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SCIENTIFIC JOURNAL OF PHARMACEUTICAL DEVELOPMENT AND MEDICAL APPLICATION



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hal. 45

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Ansietas pada Lansia: Prevalensi, Faktor Penanda, dan Penanganannya

Raymond R. Tjandrawinata

School of Bioscience, Technology and Innovation. Atma Jaya Catholic University of Indonesia

Abstrak

Ansietas pada lansia merupakan masalah kesehatan mental dengan prevalensi yang cukup tinggi, namun sering kurang terdeteksi akibat tumpang tindih gejala dengan penyakit fisik serta perubahan psikososial yang menyertai proses penuaan. Artikel ini membahas prevalensi global ansietas pada lansia, faktor penanda utama, serta pendekatan penatalaksanaan berbasis bukti. Berbagai penelitian menunjukkan bahwa ansietas pada lansia berkaitan dengan beban penyakit kronis (termasuk nyeri), gangguan gastrointestinal fungsional seperti *irritable bowel syndrome* (IBS), tingkat aktivitas fisik rendah, serta pola makan yang tidak sehat. Hubungan langsung antara kadar vitamin D serum dan tingkat ansietas pada lansia masih menunjukkan hasil yang inkonsisten; namun terdapat bukti yang mengindikasikan adanya hubungan tidak langsung melalui peran vitamin D dalam kesehatan gastrointestinal dan peradangan. Penatalaksanaan yang direkomendasikan untuk kasus ansietas pada lansia bersifat biopsikososial, dengan intervensi psikologis seperti *cognitive behavioral therapy* (CBT) dan modifikasi gaya hidup sebagai lini pertama serta farmakoterapi selektif pada kasus dengan tingkat keparahan sedang hingga berat.

Kata kunci: ansietas lansia, kesehatan mental geriatri, vitamin D, *irritable bowel syndrome*, penatalaksanaan biopsikososial

Abstract

Anxiety in older adults is a prevalent mental health issue, yet it is frequently underrecognized due to the overlap symptoms with physical illnesses and age-related psychosocial changes. This article reviews the global prevalence, key risk markers, and evidence-based management approaches. Numerous studies indicate that anxiety in older adults is associated with chronic medical conditions (including pain), functional gastrointestinal disorders such as *irritable bowel syndrome* (IBS), low level of physical activity, and unhealthy dietary patterns. Evidence regarding direct association between serum vitamin D levels and anxiety in older adults remains inconsistent; however, emerging evidence suggests an indirect association mediated through the role of vitamin D in gastrointestinal health and inflammatory process. Management of anxiety in older adults is recommended to follow a biopsychosocial approach, prioritizing psychological interventions such as cognitive behavioral therapy (CBT) and lifestyle modification, and selective pharmacotherapy reserved for moderate to severe cases.

Keywords: anxiety in elderly, geriatric mental health, vitamin D, *irritable bowel syndrome*, biopsychosocial management

Kecemasan (ansietas) merupakan gangguan mental dengan prevalensi yang cukup tinggi dan cukup banyak dialami oleh populasi lanjut usia. Studi metaanalisis global terbaru menunjukkan bahwa sekitar 16,5% lansia di seluruh dunia mengalami gejala kecemasan. Angka ini bervariasi di berbagai wilayah, misalnya, prevalensi kecemasan pada lansia tercatat lebih tinggi di beberapa negara Afrika dibandingkan kawasan lain (Jalali *et al.*, 2024). Meskipun prevalensi gangguan kecemasan yang terdiagnosis pada lansia dilaporkan sekitar 1–14% dalam populasi umum, proporsi lansia dengan gejala kecemasan subklinis dapat mencapai 15–52% menurut berbagai studi (Crocco *et al.*, 2017; Wolitzky-Taylor *et al.*, 2010). Penting dicatat bahwa gejala kecemasan yang tidak memenuhi kriteria diagnosis penuh sekalipun dapat menyebabkan gangguan fungsi dan penurunan kualitas hidup pada lansia (Lenze dan Wetherell, 2011). Kecemasan pada lansia sering kali terjadi bersamaan dengan depresi, dan hal ini dapat memperburuk kesehatan fisik, kognitif, serta kemampuan fungsional sehari-hari (Bryant *et al.*, 2008).

Kecemasan memiliki dampak yang sangat signifikan pada kualitas hidup lansia. Selain menurunkan kualitas hidup, kecemasan juga dapat meningkatkan risiko komplikasi kesehatan fisik. Sebagai contoh, lansia dengan penyakit kronis seperti penyakit jantung koroner, diabetes, atau penyakit paru obstruktif kronis (PPOK) dilaporkan memiliki tingkat kecemasan yang lebih tinggi, yang selanjutnya berkorelasi dengan kontrol penyakit yang lebih buruk dan frekuensi rawat inap yang lebih tinggi (Crocco *et al.*, 2017). Kecemasan juga umum ditemukan pada lansia penderita demensia atau penyakit Parkinson, dan gejala kecemasan dapat mempercepat penurunan kognitif serta kemampuan fungsional pada kondisi neurodegeneratif tersebut (Lenze dan Wetherell, 2011). Dengan demikian, kecemasan di usia lanjut bukan hanya masalah psikologis semata, melainkan berhubungan erat dengan kondisi kesehatan fisik, sehingga membutuhkan perhatian serius.

Banyak faktor yang dapat memengaruhi kejadian maupun tingkat keparahan kecemasan pada lansia. Status kesehatan umum merupakan salah satu penanda penting, mengingat lansia dengan banyak penyakit kronis atau penurunan fungsi fisik cenderung lebih rentan mengalami kecemasan (Crocco *et al.*, 2017). Sebagai contoh, adanya nyeri kronis, keterbatasan mobilitas, atau penyakit pencernaan fungsional seperti *irritable bowel syndrome* (IBS) dapat menjadi pemicu atau faktor yang memperberat kecemasan. IBS dan gangguan saluran pencernaan fungsional lain diketahui memiliki hubungan dua arah dengan kecemasan: pasien IBS lebih sering mengalami kecemasan dibanding populasi umum, dan sebaliknya individu dengan gangguan kecemasan sering melaporkan gejala IBS. Hal ini diduga terkait disfungsi *brain-gut axis*, di mana stres dan kecemasan dapat memengaruhi aktivitas usus, sedangkan gangguan pencernaan kronis turut meningkatkan beban psikologis (Zhang *et al.*, 2021). Dengan demikian, kondisi kesehatan fisik (seperti ada tidaknya IBS, nyeri, atau penyakit kronis lain) dapat berperan sebagai penanda risiko kecemasan pada lansia.

Tingkat aktivitas fisik juga merupakan faktor penting yang berkaitan dengan kecemasan pada populasi yang berusia lanjut. Lansia yang aktif secara fisik umumnya memiliki kesehatan mental yang lebih baik. Penelitian menunjukkan bahwa olahraga teratur berhubungan dengan penurunan gejala kecemasan pada lansia. Dalam suatu tinjauan sistematis, semua studi yang melibatkan latihan fisik teratur pada lansia menunjukkan adanya penurunan signifikan dalam gejala kecemasan dibanding sebelum intervensi. Aktivitas fisik diyakini memberikan manfaat pada kesehatan mental melalui berbagai mekanisme, di antaranya meningkatkan regulasi neuroendokrin dan menurunkan peradangan, serta memperbaiki kualitas tidur dan rasa percaya diri. Oleh karena itu, kurangnya aktivitas fisik dapat menjadi penanda risiko meningkatnya kecemasan, sedangkan rutinitas olahraga ringan hingga sedang bisa menjadi strategi protektif untuk kesehatan mental lansia (Mochcovitch *et al.*, 2016).

Pola makan dan status gizi merupakan aspek lain yang berpengaruh terhadap kecemasan pada lansia. Asupan nutrisi yang seimbang, misalnya, pola *Mediterranean diet* yang kaya sayur, buah, biji-bijian, dan lemak sehat dikaitkan dengan risiko lebih rendah terhadap gangguan *mood* dan kecemasan pada usia lanjut (Masana *et al.*, 2019). Sebaliknya, pola diet tinggi lemak jenuh dan gula tambahan tampak berhubungan dengan tingkat kecemasan yang lebih tinggi pada lansia. Analisis dalam studi ATTICA melaporkan bahwa lansia dengan pola diet tinggi lemak jenuh dan gula tambahan memiliki skor kecemasan yang lebih tinggi dibanding mereka yang menerapkan pola makan yang sehat (Masana *et al.*, 2019). Di samping itu, defisiensi nutrisi tertentu dapat berdampak pada kesehatan mental. Vitamin D adalah salah satu mikronutrien yang akhir-akhir ini banyak diteliti, yang berperan penting dalam fungsi sistem saraf dan imunitas. Lansia merupakan kelompok yang lebih rentan mengalami kekurangan vitamin D. Kadar vitamin D serum sempat diduga sebagai penanda biologis yang memengaruhi kecemasan. Namun, temuan penelitian masih beragam. Beberapa penelitian *cross-sectional* pada populasi dewasa menunjukkan adanya korelasi terbalik antara kadar 25(OH)D dengan gejala kecemasan. Analisis data National Health and Nutrition Examination Survey (NHANES) di Amerika Serikat melaporkan bahwa kelompok dengan kadar vitamin D tertinggi memiliki risiko kecemasan lebih rendah secara signifikan dibanding kelompok dengan

kadar terendah setelah mengontrol berbagai variabel. Meskipun demikian, terdapat pula riset yang tidak menemukan hubungan langsung yang bermakna antara kadar vitamin D dan skor kecemasan (Wen *et al.*, 2024). Dalam populasi lansia, hasil korelasi langsung vitamin D dengan kecemasan masih inkonsisten.

Menariknya, terdapat indikasi mengenai hubungan tidak langsung melalui peran vitamin D terhadap kondisi kesehatan lain yang memengaruhi kecemasan. Vitamin D diketahui berpengaruh positif terhadap IBS dan gangguan pencernaan inflamasi, yang dapat memengaruhi kesehatan mental. Suplementasi vitamin D dilaporkan efektif mengurangi gejala IBS dan meningkatkan kualitas hidup pasien. Tinjauan sistematis menunjukkan bahwa pasien IBS atau *inflammatory bowel disease* (IBD) pada sebagian besar uji klinis mengalami perbaikan yang signifikan pada tingkat kecemasan dan depresi setelah suplementasi vitamin D (Głabska *et al.*, 2021). Hal ini mengindikasikan bahwa vitamin D dapat secara tidak langsung menurunkan kecemasan melalui perbaikan kesehatan gastrointestinal. Oleh karena itu, disarankan agar penelitian selanjutnya mengeksplorasi interaksi vitamin D dengan faktor lain seperti status kesehatan umum, aktivitas fisik, dan pola makan dalam memengaruhi kecemasan pada lansia (Wen *et al.*, 2024).

