. Approximately 60% of all epilepsy cases are focal, with the majority originating in the temporal lobe. About 48-56 percent of these occurrences occur bilaterally.[1] The postictal phase, which occurs after a seizure, is a period of impaired brain function that can last from minutes to days.[2] One of the less commonly documented phenomena during this phase is postictal fugue, a state of altered

consciousness and amnesia that can lead to unusual behaviors without the patient's awareness.

The underlying mechanism of the postictal fugue is not yet fully understood; however, it is associated with changes in cerebral blood flow, neurotransmitter function, and may be induced by the side effects of substances. The exact prevalence is difficult to determine due to its transient nature and challenge of capturing these episodes in clinical settings. This case report aims to describe a rare case of postictal fugue episodes in adult-onset TLE.

Case Presentation

A 27-year-old man presented with a six-year history of recurrent seizures, which had improved over the past year after receiving treatment from a neurologist. The seizures experienced by the patient involved a blank stare, similar to zoning out, followed by purposeless actions, such as adjusting an apron, with his eyes directed downward and occasionally with lip-smacking. The episodes typically lasted 5-10 minutes, with the longest duration lasting 30 minutes. During these episodes, he was able to ride a motorcycle for a considerable distance, squat, walk, or engage in other activities unconsciously. He reported falling off a motorcycle four times and hurting himself with a cigarette once, without feeling any pain. There were no specific triggers for the seizures, and he denied any auras beforehand, such as smelling odors, hearing sounds, or seeing flashes of light. No tonic- clonic seizures were reported, and the patient could not recall events during the episodes. He also denied any personality changes during the seizures. The seizure could be terminated by receiving a strong blow. After a seizure, he quickly regained consciousness without confusion, fatigue, or difficulty speaking.

The patient also complained of intermittent headaches around his eyes but denied experiencing any severe headaches. This was accompanied by the loss of some long-term memories, such as experiences from elementary school or the names of friends from the middle school, though his short-term memory remained intact. There was no history of head injury or severe head trauma. He denied any history of fainting, neck stiffness, brain infections, hemiparesis, facial weakness, speech difficulties, or childhood seizures. There were no traumatic experiences prior to the onset. His other cognitive functions remained intact, and he was able to carry out daily activities independently.

The patient reported a history of alcohol consumption and psychoactive substance use since he was 12 years old, specifically tramadol, heroin, and trihexyphenidyl for 6 years, along with marijuana for 7 years, methamphetamine for 8 years, and alcohol for 11 years. The patient has denied the use of any psychoactive substances since 2020 but still smokes 20 cigarettes per day. Family history of neurological disease was unremarkable, and the family denied any relatives with similar complaints.

On electroencephalogram (EEG) examination, one spike-and-wave discharge was observed in the bilateral anterotemporal region, along with one interictal spike in the bilateral temporal region. Based on the ILAE criteria of epilepsy and EEG findings, the patient has

been diagnosed with epilepsy for the past 4 years, specifically temporal lobe epilepsy. The patient has been prescribed several antiepileptic drugs, including sodium divalproex 500 mg twice daily, phenytoin 100 mg twice daily, and carbamazepine 200 mg twice daily.

Discussion

Postictal fugue in temporal lobe epilepsy refers to a fugue or confusional state that occurs after the ictal phase, characterized by altered consciousness with varying degrees of motor activity and amnesia during the event.[3] We present a rare case of postictal fugue in temporal lobe epilepsy (TLE) with a history of substance abuse. The patient fulfilled the criteria for epilepsy shown in Table 1. The patient reported experiencing seizures four times a month. EEG findings indicate that the patient experienced focal epilepsy, specifically mesial temporal lobe epilepsy as the seizures were accompanied with impaired consciousness. The motoric action following the non-motoric seizure was thought to be a manifestation of postictal epilepsy, specifically a postictal fugue.

Table 1. Criteria of Epilepsy based on International League Against Epilepsy (ILAE)[4]

Criteria
1. At least two unprovoked (or reflex) seizures occurring >24 h apart
2. One unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years
3. Diagnosis of an epilepsy syndrome

The disorder experienced by the patient resembles dissociative fugue (Table 2 and Table 3), but it is attributable to an organic etiology. The distinguishing characteristics in postictal fugue typically include a history of epilepsy, the absence of stress-inducing events, and less purposeful and more fragmented activities and travel patterns observed in epilepsy patients. Therefore, the patient is thought to have organic dissociative disorder, a condition that meets the criteria for one of the disorders within Dissociative Disorders (F44.-) and also fulfills the general criteria for an organic cause.

Table 2. Criteria of Dissociative Amnesia (F44.0) based on DSM-V-TR[5]

Criteria
a. An inability to recall important autobiographical information, usually of a traumatic or stressful nature, that is inconsistent with ordinary forgetting.
b. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
c. The disturbance is not attributable to the physiological effects of a substance (e.g., alcohol or other drug of abuse, a medication) or a neurological or other medical condition (e.g., partial complex seizures, transient global amnesia, sequelae of a closed head injury/traumatic brain injury, other neurological condition).
d. The disturbance is not better explained by dissociative identity disorder, posttraumatic stress disorder, acute stress disorder, somatic symptom disorder, or major or mild neurocognitive disorder.