Penanganan ansietas pada lansia perlu mempertimbangkan kondisi fisik, kognitif, dan sosial. Pendekatan nonfarmakologis dianjurkan sebagai lini pertama, terutama untuk kasus ringan hingga sedang. Terapi psikologis seperti *cognitive behavioral therapy* (CBT) terbukti efektif mengurangi gejala kecemasan pada usia lanjut (Stanley *et al.*, 2013). Metaanalisis menunjukkan bahwa CBT menghasilkan tingkat remisi diagnostik yang lebih tinggi dibanding farmakoterapi saja (Wolitzky-Taylor *et al.*, 2010). Intervensi lain seperti terapi relaksasi, *mindfulness-based stress reduction*, dan konseling suportif juga bermanfaat, terutama bila disertai dukungan keluarga dan sosial (Shamseer *et al.*, 2023).

Pendekatan gaya hidup sehat perlu dilakukan bersamaan, termasuk peningkatan aktivitas fisik, pola tidur teratur, dan nutrisi seimbang. Terapi farmakologis dipertimbangkan bila gejala berat atau tidak merespons pendekatan awal. Pedoman merekomendasikan penggunaan obat golongan antidepresan seperti *selective serotonin reuptake inhibitor* (SSRI) dan *serotonin-norepinephrine reuptake inhibitor* (SNRI) sebagai lini pertama karena efektivitas dan profil keamanannya yang tergolong baik pada lansia. Obat golongan *benzodiazepine* sebaiknya dihindari atau dibatasi dengan ketat karena adanya risiko sedasi, jatuh, dan gangguan kognitif (Crocco *et al.*, 2017).

Ansietas pada lansia merupakan masalah kesehatan mental dengan tingkat prevalensi yang tinggi dan berdampak luas. Berbagai faktor penanda seperti status kesehatan fisik, adanya penyakit *irritable bowel syndrome* (IBS), aktivitas fisik, pola makan, dan vitamin D, berperan dalam memengaruhi risiko dan derajat keparahan kecemasan. Meskipun hubungan langsung antara vitamin D dan kecemasan masih inkonsisten, peran vitamin D dalam kesehatan tubuh secara umum dan pencegahan gangguan seperti IBS menunjukkan potensi mekanisme yang tidak langsung. Pendekatan holistik berbasis biopsikososial tetap menjadi strategi terbaik dalam pencegahan dan terapi kecemasan pada lansia.

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Relationship between Serum Vitamin D Levels and Anxiety Severity in Elderly Patients at the Internal Medicine and Psychiatry Clinic of RSUP Prof. dr. I.G.N.G. Ngoerah, Denpasar

Helen Widiani¹, Tuty Kuswardhani²

¹Medical Specialist Education Program in Internal Medicine, Faculty of Medicine Udayana University/RSUP Prof. dr. I.G.N.G. Ngoerah, Denpasar, Bali, Indonesia

²Department of Internal Medicine, Faculty of Medicine Udayana University/RSUP Prof. dr. I.G.N.G. Ngoerah, Denpasar, Bali, Indonesia

Abstract

Serum vitamin D plays an important role in both physical and mental health. Decreased serum vitamin D levels in the elderly are often associated with anxiety. This study aims to determine the relationship between serum vitamin D levels and anxiety severity in elderly patients. A cross-sectional analytical study was conducted and subjects were recruited using consecutive sampling at RSUP Prof. dr. I.G.N.G. Ngoerah. Serum vitamin D levels were measured using the human vitamin D Chemiluminescent Microparticle Immunoassay (CMIA), and anxiety severity were assessed using the Geriatric Anxiety Inventory (GAI). The median age of the participants was 66.5 years (range: 60–83 years). The most common anxiety severity observed was mild (40%) and the most prevalent vitamin D status was insufficient (40%). Statistical analysis showed no significant correlation between serum vitamin D levels and anxiety severity ($p=0.816$). The Spearman correlation test yielded a p -value of 0.214 with a correlation coefficient of -0.125. However, path analysis revealed that vitamin D indirectly affects anxiety severity through inflammatory bowel syndrome (IBS), with an effect size of -0.06 ($p=0.035$).

Keywords: serum vitamin D levels, anxiety levels, elderly.

Abstrak

Serum vitamin D berperan penting dalam kesehatan fisik maupun mental. Penurunan kadar serum vitamin D pada lansia sering dikaitkan dengan kecemasan. Penelitian ini bertujuan untuk mengetahui hubungan antara kadar serum vitamin D dengan derajat keparahan kecemasan pada pasien lansia. Penelitian yang dilakukan di RSUP Prof. dr. I.G.N.G. Ngoerah Denpasar ini menggunakan pendekatan analitik potong lintang (*cross-sectional*) dengan rekrutmen subjek melalui metode *consecutive sampling*. Kadar serum vitamin D diukur dengan menggunakan *human vitamin D Chemiluminescent Microparticle Immunoassay* (CMIA), dan derajat keparahan kecemasan dinilai dengan menggunakan kuesioner *Geriatric Anxiety Inventory* (GAI). Median usia subjek penelitian adalah 66,5 tahun (rentang: 60–83 tahun). Derajat keparahan kecemasan yang paling sering ditemukan adalah kecemasan ringan (40%), dan status kadar serum vitamin D yang paling umum adalah insufisiensi (40%). Analisis statistik menunjukkan tidak ada korelasi yang signifikan antara kadar serum vitamin D dengan derajat keparahan kecemasan ($p=0,816$). Uji korelasi Spearman menghasilkan nilai $p=0,214$ dan koefisien korelasi -0,125, namun *path analysis* menunjukkan bahwa vitamin D berpengaruh tidak langsung terhadap derajat keparahan kecemasan melalui *inflammatory bowel syndrome* (IBS), dengan besaran efek -0,06 ($p=0,035$).

Kata kunci: kadar vitamin D serum, derajat keparahan kecemasan, lanjut usia.

Introduction

As global life expectancy increases, the elderly population continues to grow, affecting nearly every aspect of society. The global elderly population is projected to reach 1.4 billion by 2030 and 2.1 billion by 2050.¹ According to the 2010 census, Indonesia ranked among the five countries with the largest elderly populations, with approximately 18.1 million individuals,

representing 7.6% of the total population. Projections by the Biro Pusat Statistik (BPS) estimate that this number will increase to 27.1 million by 2020, 33.7 million by 2025, and 48.2 million by 2035.²

Elderly individuals are particularly vulnerable to mental disorders, especially anxiety and depression. Anxiety is a psychological condition characterized by excessive fear and worry related to uncertain future events.³ The reported prevalence of anxiety among elderly populations ranges from approximately 14.2 to 39.4%.^{4,5,6}

Epidemiological studies have found that in developed countries, 35.5 to 50.3% of patients with severe anxiety disorders receive inadequate treatment, and this proportion rises to 76.3–85.4% in developing countries. In Switzerland and France, the prevalence of anxiety disorders ranges from 3.2 to 14.2%. In Chongqing, China, 21.63 % of the elderly, particularly those with physical illnesses, experience anxiety.⁷ Two recent studies in India reported an overall prevalence of anxiety disorders among the elderly populations of 10.8 and 10.7%.⁸ In Indonesia, the prevalence of anxiety disorder is 6.9 % among individuals aged 55–65; 9.7 % among those aged 65–75, and 13.4 % in those aged 75 and older.²

Several hypotheses have been proposed to explain on the pathophysiology of anxiety disorders, including alterations in neurotransmitters, brain chemical imbalances, inflammation, reduced neuroplasticity, chronic stress, and nutritional deficiencies. Decades of research have emphasized the critical role of malnutrition in both anxiety and depression. Recent studies indicate that vitamin D deficiency may play a complex role in mood disorders, including anxiety.^{9,10} Vitamin D, a steroid hormone, can be obtained through dietary intake or synthesized from 7-dehydrocholesterol under ultraviolet (UV) B radiation in the skin. Both genetic and environmental factors influence vitamin D status and metabolism. Vitamin D exerts multiple effects on the brain, including maintaining calcium homeostasis, regulating neurotrophic factors, providing neuroprotection, modulating neurotransmission, as well as promoting synaptic plasticity. Research on vitamin D's role in the brain has opened new directions in psychiatric studies.^{10,11} Studies have reported a significant inverse association between serum vitamin D levels and anxiety risk. For example, one large-scale analysis found an odds ratio of 0.92 ($p=1.46 \times 10^{-23}$), while another study highlighted an inverse β -coefficient ($\beta=-0.030$, $SE=0.00$, $p=1.21 \times 10^{-21}$) for generalized anxiety disorder (GAD) scores relative to vitamin D level.¹⁰

Proposed mechanisms underlying the anxiolytic effects of vitamin D, as demonstrated in experimental studies include enhanced neuronal glutamate and glutamine metabolism, which affects neurotransmitter levels.¹² Other studies indicate that vitamin D is associated with the expression of neurotrophic factor genes, stimulates neurogenesis, and promotes antioxidant capacity in neurons, thereby protecting against oxidative degeneration. Furthermore, vitamin D also serves as an essential coenzyme in the synthesis of monoamines neurotransmitters, including norepinephrine and dopamine.⁹

In the United States, approximately 20% of individuals over the age 50 are vitamin D deficient.¹³ Although numerous studies have investigated the relationship between anxiety and serum vitamin D levels, the findings remain inconsistent. Some studies report that vitamin D deficiency is associated with anxiety symptoms and that supplementation may reduce the symptoms.^{9,10,11} In a cohort study by Zhu et al. (2020), participants with vitamin D deficiency (25[OH]D less than 75 nmol/l) who received vitamin D supplementation at a dose of 1,600 IU/day for six months showed greater improvements in anxiety compared to controls. Significant between-group differences were observed at three and 6 months using the Hamilton Anxiety Rating Scale (HAMA), Hamilton Depression Rating Scale (HAMD), and Revised Social Anhedonia Scale (RSAS) ($p<0.05$).

A randomized controlled trial assigned participants to receive weekly vitamin D₃ at a dose of 25,000 IU (n=45) or no supplementation (n=45). Serum 25-hydroxyvitamin D levels increased significantly in the supplemented group, rising from 19.98±6.73 ng/ml at baseline to 26.56±8.64 ng/ml at 6 months and 28.71±9.03 ng/ml at 12 months ($p<0.001$). At

six months, anxiety scores assessed via PHQ-9 were significantly lower in the supplemented group (38.02 ± 9.03 vs. 43.91 ± 7.18 ; $p=0.003$), with further improvement at 12 months (32.35 ± 7.77 vs. 44.97 ± 7.78 ; $p<0.001$). Similarly, PHQ-9 depression scores decreased significantly at both follow-up time points ($p=0.021$ and $p<0.001$). The authors concluded that weekly vitamin D supplementation effectively reduced anxiety in high-risk populations.¹⁴

However, Granlund et al. (2020) reported no association between vitamin D status and anxiety disorders in a cohort of Middle Eastern- and African-born immigrants living in Sweden. In their study, 71% of participants had serum 25-hydroxyvitamin D [25(OH)D] levels below 50 nmol/l, and 11% of them had levels below 25 nmol/l. Overall, anxiety, depression, and health-related quality of life (HRQOL) were not associated with 25(OH)D concentrations in the study population. Although anxiety was relatively common among Middle Eastern immigrant women (32.7%), only in this subgroup, after adjustment, lower 25(OH)D levels (≤ 49 nmol/l vs. ≥ 50 nmol/l) were associated with an increased risk of anxiety (OR=23.2; 95% CI=1.97–271.9; $p=0.012$). However, reverse causality could not be excluded. The study did not demonstrate an association between vitamin D status and depression, anxiety, or HRQOL in that group.¹⁵

The relationship between anxiety and serum vitamin D levels remains inconclusive and controversial, highlighting the need for further research. Previous studies have primarily focused on general adult or immigrant populations, predominantly in developed countries, and have not specifically examined older adults. Therefore, this study was designed to investigate the association between serum vitamin D levels and anxiety severity among elderly.