Table 3. Criteria of Dissociative Fugue (F44.1) based on ICD-10[6]

Criteria
a. The features of dissociative amnesia (F44.0);
b. Purposeful travel beyond the usual everyday range (the differentiation between travel and wandering must be made by those with local knowledge); and
c. Maintenance of basic self-care (eating, washing, etc.) and simple social interaction with strangers (such as buying tickets or petrol, asking directions, ordering meals)

Based on the location of neuronal activity, epilepsy can be categorized into focal and generalized types. Focal epilepsy is related to specific regions of the brain, while generalized epilepsy involves the entire cerebral hemisphere simultaneously. Focal (or partial) epilepsy can be further divided into simple (aware), complex (with impaired awareness), and secondarily generalized types. Simple partial seizures are characterized by jerking movements in one extremity or one part of the body without loss of consciousness. Complex partial seizures involve impaired consciousness, with or without motor activity. If the seizure affects areas of the brain responsible for motor control, it may present with motor manifestations. Conversely, disruptions in other brain regions, such as the temporal lobe, are more likely to manifest non-motor symptoms. EEG findings in simple partial seizures show focal spikes in the contralateral hemisphere, while EEG findings in complex partial seizures reveal focal spikes in the frontal or temporal lobes. Secondary generalized seizures are marked by focal epilepsy that can spread from one focus to other areas of the brain, also known as focal-to-generalized, where the initial onset involves abnormalities in a focal brain structure.[7]

Temporal lobe epilepsy (TLE) is the most common form of focal epilepsy. In TLE, mossy fiber sprouting occurs, where axons from the dentate gyrus not only project to the cornu ammonis (CA3) in the hippocampus but also form new and abnormal synaptic connections in the molecular layer of the dentate gyrus. This sprouting creates excitatory feedback loops, leading to the formation of epileptogenic foci. According to the ILAE classification, TLE can be divided into mesial/limbic TLE (mTLE) and neocortical/lateral TLE (nTLE) shown in Table 4.[8,9]

In temporal lobe epilepsy (TLE), non-motor areas of the brain are often involved, including the thalamus and limbic system. The thalamus plays a crucial role in sensory information processing before it reaches the cortex, which results in impaired awareness of the environment.[10] Limbic system is a group of brain structures that located lateral to the thalamus, between cerebral cortex and hypothalamus, above the brainstem. Connected with other parts of the brain, the limbic system is involved in emotional, motivation, behavior processes, and also important to memory.[11] Memory, an essential cognitive process, can be divided into short-term (working memory) and long-term memory, which includes explicit (declarative) and implicit (procedural) memory.[12,13]

Table 4. Comparison of mTLE and nTLE[8,9]

	mTLE	nTLE
Region	Hippocampus, entorhinal cortex, amygdala, parahippocampal gyrus, and dentate gyrus	Temporal neocortex, specifically the superior, medial, and inferior temporal regions, as well as the temporo-occipital and temporo-parietal junctions and associative areas for auditory, visual, and language functions
Onset	10-year-old, particularly in individuals with a history of febrile seizures	23-year-old
Aura	Visceral sensations (such as epigastric discomfort) and déjà vu	Auditory or visual hallucinations, somatosensory symptoms
Ictal	Loss of consciousness, all activity ceases, blank stare, pupil dilation, and automatisms like chewing, smacking, or swallowing. Automatisms in the ipsilateral hand (e,g,. touching and picking) and dystonic posturing of the contralateral arm may also be observed	Motor manifestations such as jerking movements or sensory disturbances
Postictal	Present in 85% of cases, characterized by confusion, language disturbances, or psychiatric symptoms	Motor weakness (Todd's paresis) or sensory deficits may also occur. The postictal phase tends to be shorter than in mTLE
EEG	During the ictal phase, there is rhythmic focal activity between 5-9 Hz. In the interictal phase, unilateral spike-wave activity is observed in the anterior, mesial, and posterior temporal regions, which may become bilateral if the limbic system is involved	During the ictal phase, there is more prominent focal activity compared to mTLE. In the interictal phase, sharp waves, spikes, or spike-wave activity may be observed in the lateral temporal lobe

Explicit memory, which is stored in the hippocampus and medial temporal lobe, involves conscious recall of information such as events and facts. Implicit memory, stored in areas like the cerebellum and amygdala, includes skills and conditioned responses.[12,13] The Papez circuit, which begins and ends in the hippocampus and connects with the hypothalamus, thalamus, and other regions, is key in processing both memory and emotion. Disruptions in this system, particularly in the dominant hemisphere, can impair memory, language, and orientation, while disruptions in the non-dominant hemisphere may affect visual memory, such

as facial and spatial recognition.[14,15]

The postictal phase is a temporary state that occurs after a seizure has ended, lasting from several minutes to days. Postictal fugue in epilepsy can be observed in absence seizures, non-convulsive complex partial seizures, or generalized seizures. During this phase, patients may experience drowsiness, confusion, impaired consciousness, focal neurological deficits, cognitive disturbances, or psychiatric issues. The underlying mechanisms of the postictal state are not yet fully understood, but changes in brain blood flow, neurotransmitter function, and medication side effects are believed to play a role. In temporal lobe epilepsy (TLE), abnormal electrical activity in the hippocampus and surrounding structures can disrupt memory formation and spatial navigation. Cognitive function can be compromised due to reduced blood flow to the brain during the postictal phase decreases oxygen and glucose supply, which can worsen cognitive function in postictal fugue. Additionally, neurotransmitter imbalances persist during the postictal phase, with GABA reducing normal cognitive function. Lastly, consciousness is also impaired as the thalamus and the brain's ability to process sensory information are disrupted. As a result, individuals in postictal TLE exhibit purposeful motor behavior that occurs automatically, yet unaware of their surroundings, making them appear outwardly normal while being unresponsive to external stimuli.[3,16]

As happened in this patient, no motor areas were involved, rather, the thalamus and limbic system were affected. Consequently, the patient was able to move and maintain consciousness but was unaware and unresponsive to external stimuli because the thalamus could not relay sensory information to the cortex. Disruption in the limbic system, particularly the dentate gyrus and entorhinal cortex of the hippocampus, impaired the patient's ability to remember the events during the seizure, the postictal phase, as well as long-term memory.