Methods

This was an observational analytic study with a cross-sectional design, aimed to determine the relationship between serum vitamin D levels and anxiety among patients attending the internal medicine and psychiatry polyclinics of RSUP Prof. dr. I.G.N.G. Ngoerah, Denpasar, between February and July 2024.

The study sample consisted of individuals aged ≥ 60 years who met the inclusion criteria. Exclusion criteria included severe mental disorders (schizophrenia, bipolar disorder, or depression), dementia, ongoing treatment for anxiety, and refusal to participate. The required sample size was 100 participants. Data analysis was divided into descriptive statistical analysis, Chi-square test, Spearman's correlation test, ordinal logistic regression analysis, and path analysis. Descriptive statistical analysis was used to describe general characteristics. Normally distributed numerical variables were presented as mean and standard deviation (SD), whereas non-normally distributed variables were presented as median and interquartile range. Categorical variables were expressed as relative frequencies or counts and percentages. The Kolmogorov-Smirnov test was used to assess data normality. Bivariate analysis was conducted to compare the proportions of anxiety levels across serum vitamin D categories using a 2 x 2 comparison table. The Chi-square test or Fisher's exact test was applied when Chi-square assumptions were not met. Multivariate analysis was performed to evaluate the relationship between serum vitamin D categories and anxiety severity using ordinal logistic regression. Results were considered significant if $p<0.05$. All statistical analysis were conducted using SPSS.

Path analysis was performed to assess the relationship between serum vitamin D levels and anxiety severity by constructing a diagram or schematic model based on the research concept within statistical software. This analysis enables identification of direct, indirect, and total effects among variables. All stages of path analysis were performed using Statistical Software SE version 12.

Results

Based on the results of the study involving 100 participants, their characteristics are summarized in **Table 1**. The median age of the participants was 66.5 years (range 60–83 years), with a majority of participants were male (52%). Regarding educational attainment, the most common category was low education (no formal schooling, elementary school, or junior high school), accounting for 53% of the participants. Most participants were unemployed or retired (87%). The mean body mass index (BMI) was 22.62%. In terms of marital status, 64% of participants were married. The most prevalent comorbidities were hypertension (54%), diabetes mellitus (38%), coronary heart disease (30%), irritable bowel syndrome (11%), malignancies (10%), thyroid disease (6%), and chronic obstructive pulmonary disease (6%). Overall, 54% of participants had two or more comorbidities.

Tabel 1. Characteristics of study participant

Variable	n=100
Age (year) median (min-max)	66.5 (60-83)
60-69 years, n (%)	67 (67)
≥ 70 years, n (%)	33 (33)
Sex, n (%)	
Male	52 (52)
Female	48 (48)
Education, n (%)	
No formal schooling	12 (12)
Elementary	33 (33)
Junior high school	13 (13)
Senior high school	18 (18)
Bachelor or master degree	24 (24)
Education group, n (%)	
Low education (no formal schooling-junior high school)	58 (58)
High education (senior high school-bachelor/master)	42 (42)
Employment status, n (%)	
Working	13 (13)
Not working	87 (87)
BMI (kg/m2), mean±SD	22.62±4.17
<18.5 (underweight)	13 (13)
18.5-22.9 (normal)	44 (44)
23-24.9 (overweight)	13 (13)
≥ 25 (obese)	30 (30)
Marital status, n (%)	
Married	64 (64)
Unmarried	36 (36)
Comorbid, n (%)	
Diabetes Mellitus	38 (38)
Hypertension	54 (54)
Coronary heart disease	30 (30)
Tyroid disease	6 (6)
Chronic obstructive pulmonary disease	9 (9)
Irritable bowel syndrome	11 (11)
Malignancy	10 (10)
Number of Comorbidities, n (%)	
No comorbidities	23 (23)
1 Comorbidity	23 (23)
≥2 Comorbidities	54 (54)

Based on the results of the bivariate analysis using the Chi-square test, none of the variables were significantly associated with anxiety severity. Specifically, no statistically significant relationship was observed between serum vitamin D levels and anxiety severity, with a *p*-value of 0.816. Similarly, the Spearman's correlation test also revealed that the correlation between serum vitamin D levels and anxiety severity was not statistically significant, with a *p*-value of 0.214. The correlation coefficient was -0.125, suggesting a negative correlation with a weak correlation strength.

Table 2. Bivariate analysis between serum vitamin D levels and anxiety severity

		Anxiety severity				p value
		Not anxiety, n (%)	Mild, n (%)	Moderate, n (%)	Severe, n (%)	
Vitamin D status	Deficiency	3(11.5%)	9(34.6%)	4(15.4%)	10(38.5%)	0.81
	Insufficiency	5(12.5%)	15(37.5%)	9(22.5%)	11(27.5%)	
	Normal	5(14.7%)	16 (47%)	4(11.8%)	9(26.5%)	
Age (years)	60- 69	8(11.9%)	30(44.8%)	13(19.4%)	16(23.9%)	0.21
	≥70	5(15.1%)	10(30.3%)	4 (12.1%)	14(42.4%)	
Sex	Male	8(15.4%)	18(34.6%)	10(19.2%)	16(30.8%)	0.66
	Female	5(10.4%)	22(45.8%)	7 (14.6%)	14(29.2%)	
Education	Low	6(10.3%)	28(48.3%)	10(17.2%)	14(24.1%)	0.19
	High	7(16.7%)	12(28.6%)	7 (16.7%)	16(38.1%)	
Employment status	Working	2(15.4%)	5(38.5%)	2 (15.4%)	4 (30.8%)	0.99
	Not working	11(12.6%)	35(40.2%)	15(17.2%)	26 (30%)	
BMI	<18,5	0 (0%)	8(61.5%)	1 (7.7%)	4(30.8%)	0.20
	18.5-22.9	4 (9.1%)	20(45.5%)	6(13.6%)	14(31.8%)	
	23-24.9	2(15.4%)	2(15.4%)	4(30.8%)	5(38.5%)	
	≥25	7 (23.3%)	10(33.3%)	6 (20%)	7 (23.3%)	
Marital status	Married	8(12.5%)	25 (39%)	13(20.3%)	18(28.1%)	0.69
	Unmarried	5 (14%)	15 (42%)	4 (11%)	12(33%)	
DM	Yes	5(13.2%)	16(42.1%)	7(18.4%)	10(26.3%)	0.94
	No	8 (13%)	24 (39%)	10 (16%)	20 (32%)	
HT	Yes	8 (15%)	23(42.5%)	10(18.5%)	13(24%)	0.57
	No	5(10.8%)	17 (37%)	7(15.2%)	17(37%)	
CAD	Yes	4(13.3%)	11(36.7%)	5(16.7%)	10(33.3%)	0.96
	No	9(12.8%)	29(41.4%)	12(17.1%)	20(28.6%)	
Thyroid	Yes	1 (16.7%)	2 (33.3%)	1 (16.7%)	2 (33.3%)	0.98
	No	12(12.8%)	38(40.4%)	16 (17%)	28(29.8%)	
COPD	Yes	1 (11.1%)	5 (55.5%)	1 (11.1%)	2 (22.2%)	0.79
	No	12(13.2%)	35(38.5%)	16(17.6%)	28(30.7%)	
IBS	Yes	0 (0%)	3 (27.3%)	1 (9.1%)	7 (63.6%)	0.06
	No	13(14.6%)	37(41.6%)	16 (18%)	23(25.8%)	
Malignancy	Yes	0 (0%)	6 (60%)	1 (10%)	3 (30%)	0.41
	No	13(14.4%)	34(37.8%)	16(17.8%)	27 (30%)	
Comorbid	0	3 (13%)	9 (39.2%)	4 (17.4%)	7 (30.4%)	0.99
	1	3 (13%)	8 (34.8%)	5 (21.7%)	7 (30.4%)	
	≥ 2	7 (13%)	23(42.6%)	8 (14.8%)	16(29.6%)	

BMI: body mass index
 DM: diabetes mellitus
 HT: hypertension
 CAD: coronary artery disease
 COPD: chronic obstructive pulmonary disease
 IBS: inflammatory bowel syndrome

This study evaluated the associations and effects of independent variables on anxiety. Multivariate analysis using ordinal regression was performed to determine the effect of each variable on anxiety. The results indicated that irritable bowel

syndrome (IBS) was significantly associated with anxiety, with an effect size of 1.697 (95% CI= 0.18–3.215, $p=0.028$). No other variables demonstrated statistically significant association with anxiety.

Table 3. Multivariate analysis results for anxiety

Variable	Effect size	CI 95%		p value
		Lower bound	Upper bound	
Age	-0.311	-1.224	0.602	0.505
Education	-0.538	-1.339	0.263	0.188
BMI	0.449	-0.743	1.642	0.460
Irritable bowel syndrome	1.697	0.18	3.215	0.028
Vitamin D deficiency	0.572	-0.573	1.717	0.327
Vitamin D insufficiency	0.197	-0.720	1.114	0.673
Normal vitamin D	0	-	-	-

BMI: body mass index

Based on the results of the Structural Equation Modeling (SEM) analysis, vitamin D demonstrated an indirect effect on anxiety scores through the pathway of irritable bowel syndrome (IBS). Indirectly, vitamin D showed a negative correlation with anxiety scores, with an effect size of -0.06 ($p=0.035$). However, no significant direct or total effects of vitamin D on anxiety scores were observed. In contrast, IBS showed a direct and significant correlation with anxiety scores. Other variables, including employment status, body mass index (BMI), hypertension, thyroid disease, diabetes mellitus, chronic obstructive pulmonary disease (COPD), malignancy, and coronary heart disease (CHD) possessed no significant direct or indirect correlation with anxiety.

Table 4. Direct and indirect effects of the variables on anxiety scores

	Total effect	Direct effect	Indirect effect
Vitamin D	-0.11	-0.04	-0.06*
Sex	-0.93	-2.23	1.30
Employment status	0.57	0.43	0.14
BMI	-0.07	0	-0.07
IBS	-4.69*	-4.69*	0
Hypertension	0.75	0.50	0.24
Thyroid disease	-0.88	-0.54	-0.34
Diabetes mellitus	1.08	1.29	-0.21
COPD	0.74	1.19	-0.45
Malignancy	0.84	0.59	0.24
CAD	-0.20	-0.29	0.09

* $p<0.05$

Discussion

In this study, the median age of the 100 participants was 66.5 years (range 60–83 years). When participants were categorized into the 60–69 year (67%) and ≥ 70 year (33%) age groups, no statistically significant difference was observed ($p=0.207$). Consistently, multivariate analysis showed an effect size of -0.311 (95% CI=-1.224 to 0.602, $p=0.505$), which was also not statistically significant.