The underlying mechanism behind the incidence of epilepsy in this patient is thought to be related to the prolonged history of substance abuse. Particularly the use of alcohol which has been associated with seizures upon withdrawal. The chronic use of alcohol can disrupt the neurotransmitter systems, especially the gamma-aminobutyric acid (GABA) and glutamate as the major inhibitory and excitatory neurotransmitters, respectively. Evidence has suggested that alcohol potentiates the effects of GABA, which accounts for the sedation effect upon initial ingestion. Over time, chronic and excessive consumption of alcohol reduces the number of GABA receptors. Another effect is the increase in glutamate receptors in the hippocampus, an area in the brain that is responsible for memory and involved in epileptic seizures. During alcohol withdrawal, alteration in glutamate and GABA receptors occur. Glutamate receptors that have adapted to the long-term presence of alcohol become upregulated. This effect combined with the deficiency of GABA receptors lead to the overexcitation throughout the brain and subsequently causing seizures within 1 - 2 days upon stopping ingestion of alcohol.[17]

Other drugs commonly associated with seizures are cocaine, amphetamine and other stimulants, cannabinoids and psychedelic agents through their ability to produce excitation of the central nervous system.[18] Among the drugs frequently associated with seizures, the patient had a history of abusing methamphetamine and cannabinoids. Amphetamines-induced-seizures occur with use at high doses and are mediated by the stimulation of N-methyl-D-aspartate (NMDA) receptors and inhibition of GABA receptors. Cannabinoids were thought to reduce the GABA turnover at low doses but increase it at high doses.[18] Other study revealed that cannabis and heroin, a type of opioid, were associated with a lower seizure incidence compared to other drugs.[19] Tramadol, another opioid used by the patient, has been proposed to lower the seizure threshold by inhibition of serotonin and norepinephrine reuptake pathways while also exerting an inhibitory effect on GABA. Consequently, the patient's long-standing history of substance abuse may increase patient's risk of seizures.

Based on the diagnosis of postictal fugue in temporal lobe epilepsy, the patient was prescribed phenytoin as the first-line therapy for focal seizures. The patient has been on this treatment for four years, but seizures have persisted, so additional therapy was gradually introduced with two other anti-epileptic drugs (AEDs), carbamazepine and sodium divalproex.[20,21] These three medications function as anticonvulsants by blocking voltage-sensitive sodium and calcium channels, and by inhibiting GABA transaminase, thereby increasing GABA concentrations, which reduce neuronal excitability.[22]

Conclusion

This case report highlights a rare case of postictal fugue in adult patient with TLE. The characterized symptoms in this patient are purposeless actions, amnesia, and impaired consciousness following seizures. Despite optimized medical therapy, the patient's episodes of postictal fugue still occur. Although postictal fugue shares similarities with dissociative fugue, the patient is thought to have organic dissociative disorder due to history of TLE and the absence of stress-induced triggers. Recognizing this phenomenon is important for accurate diagnosis and effective treatment of epilepsy- related presentations. This case report also emphasizes the need for further research into the mechanisms underlying postictal fugue in TLE and the impact on cognitive and behavioral function.

Conflict of Interest

The authors declared no conflict of interest.

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SYSTEMATIC REVIEW

LACTATE DEHYDROGENASE AS A POTENTIAL PROGNOSTIC BIOMARKER IN SUBARACHNOID HAEMORRHAGE: A SYSTEMATIC REVIEW

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ABSTRACT

Background: Subarachnoid haemorrhage (SAH) lacks specific prognostic blood markers, but lactate dehydrogenase (LDH), linked to cellular damage, shows potential for predicting adverse outcomes in SAH patients. Elevated LDH levels may reflect anaerobic metabolism and tissue injury following SAH, providing insight into disease severity and complications. This review explores the relationship between lactate dehydrogenase levels and outcomes in SAH patients.

Method: A systematic review was conducted using PubMed, Europe PMC, ScienceDirect, and Google Scholar, searching for terms like "Lactate Dehydrogenase," "LDH," "Subarachnoid Haemorrhage," and "Outcome" up to March 3, 2025. Studies comparing LDH levels with Modified Rankin Score (mRS) and secondary outcomes such as Hunt-Hess grade, Fisher grade, complications, and mortality were included.

Result: Seven studies involving 5,985 participants met inclusion criteria. Higher LDH levels correlated with worse mRS scores, increased delayed cerebral ischemia (DCI), postoperative pneumonia, severe Hunt-Hess and Fisher grades, and higher mortality. Using the ROBINS-I tool, four studies showed low risk of bias, and three had moderate risk.

Discussion: Elevated LDH levels predict adverse outcomes in SAH, highlighting its prognostic value. As a marker of cellular damage and anaerobic metabolism, LDH reflects tissue injury and hypoxia post-SAH, explaining its link to complications like delayed cerebral ischemia (DCI) and pneumonia. This physiological basis supports its role in risk stratification, aiding early identification of high-risk patients for targeted interventions and improved outcomes.

Conclusion: Early measurement of LDH levels after SAH onset may help predict patient outcomes and complications, aiding clinical decision-making and improving patient management strategies.

Keywords: Lactate Dehydrogenase, Subarachnoid Haemorrhage, Prognosis, Outcome

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Introduction

Subarachnoid haemorrhage (SAH) is a life-threatening condition characterized by the buildup of blood between the arachnoid and pia mater.[1] Non-traumatic SAH, primarily caused by a ruptured intracranial aneurysm, remains the most common type, accounting for 85% of cases. The global incidence of SAH is 9 per 100,000 people per year, with 10% of patients dying before reaching the hospital.[2] The mortality rate within the first 24 hours can be as high as 25%, and 50% of patients die within the first 30 days.[2] Additionally, the disability rate for those who survive is 66%.[3] At present, the prediction of outcomes for patients with subarachnoid haemorrhage is mainly based on the patient's clinical grade at admission, as assessed by the World Federation of Neurological Surgeons (WFNS) score, with higher grades indicating a worse prognosis.[4] Other factors, such as age and pupillary light reflex, are also considered predictors of functional outcomes.[5] However, all of these scores are entirely dependent on clinical assessments and often disregard other factors that could affect patient outcomes.[4-5]. Thus, specific biomarkers are required promptly to predict future outcomes, enabling the optimization of treatment.