In another study, participants aged 65 years comprised 36% of the study population, whereas those over 65 years accounted for 64%, with a mean age of 67.24 ± 3.07 years. Older adults are considered at high risk for vitamin D deficiency

due to several factors, including reduced outdoor physical activity, age-related changes in UV-B absorption and cutaneous vitamin D synthesis, decreased expression of vitamin D receptors, and impaired renal function.¹⁶

Research indicates that aging can reduce the skin's capacity to produce previtamin D₃ by up to 50% compared with younger adults following UV-B exposure, in addition to reduced renal activation of vitamin D and decreased outdoor activity.¹⁷ These age-related declines in vitamin D synthesis, together with a higher burden of chronic health conditions, likely contribute to lower vitamin D levels in elderly.¹⁸

In this study, the mean of serum vitamin D level was 26.27 ± 4.17 ng/ml. Participants were categorized into three groups based on serum vitamin D status: insufficiency (21–29 ng/ml), comprising 39% of the sample; normal level (≥ 30 ng/ml), accounting for 34%; and deficiency (< 20 ng/ml), representing 27%.

Bivariate analysis between serum vitamin D levels and anxiety scores revealed no statistically significant association ($p=0.816$). Correlation analysis indicated a weak negative relationship ($r=-0.125$; $p=0.214$). In the multivariate analysis, participants with vitamin D deficiency exhibited an effect size of 0.572 (95% CI= -0.573 to 1.717 , $p=0.327$), whereas those with vitamin D insufficiency had an effect size of 0.197 (95% CI= -0.720 to 1.114 , $p=0.673$).

Armstrong *et al.* (2011) reported that serum vitamin D levels were significantly negatively correlated with anxiety ($p<0.001$). In the fourth quartile, vitamin D had a significant effect on anxiety (OR=0.774; 95% CI=0.663–0.903; $p<0.01$).¹⁸ A clinical trial found that lower vitamin D levels were associated with higher anxiety, using a cutoff of 30 ng/ml, with an area under curve (AUC) of 0.65, a sensitivity of 60%, and specificity of 58% ($p<0.05$).¹⁹ Karras *et al.* (2016) reported a vitamin D cutoff of 20 ng/ml for identifying anxiety, with an AUC of 0.70, sensitivity of 65%, and specificity of 60% ($p<0.05$).²⁰ Conversely, Black observed no significant association between serum vitamin D and anxiety: RR=1.02 (95% CI=0.98–1.07; $p=0.343$) in men, and RR=0.99 (95% CI=0.95–1.03; $p=0.484$) in women.²¹ Similarly, Granlund *et al.* (2020) reported an odds ratio (OR) of 1.10 (95% CI=0.37–3.75; $p=0.784$) for the association between vitamin D levels and anxiety. These discrepancies may reflect differences in study populations, vitamin D assay methods, or diagnostic criteria for anxiety.¹⁴

According to Zongliang, inconsistent findings regarding the association between vitamin D and anxiety may stem from variations in sample demographics, study design, environmental factors, seasonal variation, comorbidities, and dietary habits. Consistent with previous studies examining the relationship between serum vitamin D levels and anxiety, this study found that vitamin D indirectly influences anxiety severity through the pathway of irritable bowel syndrome (IBS). IBS was the only independent variable that showed a significant indirect correlation with anxiety scores. Additionally, IBS demonstrated a significant direct correlation with anxiety scores.¹

In an elderly population, a study reported that anxiety levels measured using the State-Trait Anxiety Inventory (STAI) were lower in individuals who received vitamin D supplementation compared to the control group at 6 months (38.02 ± 9.03 vs. 43.91 ± 7.18 , $p=0.003$) and at 12 months (32.35 ± 7.77 vs. 44.97 ± 7.78 , $p<0.001$). Similar findings were observed for the state anxiety subscale (STAI-S) at 6 months (37.11 ± 7.88 vs. 43.20 ± 9.33 , $p=0.003$) and at 12 months (32.59 ± 6.45 vs. 44.60 ± 9.53 , $p<0.001$). Participants with vitamin D deficiency or insufficiency at baseline showed the greatest benefit from supplementation in terms of anxiety score reduction.¹⁴ However, recent randomized controlled trials investigating the effects of vitamin D on mood in healthy individuals have shown negative results. It was hypothesized that individuals at higher risk of mood disturbances would benefit more from vitamin D supplementation. Contrary to expectations, increases in depression and anxiety scores were observed in participants who were vitamin D-deficient at baseline compared to those who had insufficiency.^{21,22}

Overall, this study yielded similar findings, as structural equation modeling (SEM) did not demonstrate a direct correlation between vitamin D levels and anxiety.

Conclusion

Based on the analysis of this study, it can be concluded that there is no direct relationship between serum vitamin D levels and anxiety severity. However, an indirect relationship was identified, whereby higher serum vitamin D levels were associated with reduced anxiety through the prevention of irritable bowel syndrome (IBS). Further research can be directed toward exploring additional factors that may influence anxiety in the elderly, including overall health status, physical activity, and dietary patterns, as well as how the interaction between these factors and serum vitamin D levels may affect anxiety outcomes.

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Hubungan antara Status Gizi dan Kejadian Dislipidemia pada Mahasiswa Program Pendidikan Dokter Spesialis Ilmu Penyakit Dalam RSUP Prof. dr. I.G.N.G. Ngoerah, Denpasar

I Dewa Gede Agung Suta Ariwangsa¹, I Made Pande Dwipayana²

¹Program Studi Ilmu Penyakit Dalam, Fakultas Kedokteran Universitas Udayana/RSUP Prof. dr. I.G.N.G. Ngoerah, Denpasar, Bali, Indonesia

²Departemen Ilmu Penyakit Dalam, Fakultas Kedokteran Universitas Udayana/RSUP Prof. dr. I.G.N.G. Ngoerah, Denpasar, Bali, Indonesia

Abstrak

Latar Belakang: Status gizi memiliki peran yang penting dalam menentukan kondisi kesehatan seseorang. Obesitas memiliki hubungan yang kuat dengan dislipidemia, terutama melalui mekanisme resistansi insulin dan adipokin proinflamasi yang berkontribusi pada terjadinya sindrom metabolik. Meskipun demikian, bukti terbaru menunjukkan bahwa dislipidemia terkait obesitas tidak selalu memiliki pola patofisiologi yang seragam, melainkan dapat bervariasi sesuai dengan karakteristik individu. Penelitian ini bertujuan untuk menilai hubungan antara status gizi dan dislipidemia pada mahasiswa Program Pendidikan Dokter Spesialis Ilmu Penyakit Dalam RSUP Prof. dr. I.G.N.G. Ngoerah, Denpasar.

Metode: Penelitian ini menggunakan desain potong lintang dan dilaksanakan pada bulan Agustus 2023 di RSUP Prof. dr. I.G.N.G. Ngoerah, Denpasar. Subjek penelitian adalah mahasiswa Program Pendidikan Dokter Spesialis Ilmu Penyakit Dalam. Data dikumpulkan melalui pengukuran indeks massa tubuh sebagai indikator status gizi dan pemeriksaan profil lipid sebagai indikator dislipidemia. Uji korelasi dilakukan menggunakan uji Chi-Square dengan tingkat signifikansi $p < 0,05$.

Hasil: Sebanyak 115 subjek berpartisipasi dalam penelitian, 60% laki-laki dan 40% perempuan, dengan rerata usia $31,25 \pm 3,82$ tahun. Sebanyak 74 (64,3%) subjek tergolong obesitas dan 57 subjek mengalami dislipidemia. Terdapat 46 subjek yang mengalami obesitas sekaligus dislipidemia, sedangkan 11 subjek mengalami dislipidemia tanpa obesitas. Sebanyak 30 subjek tidak mengalami obesitas maupun dislipidemia, dan 28 subjek hanya mengalami obesitas. Uji Chi-Square menunjukkan hubungan yang signifikan antara status gizi dan kejadian dislipidemia ($p < 0,001$). **Kesimpulan:** Terdapat hubungan yang signifikan antara status gizi dan kejadian dislipidemia. Penelitian lanjutan diperlukan untuk mengevaluasi faktor-faktor spesifik yang berkontribusi terhadap terjadinya obesitas maupun dislipidemia pada populasi mahasiswa program pendidikan dokter spesialis.

Kata kunci: status gizi, obesitas, dislipidemia, dokter residen, PPDS

Abstract

Background: Nutritional status plays an important role in determining individual's health. Obesity is closely associated with dyslipidemia, mainly through insulin resistance mechanisms and proinflammatory adipokines, which contribute to the development of metabolic syndrome. However, recent evidence suggests that obesity-related dyslipidemia does not follow a single, uniform pathophysiological pattern; instead, its characteristics may vary across individuals. This study aimed to examine the relationship between nutritional status and dyslipidemia among residents of the Internal Medicine Specialist Program at RSUP Prof. dr. I.G.N.G. Ngoerah, Denpasar. **Methods:** This cross-sectional study was conducted in August 2023 at RSUP Prof. dr. I.G.N.G. Ngoerah, Denpasar. The study subjects were residents of the Internal Medicine Specialist Program. Data were collected through measurements of body mass index (BMI) as an indicator of nutritional status and lipid profile examination as an indicator of dyslipidemia. The association between variables was analyzed using

the Chi-Square test, with statistical significance set at $p < 0.05$. **Results:** A total of 115 subjects were enrolled in the study, with 60% men and 40% women and a mean age of 31.25 ± 3.82 years. Of these, 74 subjects (64.3%) were classified as obese, and 57 subjects had dyslipidemia. Forty-six (46) subjects had presented with obesity and dyslipidemia, while 11 subjects had dyslipidemia in the absence of obesity. Meanwhile, 30 subjects had neither obesity nor dyslipidemia, and 28 participants were obese without dyslipidemia. The Chi-Square test showed a significant association between nutritional status and dyslipidemia ($p < 0.001$). **Conclusion:** This study demonstrates a significant relationship between nutritional status and dyslipidemia. Further research is needed to explore specific factors that contribute to obesity and dyslipidemia among residents in specialist medical training programs.