Lactate dehydrogenase is an enzyme present in nearly all body tissues. It plays a crucial role in the anaerobic metabolic pathway by catalyzing the conversion of pyruvate to lactate under anaerobic conditions. While lactate dehydrogenase levels have been used to predict outcomes in patients with heart disorders, cancer, trauma, central nervous system infections, and other conditions, no studies have yet explored the relationship between lactate dehydrogenase levels and the outcomes of patients with subarachnoid haemorrhage.[6-8]

Materials and Methods

The systematic review and meta-analysis were performed and documented in accordance to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta Analyses) guidelines. Additionally, the review protocol was listed in the PROSPERO International Prospective Register of Systematic Reviews, assigned registration number CRD42024576454

The data were obtained by searching in the following databases: PubMed, EuropePMC, ScienceDirect, and Google Scholar. The search strategy involved using the keywords " Lactate Dehydrogenase", "LDH", "Subarachnoid Haemorrhage", "Prognosis", "Outcome", combine using Boolen operators such as "AND" and"OR". The keyword search terms are listed in Table 1. The search and processing was conducted on March 3, 2025.

The systematic review and meta-analysis included studies published between 2014 and 2024 that investigated the association between lactate dehydrogenase (LDH) levels and outcomes or complications in patients with subarachnoid haemorrhage. Eligible studies were required to report LDH ranges, with higher LDH levels classified as the intervention group and lower levels as

the comparison group. Primary outcomes focused on functional measures, such as the modified Rankin Scale (mRS) score, while secondary outcomes included Hunt-Hess grade, Fisher Grade, Complication, and Mortality rates.

We excluded studies that were non-English, conducted on animals or cadavers, available only as abstracts or conference papers, or not accessible in full text. This was done to ensure high-quality studies and achieve the most reliable results regarding the relationship between LDH levels and predicted outcomes in patients with subarachnoid haemorrhage.

Database searches and data extraction were conducted by seven authors (YYEA, AEP, JW, ME, MA, RF, MGS, HWN). Any disagreements were resolved through consultation with a neurology expert (YS) until a consensus was reached. The data were systematically processed using Google Sheets and Microsoft Excel 2019. Each study was carefully divided into several components, including the Study ID, study design, country of origin, sample size, average age, inclusion and exclusion criteria, type of subarachnoid haemorrhage (SAH), timing of LDH sampling, measured outcome, LDH values, and study conclusions (major findings).

Results

Literature Search

The flow of included studies through selection process depicted in PRISMA diagram shown in Figure 1. Initially, 531 records were identified through database searching consisting of PubMed (10), Europe PMC (200), ScienceDirect (300), and Google Scholar (21). After removing 58 duplicates, 473 records undergone title and abstract screening, resulting in exclusion of 455 articles. The full text of 18 articles were assessed and 11 articles were excluded due to duplication (10 articles) and inaccessible article (1 study). Finally, a total of 7 studies are included in this review. [5,9-14]

Study Characteristics

Characteristics of included studies can be shown in Table 2. This systematic review included seven studies conducted across China, Japan, Belgium, and other regions, with sample sizes ranging from 19 to 3,524 patients. Most studies utilized retrospective cohort designs, while one employed a prospective cohort methodology. All studies measured serum LDH levels at admission. Key inclusion criteria varied but generally required SAH diagnosis confirmed by imaging and appropriate aneurysm treatment. Exclusion criteria included comorbid neurological or systemic conditions, incomplete data, or delayed admission.

Serum LDH and Prognostic Outcomes in Aneurismal-SAH

Table 3 provides an integrated description of the findings from studies assessing the prognostic role of serum lactate dehydrogenase (LDH) levels in aneurysmal subarachnoid haemorrhage (aSAH) patients. The analysis encompasses various outcomes, including complications, mortality, and functional recovery.

LDH Levels and Postoperative Pneumonia (POP)

One study conducted by Ding et al (2019) reported that patients with POP had significantly higher LDH levels (261.26 ± 126.51 U/L) compared to those without POP (189.00
± 69.20 U/L). A threshold LDH level of 203.5 U/L yielded a sensitivity of 63.6% and specificity of 71.3% for predicting POP, suggesting LDH's utility as a predictive marker for postoperative complications.

LDH and Delayed Cerebral Ischemia (DCI)

Study conducted by Anan et al (2020) on aSAH patients who developed DCI demonstrated slightly elevated LDH levels (222.1 ± 56.4 U/L) compared to non-DCI patients (214.7 ± 47.4 U/L). Additionally, LDH concentrations in carotid cisternal cerebrospinal fluid (CSF) were identified as potential predictive biomarkers for DCI, reflecting early brain injury (EBI).

LDH and Neurological Outcomes

Multiple studies explored the relationship between LDH levels and functional outcomes measured by the modified Rankin Scale (mRS) and Glasgow Outcome Scale (GOS):

- Study conducted by Zheng et al. (2021) and Zheng et al (2022). Poor mRS outcomes (scores 3–6) were associated with higher LDH levels compared to good outcomes (scores 0–2). For example, LDH levels for mRS 3–6 ranged from 205.918 ± 59.203 U/L to 234.188 ± 108.336 U/L
- Worse Hunt-Hess and Fisher grades, which indicate greater disease severity, were associated with progressively higher LDH levels. For instance, Hunt-Hess Grade V and Fisher Grade IV showed LDH levels of 252.851 ± 93.302 U/L and 376.806 ± 89.308 U/L, respectively as shown in studies conducted by Zheng et al (2021) and Zan et al (2022) respectively.
- Study conducted by Cavali et al (2023) shown that the Glasgow Outcome Scale (GOS) analysis showed a significant difference between favorable (176.05 ± 8.72 U/L) and unfavorable outcomes (215.29 ± 14.29 U/L), reinforcing LDH's role as a biomarker for poor recovery.