Keywords: nutritional status, obesity, dyslipidemia, resident physicians, PPDS

Pendahuluan

Seiring dengan kemajuan teknologi, transportasi, dan informasi, pola aktivitas masyarakat dalam kehidupan sehari-hari mengalami banyak perubahan, termasuk dalam hal aktivitas fisik, pola makan, gaya hidup, serta komposisi tubuh. Perubahan pada pola makan dan aktivitas fisik tersebut menyebabkan semakin banyak orang mengalami masalah gizi. Masalah gizi merupakan kondisi yang menggambarkan gangguan kesehatan pada seseorang maupun sekelompok orang atau masyarakat sebagai bentuk ketidakseimbangan antara asupan (*intake*) dan kebutuhan tubuh. Ketidakseimbangan ini dapat mengakibatkan gizi kurang maupun gizi lebih yang dapat berujung pada obesitas.¹

Obesitas merupakan suatu kondisi medis yang bersifat kompleks dan dalam jangka panjang, dengan dampak negatif yang signifikan terhadap kesehatan manusia. Kondisi ini termasuk dalam gangguan metabolik yang dipengaruhi oleh faktor gaya hidup, seperti tingkat aktivitas fisik, pola makan, serta faktor genetik. Saat ini, obesitas menjadi masalah kesehatan utama yang terus meningkat di seluruh dunia pada tingkat yang mengkhawatirkan. Diperkirakan sekitar 1,9 miliar penduduk dunia mengalami *overweight* atau obesitas. Di Indonesia, sekitar 13,5% penduduk dewasa berusia 18 tahun ke atas mengalami *overweight*, sedangkan 28,7% tergolong obesitas.² Pengukuran indeks massa tubuh (IMT) merupakan metode sederhana untuk menilai status gizi, terutama dalam menentukan seseorang dengan berat badan kurang, normal, atau berlebih.³ Status gizi lebih yang dapat berkembang menjadi obesitas menyebabkan peningkatan risiko akan berbagai penyakit, termasuk hipertensi, resistansi insulin atau diabetes melitus tipe 2, penyakit jantung koroner (PJK), dan dislipidemia.^{1,4}

Dislipidemia mencakup beberapa kelainan profil lipid, seperti peningkatan kadar kolesterol total, peningkatan kadar trigliserida (TG), penurunan *high-density lipoprotein* (HDL), serta peningkatan *low-density lipoprotein* (LDL). Komponen-komponen tersebut memiliki peran utama dalam mempercepat terjadinya aterosklerosis dan meningkatkan risiko penyakit kardiovaskular. Kolesterol total merupakan salah satu indikator yang sering digunakan untuk menilai risiko penyakit kardiovaskular. Hiperkolesterolemia, yaitu meningkatnya kadar kolesterol total, umumnya tidak menimbulkan gejala klinis. Oleh karena itu, pemeriksaan rutin kadar kolesterol menjadi salah satu langkah penting dalam upaya deteksi dini, terutama pada individu dengan risiko tinggi. Secara global, peningkatan kadar kolesterol yang berkontribusi terhadap penyakit jantung dan stroke diperkirakan menyebabkan sekitar 2,6 juta kematian setiap tahun. Angka kematian tertinggi tercatat di Eropa sekitar 54%, kemudian Amerika sebesar 48%. Sementara wilayah Afrika dan Asia Tenggara masing-masing menyumbang sekitar 22,6% dan 29,0%.¹ Kadar kolesterol yang tinggi juga berkaitan erat dengan meningkatnya prevalensi obesitas di masyarakat, yang pada akhirnya dapat memperbesar risiko terjadinya penyakit kardiovaskular akibat pola hidup yang kurang sehat.⁵

Salah satu faktor yang berperan dalam terjadinya dislipidemia adalah faktor genetik dan asupan lemak yang tinggi. Dampak lemak makanan terhadap dislipidemia berkaitan dengan kandungan asam lemak dan kolesterol dalam makanan tersebut yang dapat memengaruhi profil lipid darah. Asam lemak jenuh dan kondisi obesitas memberikan pengaruh yang kurang

baik terhadap profil lipid darah. Asupan lemak yang tinggi tanpa diimbangi dengan aktivitas fisik yang memadai akan menyebabkan penumpukan energi dalam bentuk lipid di jaringan adiposa. Kondisi ini dapat menyebabkan peningkatan berat badan yang berhubungan dengan peningkatan IMT.⁶ Berbagai penelitian mengenai status gizi dan dislipidemia telah banyak dilakukan di Indonesia, namun studi serupa yang dilakukan pada dokter residen yang sedang menempuh program pendidikan dokter spesialis masih terbatas. Pandemi Covid-19 turut menimbulkan tantangan baru bagi tenaga medis, khususnya dokter. Hal ini karena meningkatnya beban kerja fisik dan mental dapat memicu perubahan gaya hidup yang berdampak pada status gizi.⁷ Berdasarkan kondisi tersebut, penelitian ini bertujuan untuk menilai hubungan antara status gizi dan kejadian dislipidemia pada mahasiswa Program Pendidikan Dokter Spesialis Ilmu Penyakit Dalam di RSUP Prof. dr. I.G.N.G. Ngoerah, Denpasar.

Metode

Penelitian ini melibatkan 115 subjek yang merupakan mahasiswa Program Pendidikan Dokter Spesialis Ilmu Penyakit Dalam di RSUP Prof. dr. I.G.N.G. Ngoerah, Denpasar, Bali, Indonesia pada bulan Agustus 2023. Studi ini menggunakan desain potong lintang dan data dikumpulkan pada satu waktu. Data yang digunakan merupakan data primer yang diperoleh melalui pengukuran langsung terhadap subjek penelitian. Pengukuran tinggi badan dan berat badan dilakukan menggunakan timbangan digital, kemudian dilakukan perhitungan IMT sebagai indikator status gizi subjek penelitian. Selanjutnya, untuk menilai dislipidemia, dilakukan pengambilan darah vena dan pemeriksaan laboratorium meliputi *low-density lipoprotein* (LDL), *high-density lipoprotein* (HDL), dan trigliserida (TG). Status gizi diklasifikasikan menjadi 2 kategori, yaitu obesitas (IMT ≥ 25 kg/m²) dan tidak obesitas (IMT < 25 kg/m²). Subjek dinyatakan mengalami dislipidemia bila memenuhi minimal satu dari tiga kriteria berikut: 1) kadar LDL > 150 mg/dl; 2) HDL < 40 mg/dl; 3) TG > 150 mg/dl. Selain itu, data tambahan seperti jenis kelamin dan usia juga dicatat dan dikumpulkan. Seluruh data ditabulasi dan dianalisis menggunakan perangkat lunak IBM Statistical Package for the Social Science (SPSS) versi 26 untuk Windows. Analisis deskriptif dilakukan terhadap variabel jenis kelamin, usia, IMT, LDL, HDL, dan TG. Selanjutnya, analisis bivariat menggunakan uji Chi-square dilakukan untuk menilai hubungan antara status gizi dan kejadian dislipidemia. Hubungan antarvariabel, status gizi dan dislipidemia, dinyatakan signifikan secara statistik apabila menunjukkan nilai $p < 0,05$.

Hasil

Dalam penelitian ini, diperoleh total 115 subjek, terdiri atas 69 (60%) laki-laki dan 46 (40%) perempuan. Rerata usia subjek adalah $31,25 \pm 3,82$ tahun, dengan rentang antara 26 hingga 48 tahun. Rerata kadar LDL sebesar 129,89 mg/dl, dengan kadar LDL tertinggi 217 mg/dl dan terendah 53 mg/dl. Rerata kadar HDL sebesar 49,44 mg/dl, dengan kadar HDL tertinggi 88 mg/dl dan HDL terendah 32 mg/dl. Sementara itu, rerata kadar TG sebesar 104,87 mg/dl, dengan kadar TG tertinggi 488,9 mg/dl dan terendah 30,2 mg/dl. Subjek penelitian memiliki rerata IMT sebesar 27,13 kg/m², dengan IMT tertinggi sebesar 39,55 kg/m² dan IMT terendah 18,02 kg/m². Data tersaji pada **Tabel 1** berikut ini:

Tabel 1. Karakteristik subjek penelitian

Karakteristik	
Usia (tahun)	
Rerata	31,25 ± 3,82
Usia tertua	48
Usia termuda	26
Low-density lipoprotein (LDL) (mg/dl)	
Rerata	129,89
LDL tertinggi	217
LDL terendah	53
High-density lipoprotein (HDL) (mg/dl)	
Rerata	49,44
HDL tertinggi	88
HDL terendah	32
Trigliserida (TG) (mg/dl)	
Rerata	104,87
TG tertinggi	488,9
TG terendah	30,2
Indeks massa tubuh (IMT) (kg/m²)	
Rerata	27,13
IMT tertinggi	39,55
IMT terendah	18,02

Dalam penelitian ini, beberapa subjek diketahui memiliki riwayat penyakit sebelumnya (lihat **Tabel 2**), yaitu dislipidemia, diabetes melitus tipe 2, hipertensi, asma, penyakit Hashimoto, dan psoriasis artritis, masing-masing dialami oleh satu orang (0,087%) dan tidak ditemukan pada subjek yang sama. Jumlah subjek dengan IMT kategori obesitas sebesar 74 orang (64,3%), sedangkan 41 orang (35,7%) termasuk dalam kategori tidak obesitas. Berdasarkan hasil pemeriksaan laboratorium terhadap kadar LDL, HDL, dan TG, diperoleh bahwa 57 subjek (49,6%) memenuhi kriteria dislipidemia, sementara 58 subjek (50,4%) tidak menunjukkan adanya dislipidemia (lihat **Tabel 3**).

Tabel 2. Riwayat penyakit subjek penelitian

Riwayat Penyakit	Jumlah	Persentase
Dislipidemia	1	0,087%
Diabetes melitus tipe 2	1	0,087%
Hipertensi	1	0,087%
Asma	1	0,087%
Penyakit Hashimoto	1	0,087%
Psoriasis artritis	1	0,087%

Tabel 3. Proporsi subjek menurut indeks massa tubuh (IMT) dan dislipidemia

Parameter	Jumlah (n=115)	Persentase
Indeks massa tubuh		
Obesitas	74	64,3%
Tidak obesitas	41	35,7%
Dislipidemia		
Ya	57	49,6%
Tidak	58	50,4%

Hasil analisis bivariat menunjukkan bahwa 46 subjek dengan obesitas mengalami dislipidemia, sedangkan 11 subjek tanpa obesitas juga tercatat memiliki dislipidemia. Selain itu, terdapat 28 subjek yang hanya mengalami obesitas, dan 30 subjek lainnya tidak menunjukkan obesitas maupun dislipidemia. Hasil uji korelasi Chi-Square (lihat **Tabel 4**) menunjukkan bahwa status gizi memiliki hubungan yang bermakna secara statistik dengan kejadian dislipidemia ($p<0,001$).

Tabel 4. Analisis Chi-Square hubungan status gizi terhadap kejadian dislipidemia

Hubungan status gizi terhadap kejadian dislipidemia		Dislipidemia		Signifikansi (p)
		Ya	Tidak	
Indeks massa tubuh	Obesitas	46	28	0,001
	Tidak obesitas	11	30	

Diskusi

Penelitian ini menunjukkan bahwa proporsi subjek laki-laki (60%) lebih tinggi dibandingkan perempuan (40%). Temuan ini konsisten dan sejalan dengan temuan dalam studi oleh Sahara *et al.* (2022), yang juga menunjukkan bahwa mayoritas peserta studi residen berjenis kelamin laki-laki (63,5%).²

Suatu studi oleh Suryana dan Olivia (2016) melaporkan bahwa rerata kadar LDL pada subjek dengan status gizi normal adalah $130,22\pm31,29$ mg/dl, sedangkan pada subjek obesitas sebesar $148,44\pm33,06$ mg/dl. Rerata kadar HDL pada kelompok subjek dengan status gizi normal sebesar $46,17\pm12,74$ mg/dl, sementara pada kelompok obesitas sebesar $41,89\pm8,82$ mg/dl.⁸ Hal tersebut sejalan dengan penelitian ini, di mana rerata kadar LDL seluruh subjek adalah 129,89 mg/dl (<150 mg/dl) dan rerata kadar HDL yaitu sebesar 49,44 mg/dl (>40 mg/dl).

Sebanyak 64,3% subjek tergolong obesitas pada studi ini, sejalan dengan penelitian Wati dan Ernawati (2016) yang juga melaporkan proporsi responden obesitas lebih tinggi (61,4%) dibandingkan responden dengan status normal (38,6%).⁹ Hasil serupa juga ditunjukkan oleh Wongkar *et al.* (2013), yakni dari 63 subjek, 52 subjek (82,5%) tergolong obesitas.¹ Tingginya proporsi subjek dengan obesitas dapat mencerminkan beberapa kemungkinan, salah satunya adalah adanya keseimbangan energi yang positif serta kurangnya aktivitas fisik. Keseimbangan energi positif terjadi ketika energi dari makanan yang dikonsumsi lebih besar dibandingkan energi yang dikeluarkan/digunakan tubuh. Penelitian oleh Dainy *et al.* (2016) juga mendukung temuan ini, dengan 67 subjek dari 116 orang memiliki $IMT \geq 25$ kg/m².⁶ Obesitas meningkatkan risiko morbiditas dan mortalitas akibat penyakit diabetes, hipertensi, dan penyakit kardiovaskular. Prevalensi *overweight* dan obesitas pun terus meningkat pada populasi global.¹⁰ Komite konsultatif WHO menyatakan bahwa populasi Asia memiliki hubungan yang berbeda antara IMT, persentase lemak tubuh, dan risiko kesehatan dibandingkan populasi Eropa. Oleh karena itu, disarankan batas IMT sebesar $\geq 23-24,9$ kg/m² untuk kategori *overweight* dan $IMT \geq 25$ kg/m² untuk kategori obesitas.¹¹

Proporsi subjek yang mengalami dislipidemia dalam penelitian ini adalah 49,6%, sedangkan 50,4% lainnya tidak mengalami dislipidemia. Salah satu faktor yang berkontribusi terhadap peningkatan kadar kolesterol total dan LDL adalah konsumsi makanan yang tinggi lemak jenuh dan kolesterol. Sementara itu, kadar TG yang tinggi tidak hanya berasal dari proses *de novo lipogenesis*, tetapi juga dipengaruhi oleh pola makan, asupan asam lemak, faktor genetik, status gizi, serta asupan karbohidrat sederhana yang berlebihan. Trigliserida diangkut oleh *very low-density lipoprotein* (VLDL) atau kilomikron menuju jaringan tubuh untuk digunakan sebagai sumber energi atau disimpan pada jaringan adiposa. HDL berperan dalam menjaga keseimbangan kolesterol darah dengan cara mengangkut kolesterol tidak teresterifikasi dari dalam sel dan lipoprotein kembali ke hati untuk selanjutnya dieksresikan dalam bentuk garam empedu atau *bile salt*.⁶ Perubahan gaya hidup dapat memengaruhi kadar kolesterol total, HDL, LDL, dan TG. American Heart Association (AHA) merekomendasikan agar semua orang dewasa menerapkan pola makan sehat, melakukan aktivitas fisik secara teratur, dan menghindari paparan asap tembakau.¹²

The U.S. Preventive Services Task Force (USPSTF) tidak memberikan rekomendasi khusus terkait skrining rutin untuk kelainan lipid pada pria berusia 20–35 tahun atau pada wanita berusia 20 tahun atau lebih yang tidak memiliki risiko tinggi penyakit jantung koroner (PJK). Sebaliknya, The National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) merekomendasikan agar skrining lipid dimulai pada semua orang dewasa sejak usia 20 tahun, tanpa mempertimbangkan profil risiko PJK. Rekomendasi ini didasarkan pada pertimbangan bahwa skrining dapat mendorong perilaku hidup sehat, meningkatkan kesadaran masyarakat mengenai kolesterol, serta membantu mengidentifikasi individu dengan risiko tinggi PJK.¹²

Hasil analisis statistik dalam penelitian ini menunjukkan bahwa status gizi, khususnya obesitas, memiliki hubungan yang signifikan dengan kejadian dislipidemia ($p < 0,001$). Temuan ini sejalan dengan penelitian Dainy *et al.* (2016), yang menunjukkan korelasi positif signifikan antara IMT dengan TG ($p = 0,03$), serta antara *mini nutritional assessment* (MNA) dan kolesterol total ($p = 0,004$) pada kelompok lansia dan pralansia. Status gizi terbukti menjadi salah satu faktor yang berperan dalam terjadinya dislipidemia. Selain sindrom metabolik dan diabetes melitus tipe 2, obesitas merupakan salah satu komorbiditas yang dapat meningkatkan kadar trigliserida. Peningkatan kadar trigliserida juga berkontribusi pada penurunan kadar HDL, sehingga memperberat gangguan profil lipid. Individu dengan dislipidemia dan IMT tinggi cenderung memiliki tingkat inflamasi dalam tubuh yang lebih tinggi, ditandai dengan peningkatan kadar *C-reactive protein* (CRP). Oleh karena itu, menjaga status gizi dalam batas normal menjadi salah satu langkah penting untuk mencegah dampak negatif dislipidemia tahap lanjut, termasuk risiko penyakit aterosklerosis, stroke, dan berbagai penyakit lain yang terkait.⁶

Penelitian oleh Wati dan Ernawati (2016) melaporkan hasil yang serupa, yaitu terdapat hubungan bermakna antara IMT dan kadar TG ($p < 0,001$), serta korelasi antara IMT dan sindrom metabolik ($p = 0,011$). Obesitas yang dipicu oleh konsumsi karbohidrat berlebih berkaitan erat dengan peningkatan kadar trigliserida, karena karbohidrat merupakan bahan dasar pembentukan trigliserida, dan kelebihannya akan disimpan sebagai lemak di jaringan subkutan. Asupan karbohidrat yang tinggi meningkatkan pembentukan piruvat dan asetil-KoA, yang pada akhirnya meningkatkan kadar trigliserida. Baik laki-laki maupun perempuan yang mengalami obesitas juga berhubungan dengan meningkatnya tekanan darah sistolik dan diastolik, kolesterol total, kolesterol LDL, serta trigliserida, sementara kadar HDL cenderung lebih rendah.⁹

Terdapat berbagai faktor risiko yang memengaruhi terjadinya sindrom metabolik, termasuk gaya hidup (pola makan, konsumsi alkohol, merokok, dan aktivitas fisik), sosial ekonomi, genetik serta stres. Salah satu komponen utama sindrom metabolik adalah obesitas sentral, yang kini menjadi masalah kesehatan masyarakat secara global. Berbagai penelitian menunjukkan bahwa kelompok usia 20–64 tahun memiliki risiko tinggi mengalami obesitas. Obesitas umumnya terjadi ketika asupan energi melebihi energi yang digunakan tubuh untuk metabolisme basal, aktivitas fisik, pencernaan, dan

pertumbuhan. Kelebihan energi yang tidak digunakan akan disimpan dalam bentuk lemak, sehingga meningkatkan jumlah dan ukuran sel lemak. Kondisi tersebut memicu terjadinya obesitas dan berlanjut pada sindrom metabolik, di mana dislipidemia merupakan salah satu komponennya. Variasi insiden dan prevalensi sindrom metabolik dipengaruhi oleh beberapa hal antara lain perbedaan kriteria diagnosis, etnis/ras, usia, dan jenis kelamin.⁹

Berbagai bukti menunjukkan bahwa resistansi insulin merupakan mekanisme yang paling mungkin menghubungkan antara obesitas dan dislipidemia metabolik terkait obesitas. Merujuk pada studi Magkos *et al.*, Vekic *et al.* (2019) menyatakan bahwa resistansi insulin dan dislipidemia metabolik berkaitan dengan adiposopati, yaitu perubahan struktural dan fungsional pada jaringan adiposa. Kelainan ini berdampak pada struktur intraseluler adiposit, menyebabkan stres retikulum endoplasma dan disfungsi mitokondria. Adipokin, yang diproduksi oleh sel adiposit dan makrofag yang berakumulasi pada jaringan adiposa, merupakan mediator molekuler utama dari resistansi insulin terkait obesitas. Selain itu, adiposit yang menjadi resistan terhadap insulin akan meningkatkan lipolisis dan pelepasan asam lemak bebas ke dalam sirkulasi. Peningkatan konsentrasi asam lemak bebas dapat memicu lipotoksitas, yang menjadi mekanisme lain resistansi insulin terkait obesitas pada jaringan non-adiposa.¹³

Kesimpulan

Berdasarkan hasil penelitian, sebagian besar subjek tergolong obesitas dengan proporsi laki-laki lebih tinggi dibandingkan perempuan, dan sebagian subjek mengalami dislipidemia. Status gizi, khususnya obesitas, terbukti memiliki hubungan yang signifikan dengan kejadian dislipidemia pada mahasiswa Program Pendidikan Dokter Spesialis Ilmu Penyakit Dalam RSUP Prof. dr. I.G.N.G. Ngoerah. Faktor-faktor yang berkontribusi terhadap tingginya obesitas ataupun dislipidemia belum dievaluasi dalam penelitian ini. Oleh karena itu, penelitian lanjutan diperlukan untuk meninjau faktor-faktor tersebut sehingga dapat dilakukan upaya penyesuaian atau intervensi yang lebih tepat bagi para mahasiswa.

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Dermatitis Kontak Alergi Akibat Plester Penutup Luka: Sebuah Laporan kasus Jarang dan Tinjauan Literatur

Lukman Nur Rahman^{1,2}, Ilham Suropto Gani¹

¹Fakultas Kedokteran, Universitas Tadulako, Palu, Sulawesi Tengah, Indonesia

²Program Magister Ilmu Kedokteran Dasar, Fakultas Kedokteran, Universitas Airlangga, Surabaya, Jawa Timur, Indonesia

Abstrak

Pendahuluan: Penggunaan perekat medis sebagai penutup luka pascaoperasi dapat memicu sensitisasi dan kemudian menimbulkan dermatitis kontak alergi (DKA) akibat paparan terhadap berbagai bahan kimia yang terkandung di dalam produk tersebut.

Laporan kasus: Seorang perempuan berusia 32 tahun datang dengan keluhan ruam kemerahan pada area abdomen di sekitar plester luka operasi, yang muncul sekitar satu minggu setelah menjalani laparotomi atas indikasi neoplasma ovarium sistik. Ruam pertama kali timbul dua hari pascaoperasi, disertai sensasi terbakar, panas, dan gatal. Lesi kemudian berkembang menjadi bintik-bintik berisi cairan menyerupai vesikel. Pemeriksaan klinis menunjukkan adanya makula eritema disertai papul hingga vesikel berbentuk milier dan bula, dengan skuama yang tersebar difus mengikuti pola plester luka operasi. Plester yang digunakan adalah Pharmafix®, yang mengandung perekat medis berbasis akrilat (*acrylate*). Terapi yang diberikan meliputi antihistamin *cetirizine* 10 mg, *methylprednisolone* 4 mg dua kali sehari, serta krim topikal *desoximetasone* 0,25%.