Risk of Bias

The risk of bias of included studies were conducted using Cochrane Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) Tool. Most domains indicated a low risk of bias, resulting in 4 studies being classified as "low risk of bias" and 3 studies as "moderate risk of bias" in the overall final results (Figure 2).

Discussion

Our findings show that the LDH value rises alongside the mRS score, Hunt-Hess grade, and Fisher grade, and is linked to postoperative pneumonia, delayed cerebral ischemia, and mortality rates. Zheng et al. (2021) observed higher mRS scores in individuals with elevated LDH levels (mRS 5-6: 234,188 ± 108,336 U/L vs mRS 0: 179,247 ± 46,761 U/L). Similarly, Zheng et al. (2022) reported a comparable trend (mRS 3-6: 227 ± 83,125 U/L vs mRS

0-2: 180,378 ± 50,695 U/L). Subarachnoid clots in the sulci and fissures cause spreading depolarizations and acute cerebral infarction in the nearby cortex after a cerebral aneurysm rupture.[15] An increase in ischemic lesions has been associated with higher mRS scores, which contributes to the clinical condition of patients with aSAH.[16] Zheng et al. (2021) reported that higher LDH levels were seen in patients with higher Hunt-Hess (HH) grades (HH Grade 1: 163,880 ± 35,571 U/L vs HH Grade V: 252,851 ± 93,302 U/L). This aligns with the findings of Multi et al. (2024), which involved 6,130 patients, showing that the Hunt-Hess grading system can serve as a predictor for both patient outcomes and mortality in subarachnoid haemorrhage (SAH). The study indicated that higher HH grades are linked to worse outcomes and increased mortality.[15,17] Neuronal apoptosis and necrosis in SAH result in the release of LDH into the bloodstream, leading to elevated LDH levels. These results suggest that serum LDH levels can serve as an indicator of the severity of brain tissue injury. [15,17]

Higher LDH levels were also observed in the group with a higher Fisher Grade. Zen et al. (2022) noted a significant difference in LDH values between Fisher Grade 4 and Fisher Grade 1 (376,806 ± 89,308 U/L vs. 37,989 ± 14,115 U/L, respectively). Similarly, Zheng et al. (2021) reported similar findings (Fisher Grade 4: 210,811 ± 68,962 U/L vs. Fisher Grade 1: 169,492 ± 41,621 U/L). In SAH, the disruption of the blood-brain barrier leads to the breakdown of red blood cells in the cerebrospinal fluid.[18,19] The LDH released from these lysed red blood cells is absorbed into the bloodstream, which raises LDH levels. Therefore, a higher Fisher Grade is linked to higher LDH values. [18,19]

The Glasgow Outcome Scale (GOS), which categorizes recovery from death to good recovery, is a key measure of long-term neurological outcomes in subarachnoid haemorrhage (SAH) patients. Cavali et al. (2023) emphasize the role of LDH as a reliable biomarker in predicting unfavorable outcomes, particularly those with GOS scores of 1–3 (215.29 ± 14.29 U/L) versus more favorable outcomes (176.05 ± 8.72 U/L for GOS 4–5). Elevated LDH levels in patients with unfavorable GOS outcomes likely reflect severe neuronal injury and metabolic disturbances. This is further corroborated by the association between higher LDH levels and worse Hunt-Hess and Fisher grades, both of which are established indicators of disease severity. Neuronal apoptosis and necrosis, hallmarks of SAH pathology, contribute to the release of LDH into the bloodstream, further linking LDH to poorer neurological recovery.[5]

In terms of mortality, the association with LDH levels is particularly striking. Zan et al. (2022) found that patients with elevated Fisher grades (Grade IV: 376.806 ± 89.308 U/L) had significantly higher 90-day mortality rates, indicating that LDH is not only reflective of immediate injury but also of progressive secondary brain damage, such as delayed cerebral ischemia (DCI) and systemic complications. This aligns with findings by Ren et al. (2023), where higher LDH levels

were associated with mortality within seven days post-discharge. The modest difference in LDH levels between mortality and non-mortality groups in Ren's study (239.8 ± 70.5 U/L vs. 236.3 ± 12.4 U/L) suggests that LDH may be more indicative of cumulative injury over time rather than acute events. [13,14]

Interestingly, LDH's role in predicting mortality is supported by its ability to reflect systemic stress responses, including inflammation, oxidative stress, and cellular hypoxia. Elevated LDH levels in such contexts provide a snapshot of metabolic derangements and widespread tissue injury, underscoring its value in mortality risk stratification.[13,20-22]

Postoperative pneumonia (POP), a significant complication following aneurysmal SAH, is another domain where LDH demonstrates prognostic value. Ding et al. (2019) observed a clear differentiation in LDH levels between patients who developed POP (261.26 ± 126.51 U/L) and those who did not (189.00 ± 69.20 U/L), with a threshold of 203.5 U/L offering predictive utility. The higher LDH levels in POP cases likely reflect the inflammatory cascade and immune dysregulation triggered by SAH, which predispose patients to infections. Given the high morbidity associated with POP, identifying patients at risk using biomarkers like LDH could facilitate early intervention strategies, such as prophylactic antibiotics or enhanced pulmonary care.[9]

Inflammatory markers are commonly used in clinical practice. Common examples include lactate dehydrogenase (LDH), procalcitonin, interleukins, among others. These markers are known to increase in a variety of conditions such as infection, tumour, and even in cases of subarachnoid haemorrhage. To date, no studies have directly compared the effectiveness of these markers in predicting prognosis, as each plays a significant role in disease progression. However, LDH continues to be widely utilized as an inflammatory marker due to its reliability in indicating tissue damage, its broad accessibility across various laboratory settings, and its comparatively lower cost relative to other inflammatory biomarkers.[23,24]

Incorporating LDH as part of routine admission assessments for aneurysmal SAH patients could enable more tailored management strategies. For instance, patients with significantly elevated LDH levels could be earmarked for intensive monitoring, early prophylactic measures against complications, and more aggressive therapeutic interventions. Furthermore, longitudinal monitoring of LDH trends during hospitalization might provide additional insights into disease progression and the effectiveness of interventions.