Diskusi: Pasien didiagnosis dengan DKA akibat perekat medis dalam menutup luka yang mengandung akrilat. Reaksi alergi ini dipicu oleh komponen kimia perekat termasuk *diethyl-dithiocarbamate*; *tetrahydrofurfuryl acrylate*, dan *2-hydroxyethyl methacrylate*. Penatalaksanaan akut mencakup pelepasan perekat dari kulit, pembersihan area yang terkena secara hati-hati, serta penggunaan kortikosteroid topikal jangka pendek bila diperlukan.

Kata kunci: dermatitis kontak alergi, perekat medis, akrilat

Abstract

Introduction: The use of medical adhesives as postoperative wound dressings can lead to sensitization and subsequently trigger allergic contact dermatitis (ACD) due to exposure to various chemical components contained within these products.

Case report: A 32-year-old woman presented with a reddish rash on the abdominal area surrounding her postoperative wound dressing, appearing approximately one week after undergoing laparotomy for a cystic ovarian neoplasm. The rash first developed two days after surgery, accompanied by burning, warmth, and pruritus. The lesions progressed into small fluid-filled vesicle-like eruptions. Clinical examination revealed erythematous macules with papules, milia-like vesicles and bullae, along with diffuse scaling that followed the outline of the surgical adhesive. The dressing used was Pharmafix®, which contains acrylate-based medical adhesive. Treatment consisted of cetirizine 10 mg, methylprednisolone 4 mg twice daily, and topical desoximetasone cream 0.25%.

Discussion: The patient was diagnosed with ACD induced by acrylate-containing medical adhesives. The allergic reaction was triggered by chemical components within the adhesive, including diethyl-dithiocarbamate, tetrahydrofurfuryl acrylate, and 2-hydroxyethyl methacrylate. Acute management involved removal of the adhesive, gentle cleansing of the affected area, and short-term use of topical corticosteroid when indicated.

Keywords: allergic contact dermatitis, medical adhesive, acrylate

Pendahuluan

Infeksi luka operasi (ILO) merupakan salah satu komplikasi pascabedah yang paling mengkhawatirkan setelah tindakan bedah dan perlu mendapatkan perhatian secara khusus. Penggunaan perekat medis merupakan salah satu upaya untuk perawatan luka yang dapat menurunkan risiko terjadinya infeksi pascabedah. Perekat medis meliputi berbagai komponen dari sejumlah produk, termasuk pita perekat, pembalut, elektroda, perlengkapan ostomi, dan tambalan.^{1,2} Penggunaan perekat medis dalam menutup luka dapat menyebabkan terjadinya sensitisasi sehingga berakibat pada timbulnya dermatitis kontak alergi (DKA). Kejadian tersebut kemungkinan sebagai akibat dari bahan penutup luka yang digunakan.¹ DKA merupakan reaksi hipersensitivitas tipe IV yang dimediasi oleh alergen tertentu, dan berdampak pada terjadinya respons inflamasi. Pada umumnya, kondisi ini terjadi mulai hari kelima hingga hari ke-14 setelah adanya kontak dengan agen penyebab.^{3,4} DKA dikategorikan sebagai kondisi umum yang terjadi pada sekitar 20% populasi.¹

Dalam suatu literatur, dilaporkan adanya kasus yang menunjukkan terjadinya dermatitis kontak alergi (DKA) terhadap bahan kimia yang ditemukan dalam perekat medis. Bahan-bahan tersebut antara lain *cyanoacrylates*, *benzoin derivatives*, dan *mastisol*. Berbagai produk tersebut digunakan dengan cara yang sama untuk menutup luka karena fleksibilitas, kekuatan, serta kerjanya yang relatif cepat.^{5,6}

Laporan kasus ini membahas mengenai dermatitis kontak alergi yang terjadi akibat penggunaan plester penutup luka setelah operasi di rumah sakit tersier. Penulisan laporan kasus ini sesuai dengan pedoman penulisan laporan kasus standar internasional (CARE).

Laporan Kasus

Seorang perempuan berusia 32 tahun datang dengan keluhan ruam kemerahan pada bagian perut di sekitar plester luka operasi. Keluhan tersebut dilaporkan terjadi sejak kurang lebih 1 minggu setelah dilakukan operasi laparotomi salpingo-ooforektomi oleh bagian Onkologi, Obstetri, dan Ginekologi dengan indikasi neoplasma ovarium sistik. Ruam muncul pertama kali 2 hari setelah operasi, kemudian berkembang menjadi bintik-bintik berisi cairan seperti melepuh. Keluhan ruam disertai sensasi rasa terbakar, panas, dan gatal, sehingga mendorong pasien untuk menggaruk area ruam dengan tangan. Garukan tersebut menyebabkan bintik-bintik pecah dan mengering, yang mengakibatkan pasien merasakan kulit menjadi kering. Tidak dilaporkan adanya riwayat alergi dalam keluarga. Pasien tidak memiliki riwayat dermatitis atopik dan tidak diketahui adanya riwayat alergi terhadap perekat medis.

Pemeriksaan klinis pada regio abdomen bawah menunjukkan makula eritema dengan papul hingga vesikel berbentuk milier dan bula disertai skuama yang tersebar difus mengikuti bentuk plester luka operasi persegi panjang yang berukuran 24 cm x 7 cm. Pada bagian tengah tampak insisi Pfannenstiel (**Gambar 1**). Plester luka yang digunakan adalah Phamafix® dengan bahan perekat medis berbasis akrilat (**Gambar 2**).

Pemeriksaan penunjang berupa pemeriksaan darah rutin dan elektrolit menunjukkan hasil dalam batas normal. Uji tempel dan uji tusuk untuk bahan alergi perekat medis tidak dilakukan karena keterbatasan fasilitas di rumah sakit. Sebagai tata laksana, pasien diberikan antihistamin *cetirizine* 10 mg per oral sekali sehari, kortikosteroid sistemik *methylprednisolone* 4 mg per oral dua kali sehari, dan kortikosteroid topikal krim *desoximetasone* 0,25% selama 7 hari. Setelah 3 hari pemberian obat, terjadi perbaikan klinis berupa eritema yang terlihat berkurang dan lesi mengering (**Gambar 3**).



Gambar 1. Regio abdomen bawah: tampak makula eritema dengan papul hingga vesikel disertai skuama yang tersebar difus mengikuti betuk plester luka operasi



Gambar 2. Phamafix® dengan bahan perekat medis berbasis akrilat (*acrylate*)



Gambar 3. Tiga hari setelah pengobatan tampak eritema berkurang dan lesi mengering

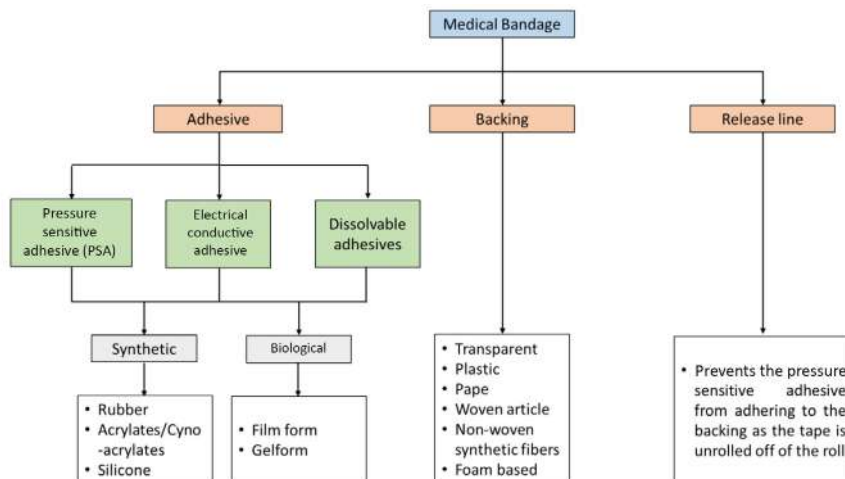
Diskusi

Dermatitis kontak alergi (DKA) merupakan bentuk dermatitis yang muncul akibat paparan terhadap bahan alergen yang bersentuhan atau melekat pada kulit, dan prosesnya dimediasi oleh reaksi hipersensitivitas tipe IV.⁷ Sebelum membahas

reaksi alergi yang berkaitan dengan penggunaan pita perekat, penting untuk memahami terlebih dahulu mengenai jenis-jenis pita perekat medis yang tersedia. Perban berperekat, sering disebut sebagai plester tempel, plester medis, atau plester, berfungsi melindungi luka dari gesekan, kontaminasi bakteri, kerusakan, serta paparan kotoran. Sebagian besar pita perekat medis terdiri atas tiga komponen utama, yaitu sisi perekat, sisi belakang (*carrier*), dan lapisan pelepas (**Gambar 4**). Jenis perekat standar yang umum digunakan dalam aplikasi medis mencakup tiga kategori utama, yaitu perekat yang sensitif tekanan, perekat yang dapat larut, serta perekat dengan sifat konduktivitas listrik. Secara umum, berdasarkan komposisi utama dalam formulasinya, perekat medis dikelompokkan menjadi dua kategori yaitu bahan perekat sintetis dan bahan perekat biologis. Setiap formulasi perekat medis harus melalui pengujian untuk memastikan pemenuhan standar keamanan medis. Jenis perekat yang paling sering digunakan meliputi akrilik, silikon, karet, dan perekat berbasis bio, yang dapat meliputi berbagai bahan berikut: *hydroabietic acid*, *tricresyl phosphate*, *2,5-di(tert-amyl)hydroquinone*, *benzoyl peroxide*, *epoxy resin*, *dodecyl maleamic acid* dan *octadecyl maleamic acid*, *diethyldithiocarbamate*, *tetrahydrofurfuryl acrylate resin*, serta *p-tert-butylphenol formaldehyde*.²