This study has several limitations. First, there are still few studies that examine the relationship between LDH levels and outcomes in subarachnoid haemorrhage (SAH). Additionally, limited research reports on subgroup outcomes, and more studies are needed to compare factors such as the mRS score, HH Grade, Fisher Grade, complications, and mortality in SAH patients to strengthen the findings. The cutoff value for LDH to determine

prognosis cannot be established due to varying outcomes across studies. Another issue is the unclear timing of LDH measurements, particularly regarding how long after the event they were taken. Future research should aim to clarify the timing of LDH measurements from the onset of SAH to provide more reliable evidence.

Conclusion

The relationship between LDH levels and outcomes in SAH patients highlights its potential as a prognostic biomarker in aneurysmal SAH. LDH not only reflects the severity of initial injury but also serves as a harbinger of secondary complications and outcomes. Its routine application could refine prognostication and guide individualized treatment strategies, ultimately improving patient outcomes.

Conflict of Interest

The authors declared no conflict of interest.

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Table 1. Keywords search term

Databases	Search terms
PubMed	("LDH"[All Fields] OR ("l lactate dehydrogenase"[MeSH Terms] OR ("l lactate"[All Fields] AND "dehydrogenase"[All Fields]) OR "l lactate dehydrogenase"[All Fields] OR ("lactate"[All Fields] AND "dehydrogenase"[All Fields]) OR "lactate dehydrogenase"[All Fields])) AND ("prognosis"[MeSH Terms] OR "prognosis"[All Fields] OR "prognoses"[All Fields] OR ("outcome"[All Fields] OR "outcomes"[All Fields])) AND ("subarachnoid haemorrhage"[All Fields] OR "subarachnoid haemorrhage"[MeSH Terms] OR ("subarachnoid"[All Fields] AND "haemorrhage"[All Fields]) OR "subarachnoid haemorrhage"[All Fields])
Europe PMC	(Lactate Dehydrogenase OR LDH) AND (prognosis OR outcomes) AND Subarachnoid haemorrhage
ScienceDirect	(Lactate Dehydrogenase OR LDH) AND (prognosis OR outcomes) AND Subarachnoid haemorrhage
Google Scholar	(Lactate Dehydrogenase OR LDH) AND (prognosis OR outcomes) AND Subarachnoid haemorrhage

Table 2. Characteristic of the study

Study ID	Study Design	Country	Sample Size	Median/Mean Age	Inclusion Criteria	Exclusion Criteria
Ding, et al (2019)	Prospective Cohort	China	647	54.82 ± 11.30	**(1)** subarachnoid haemorrhage was caused by intracranial aneurysm, as confirmed by computed tomography angiography or digital subtraction angiography; (**2)** patient was admitted to hospital within 7 days of symptom onset; (**3)** admission serum LDH level was obtained; (**4)** treatment of aneurysm (clipping or interventional) was performed.	**(1)** age <18 years old; **(2)** MV use or diagnosis of pneumonia before surgical treatment; **(3)** patient death within first 48 hours of admission; **(4)** previous use of antiplatelet or anticoagulant medication, steroids, or immunosuppressants; **(5)** history of other neurologic diseases, such as intracranial tumor, stroke, or severe head trauma; and; **(6)** other systemic diseases, such as autoimmune disease, uremia, cirrhosis, cancer, and chronic lung and heart diseases.

Anan, et al (2020)	Retrospective Cohort	Japan	19	NA	**(1)** patients within 14 days of acute SAH	**(1)** cases with suspected meningitis (elevated white blood cells in CSF); **(2)** posterior aneurysm location; **(3)** patients treated with endovascular
Zheng, et al (2021)	Retrospective Cohort	China	202	NA	**(1)** diagnosis of SAH confirmed by CT; **(2)** presence of intracranial aneurysms confirmed using CT angiography (CTA) or digital subtraction angiography (DSA); **(3)** all aneurysms treated using microsurgical clipping; **(4)** CTA and/or DSA performed postoperatively; **(5)** patients were admitted 24 h after the onset of SAH.	**(1)** aSAH detected > 24 h after occurrence; **(2)** other cerebrovascular diseases (such as cerebral arteriovenous malformations, intracranial arteriovenous fistula, or moyamoya syndrome/disease) or intracranial tumors; **(3)** history of myocardial infarction, hepatitis, malignant tumor, pulmonary infarction, leukemia, hemolytic anemia, kidney disease, or progressive muscular atrophy
Zheng, et al (2022)	Retrospective Cohort	China	856	54.5 (10–86)	**(1)** aneurysmal subarachnoid haemorrhage (aSAH) was diagnosed by computed tomography (CT) and computerized tomography angiography (CTA) or digital subtraction angiography (DSA); **(2)** the patients were admitted 24 h after the occurrence of SAH; (3) cerebral aneurysms were treated by microsurgical clipping.	**(1)** aSAH detected > 24 h after the onset; **(2)** the presence of intracranial tumors in patients with other cerebrovascular diseases (such as intracranial arteriovenous malformations, arteriovenous fistula, and Moyamoya syndrome/disease); **(3)** patients with myocardial infarction, pulmonary infarction, hepatitis, kidney disease or progressive muscular atrophy, malignant tumor, leukemia, hemolytic anemia, etc.
Zan, et al (2022)	Retrospective Cohort	China	3524	51.77 (11.68) low ldh vs 56.76 (11.99) high ldh	(1) subarachnoid haemorrhage diagnosed via head computed tomography, magnetic resonance imaging, or angiography, and an aneurysm confirmed with cerebral angiography, magnetic resonance angiography, or computed tomography	(1) aneurysms caused by trauma or arteriovenous malformations; (2) fusiform aneurysms, and nondefinitive aneurysms; aneurysms were treated before ictus or; (3) lack of admission LDH, (4) wrong or non-existent registration in sichuan province

					angiography.	
Cavali, et al (2023)	Retrospective Cohort	Belgium	547	54.044 (±12.9)	1) age > 18 years; 2) diagnosis of ruptured aneurysm as the primary cause of SAH on computed tomography (CT) with angiographic confirmation (either computed tomography angiography or cerebral angiography)	1) pregnancy; 2) patients without 3 months follow up assessment reported in the medical records.
Ren, et al (2023)	Retrospective Cohort	China	190	62 [53–68]	(1) aSAH confirmed on brain computed tomography (CT) and CT angiography or digital subtraction angiography; (2) age ≥18 years	(1) incomplete or unavailable records; (2) refusal to consent; or (3) late admission (>7 days after the ictus of aSAH)

Table 3. Outcome measurement and LDH Values

Study, ID	Type of SAH	LDH Taken	Measured Outcome	LDH Values	Major Findings
Ding, et al (2019)	Aneurysmal Subarachnoid Haemorrhage	Admission	Postoperative Pneumonia (POP)	• **w/o POP**: 189.00 ± 69.20 U/L • **POP**: 261.26 ± 126.51 U/L	LDH might be a helpful predictor of POP occurrence in patients with aSAH. LDH level had a sensitivity of 63.6% and a specificity of 71.3% for predicting POP based on best threshold of 203.5 U/L associated with POP in patients with aSAH, even after adjusting for possible confounding factors.

Anan, et al (2020)	Aneurysmal Subarachnoid Haemorrhage	14 days post operation	Delayed Cerebral Ischemia (DCI)	• **Non-DCI**: 214.7 ± 47.4 U/L • **DCI**: 222.1 ± 56.4 U/L	Venous LDH was found to be higher in the DCI group. Lactate and LDH concentrations in carotid cisternal CSF may vividly reflect EBI and thus may provide predictive biomarkers for DCI following aSAH
Zheng, et al (2021)	Aneurysmal Subarachnoid Haemorrhage	Admission	Clinical Outcome based on mRS 0-2: Good Outcome 3-6: Poor Outcome	• **Good Outcome**: 205.356 ± 76.785 U/L • **Poor Outcome**: 227.119 ± 86.469 U/L	Serum levels of LDH correlated with Hunt–Hess grade, Fisher grade, and neurological functional outcome, and predicted the outcome of aSAH.
			Functional Outcome based on mRS 0: no symptoms 1-2: slight disability 3-4: moderate to serious disability 5-6: Severe Disability to death	• **mRS 0:** 179.247 ± 46.761 U/L • **mRS 1-2:** 193.977 ± 69.399 U/L • **mRS 3-4:** 205.918 ± 59.203 U/L • **mRS 5-6**: 234.188 ± 108.336 U/L	Serum levels of LDH correlated with Hunt–Hess grade, Fisher grade, and neurological functional outcome, and predicted the outcome of aSAH. Serum LDH was higher in patients, with higher mRS Score, howerver phosphate level might play a role. The LDH to phosphate ratio was a potential biomarker and could predict the unfavorable outcome of microsurgical clipping for rIA in 3 month.

			Hunt-Hess Grade	• **HH Grade 1:** 163.880 ± 35.571 U/L • **HH Grade II:** 174.981 ± 49.616 U/L • **HH Grade III:**188.306 ± 50.702 U/L • **HH Grade IV**:225.609 ± 69.509 U/L • **HH Grade V:** 252.851 ± 93.302 U/L	
			Fisher Grade	• **Fisher Grade 1:** 169.492 ± 41.621 U/L • **Fisher Grade 2:** 177.097 ± 42.621 U/L • **Fisher Grade 3:** 198.709 ± 72.553 U/L • **Fisher Grade 4:** 210.811 ± 68.962 U/L	
Zheng, et al (2022)	Aneurysmal Subarachnoid Haemorrhage	Admission	mRS Score 0-2 : Good Outcome 3-6 : Poor Outcome	• **Good Outcome:** 180.378 ± 50.695 U/L • **Poor Outcome:** 227 ± 83.125 U/L	Serum LDH was seen higher in Poor outcome group patients. LDH may be related to neuronal damage, cerebral hypoxia, and early brain injury after aneurysm ruptures.

Zan, et al (2022)	Aneurysmal Subarachnoid Haemorrhage	Admission	Mortality at 90 days	• **Fisher Grade 1:** 37.989 ± 14.115 U/L • **Fisher Grade 2:** 135.508± 18.017 U/L • **Fisher Grade 3:** 103.865 ± 23.384 U/L • **Fisher Grade 4:** 376.806 ± 89.308 U/L	In patients with aSAH, both baseline and longitudinal high-serum LDH levels were associated with all-cause mortality. Mortality was seen higher in patients with higher LDH at admission.
Cavali, et al (2023)	Aneurysmal Subarachnoid Haemorrhage	Admission	**GOS Score** 1: dead 2: persistent vegetative state 3: severe disability 4: moderate disability 5: good recovery 1-3: Unfavorable Outcome 4-5: Favorable Outcome	• **Favorable Outcome:** 176.05 ±8.72 U/L • **Unfavorable Outcome:** 215.29 ± 14.29 U/L	Lactate dehydrogenase is an easily available biomarkers for short term neurological outcome in acute SAH in and hospital mortality

			In Hospital Mortality	• **Non-mortality group:** 180.1 ± 9.7 U/L • **Mortality group:** 221.58 ± 15.45 U/L	
Ren, et al (2023)	Aneurysmal Subarachnoid Haemorrhage	Admission	Mortality 7 days after discharge	• **Non-mortality group:** 236.3 ± 12.4 U/L • **Mortality Group:** 239.8 ± 70.5 U/L	Laboratory screening may provide a useful tool for the management of aSAH patients requiring MV in stratifying risk levels for mortality and for better clinical decision-making

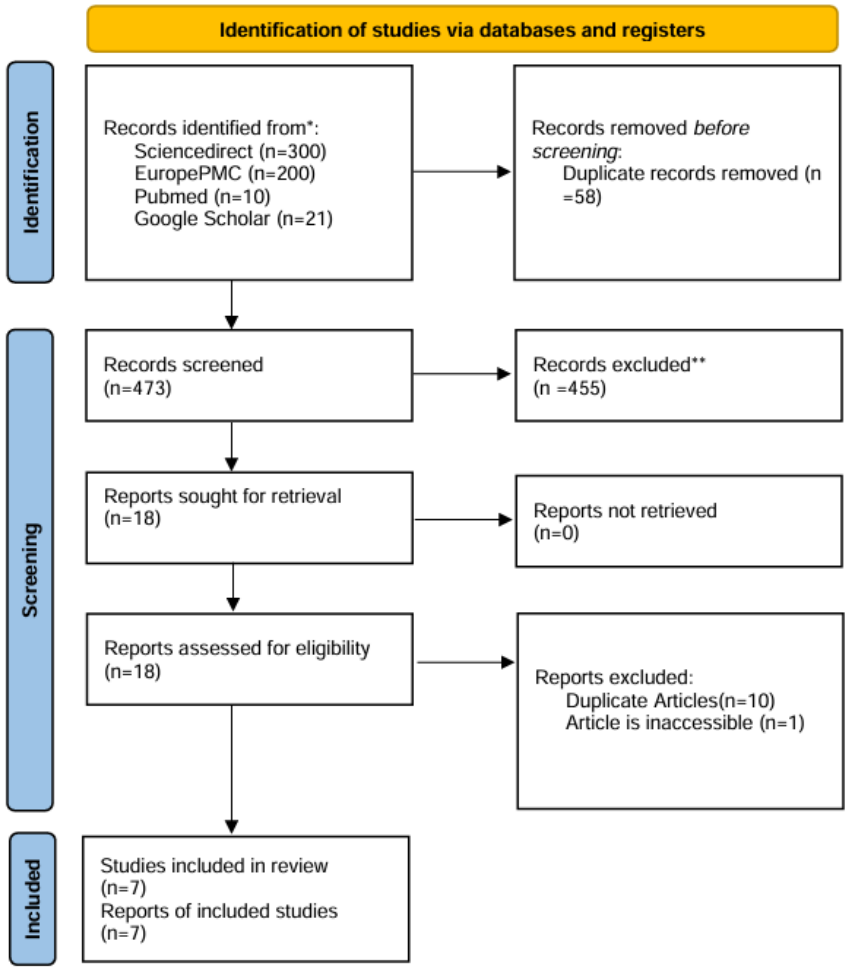

Figure 1. PRISMA Guidelines

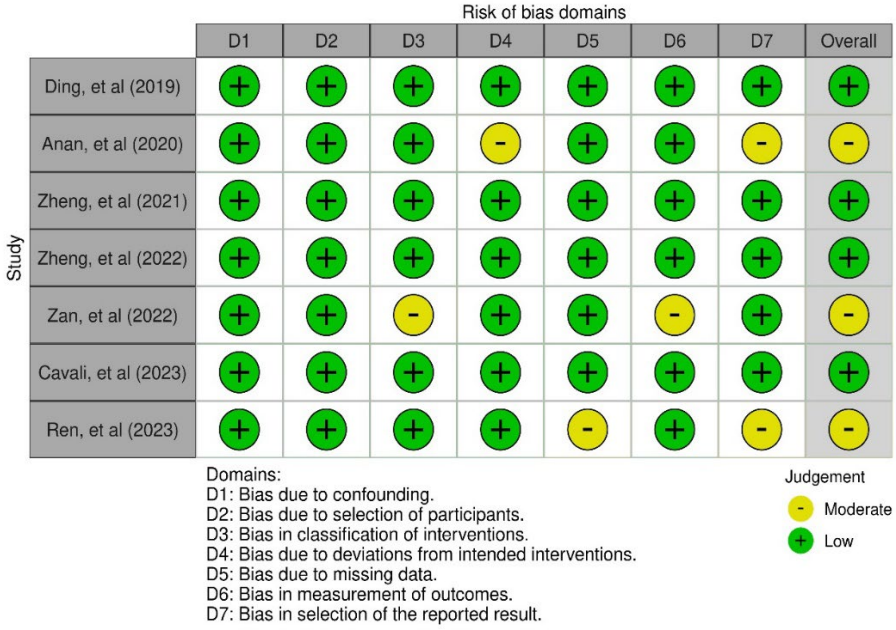

Figure 2. Risk of Bias of each study

Author Guidelines

Submission

The submitted manuscript should be addressed to the Editor-in-chief of Lumina: Indonesian Journal of Neurology. The manuscript will be submitted through online submission by a registered user at https://ojs.uph.edu/index.php/lumina/index. For further questions, please kindly contact us at (email)

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- ICMJE Conflict of Interest Statement Form (*[Insert Link]*)
- Copy of Ethical Approval (if applicable)
- Final Checklist signed by all authors

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