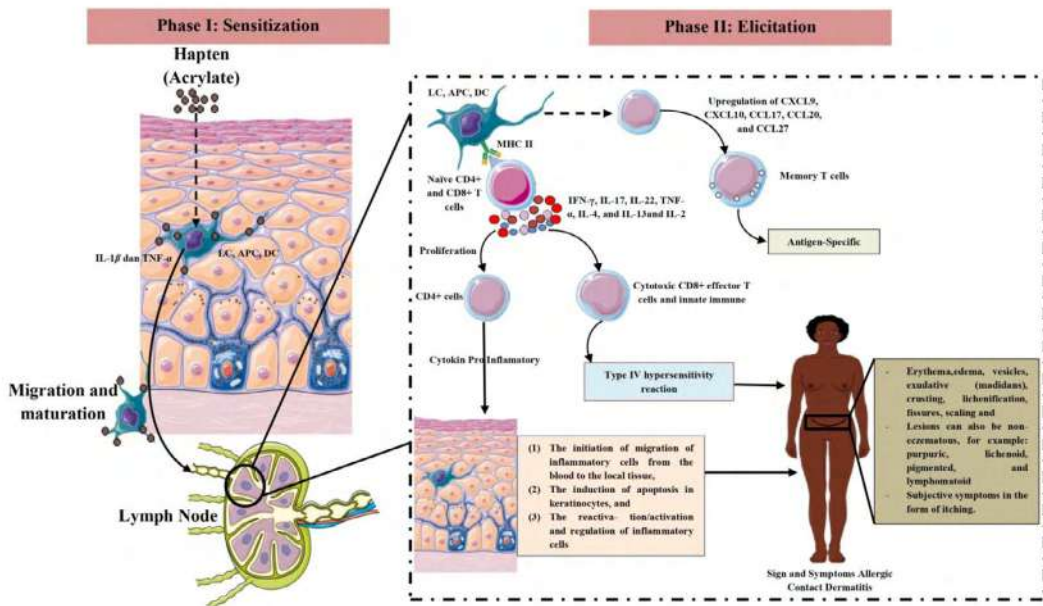
Suatu laporan kasus (Widman dkk. 2007) menunjukkan terjadinya dermatitis kontak alergi (DKA) terhadap bahan kimia yang ditemukan dalam perekat medis berupa *hydroabietic acid* (*derivative of colophony*), *tricresyl phosphate*, *2,5-di(tert-amyl)hydroquinone*, *benzoyl peroxide*, *epoxy resin*, *dodecyl maleamic acid* dan *octadecyl maleamic acid*, *diethyldithiocarbamate*, *tetrahydrofurfuryl acrylate*, serta *p-tert-butylphenol formaldehyde resin*.⁵ Analisis *cross-sectional* yang dilakukan oleh Atwater dkk. (2021) berdasarkan data The North American Contact Dermatitis Group periode 2001–2018, menemukan bahwa alergen yang paling umum menjadi penyebab terjadinya dermatitis kontak alergi akibat plester penutup luka adalah *colophony* (80,7%), *balsam of Peru* (3,9%), *2-hydroxyethyl methacrylate* (2,7%), dan *carba mix* (2,7%).⁸ Pada kasus yang disajikan berikut, DKA kemungkinan disebabkan oleh perekat medis berbahan akrilat.

Mekanisme terjadinya dermatitis kontak alergi (DKA) akibat akrilat pada prinsipnya serupa dengan mekanisme yang dipicu oleh alergen lainnya. Proses DKA meliputi dua fase utama, yaitu fase sensitisasi, ketika sistem imun mulai mengenali dan membentuk kesiapan terhadap alergen, kemudian fase elisitasi, yaitu respons imunologis yang muncul setelah paparan berulang terhadap alergen. Keseluruhan proses ini termasuk dalam reaksi hipersensitivitas tipe IV (tipe tertunda) (**Gambar 5**).^{2,3,6,9–11}



Gambar 4. Klasifikasi pita perekat medis²

Fase sensitisasi dimediasi oleh berbagai komponen sistem imun bawaan. Bahan perekat medis dengan berat molekul rendah, seperti akrilat, berperan sebagai haptan, yaitu suatu molekul kecil yang secara intrinsik tidak bersifat imunogenik, namun dapat dikenali oleh sistem imun setelah berikatan dengan protein pada sel penampil antigen (*antigen-presenting cell/APC*), termasuk sel dendritik (*dendritic cell/DC*) dan sel Langerhans (*Langerhans cell/LC*). Interaksi antigenik pada kulit memicu pelepasan interleukin-1 β dan *tumor necrosis factor- α* (TNF- α) oleh LC dan keratinosit, yang selanjutnya mendorong migrasi DC dan LC menuju kelenjar getah bening. Pada fase sensitisasi awal ini, alergen dikenali dan diproses oleh sel dendritik dermal, kemudian dipresentasikan kepada sel T dan sel B. Sel T naif mengalami proliferasi klonal dan berdiferensiasi menjadi sel T efektor, yang merupakan ciri khas reaksi hipersensitivitas tipe IV. Sementara itu, sel B menghasilkan IgE spesifik terhadap alergen, yang kemudian berikatan dengan reseptor IgE pada sel mast dan basofil, mencerminkan mekanisme reaksi hipersensitivitas tipe I.^{2,3,6,9-11}



Gambar 5. Mekanisme DKA akibat perekat medis berbasis akrilat¹¹.

APC: *antigen-presenting cells*, LC: *Langerhans cells*, DC: *dendritic cells*, MHC II: *major histocompatibility complex II*, IL-1 β : *interleukin-1 β* , TNF- α : *tumor necrosis factor- α* , IFN- γ : *interferon- γ* , IL-47: *interleukin-47*, IL-22: *interleukin-22*, IL-4: *interleukin-4*, IL-2: *interleukin-2*.

Fase elisitasi berlangsung di dalam kelenjar getah bening, ketika sel Langerhans (LC) dan sel dendritik dermal (dDC) menyajikan antigen melalui molekul histokompatibilitas utama kelas I (MHC-I) dan kelas II (MHC-II). Mekanisme ini masing-masing mengaktivasi sel T CD8+ dan CD4+ naif, yang kemudian menstimulasi pelepasan berbagai sitokin, termasuk interleukin (IL)-12, IFN- γ , IL-17, IL-22, TNF- α , IL-4, dan IL-13. Rangkaian sinyal tersebut mendorong terjadinya proliferasi lanjutan sel T CD4+ yang membawa antigen (Ag), serta aktivasi sel T CD4+ dan CD8+ naif yang menghasilkan IFN- γ dan memicu diferensiasi sel Tc1 dan Th1. Selain itu, subpopulasi sel T CD4+ efektor spesifik haptan, termasuk sel T pembantu (Th) dan sel T regulator, berkontribusi terhadap (1) inisiasi migrasi sel inflamasi dari sirkulasi menuju jaringan lokal, (2) induksi apoptosis pada keratinosit, serta (3) reaktivasi atau aktivasi serta regulasi sel inflamasi. Sementara itu, sel T CD8+ sitotoksik berperan sebagai efektor utama spesifik haptan di epidermis dan dermis, sehingga memicu perubahan histologis dan infiltrasi sel inflamasi yang didominasi oleh limfosit dan neutrofil. Sel T naif yang mengekspresikan reseptor sel T (*T-cell receptor/TCR*) yang spesifik terhadap haptan mengalami ekspansi klonal, diikuti oleh pembentukan serta

distribusi sel T memori dan efektor ke berbagai jaringan, termasuk kulit, kelenjar getah bening, serta sistem vaskular dan limfatik. Sel T efektor ini dapat dengan cepat diaktivasi kembali ketika terjadi paparan berulang terhadap alergen yang sama, sehingga memicu pelepasan berbagai sitokin dan menarik sel inflamasi lain seperti granulosit dan makrofag. Proses ini merupakan ciri khas dari reaksi hipersensitivitas tipe IV. Pada saat yang sama, alergen yang identik dapat berikatan dengan IgE spesifik yang terikat pada reseptor permukaan sel *mast* dan basofil. Ikatan silang (*cross-linking*) dari dua reseptor yang berdekatan memicu degranulasi, yang ditandai dengan pelepasan berbagai mediator, termasuk histamin, protease, heparin, prostaglandin D2, dan faktor pengaktif trombosit (*platelet activating factor*). Hal ini dikenal sebagai degranulasi (reaksi hipersensitivitas tipe I). Kombinasi aktivasi sel inflamasi dan pelepasan mediator inilah yang pada akhirnya menghasilkan manifestasi klinis dermatitis kontak.^{2,3,6,9-11}

Tabel 1. Daftar alergen standar yang disarankan untuk uji tempel (*patch-test*) pada kasus dengan kecurigaan alergi terhadap perekat dan perban medis oleh North American Contact Dermatitis Group (NACDG)⁵

1. Tetrahydrofurfuryl methacrylate 2.0% pet	44. Triglycidyl isocyanurate 0.5% pet
2. Zinc ethylenebis (dithiocarbamate) 1.0% pet	45. Isophorone diisocyanate 1% pet
3. Isooctyl acrylate 1.0% pet	46. Triethylene glycol dimethacrylate 0.1% pet
4. Mastisol Liquid Adhesive (as is)	47. Ethyl alpha-cyanoacrylate (super glue) as is
5. Dimethylphthalate 5.0% pet	48. Hydroxypropyl acrylate 0.1% pet
6. Compound benzoin tincture (as is)	49. 2-Hydroxy propyl methacrylate 0.2% pet
7. Octadecyl maleamic acid 1.0% EtOH	50. 1,6-Hexanediol diacrylate 0.1% pet
8. N,n-dimethyl-p-toluidine 2.0% pet	51. Tetraethylene glycol dimethacrylate 2.0% pet
9. Triethylenetetramine 0.5% pet	52. Butyl acrylate 0.1% pet
10. Diethylenetriamine 0.5% pet	53. 2-Ethylhexyl acrylate 0.1% pet
11. Isophorone diamine 0.1% pet	54. Triethylene glycol dimethacrylate 2.0% pet
12. Hexamethylenetetramine 1.0% pet	55. 4-tert-Butylcatechol (PTBC) 0.5% pet
13. Bisphenol A 1.0% pet	56. Colophony 20% pet*
14. Dioctyl phthalate 2.0% pet	57. p-Phenylenediamine 1% pet*
15. 2-(2-Hydroxy-5-methylphenyl) benzotriazol 1.0% pet	58. Epoxy resin (bis-A) 10% pet*
16. Benzoyl peroxide 1.0% pet	59. p-tert-Butylphenol formaldehyde resin 1% pet*
17. Dibutyl phthalate 5.0% pet	60. 2,6-di-tert-Butyl-4-cresol 2% pet*
18. Tricresyl phosphate 5.0% pet	61. 2-tert-Butyl-4-cresol 2% pet*
19. Triphenyl phosphate 5.0% pet	62. Phenol formaldehyde resin 1% pet*
20. Resorcinol monobenzoate 1.0% pet	63. Ethylene glycol dimethacrylate 2% pet*
21. Hydroquinone 1.0% pet	64. 2-Hydroxyethyl methacrylate 1% pet*
22. Abitol 10% pet	65. Methyl methacrylate 2% pet*
23. 4-tert-Butylphenol 1.0% pet	66. Ethyl acrylate 0.1% pet*
24. Diphenylthiourea 1.0% pet	67. Mercaptobenzothiazole 1% pet*
25. Toluene-2,4-diisocyanate 2.0% pet	68. Carba mix 3% pet*
26. Diphenylmethane-4,4-diisocyanate 2.0% pet	69. Thiuram mix 1% pet*
27. N,n'-dimethyl thiourea 1.0% pet	70. Tegaderm (3M) as is, cut in quarters (3 × 3 cm)
28. Ethylbutyl thiourea 1.0% pet	71. Micropore™ 1530 (3M) as is, 2.5 × 2.5 cm
29. Niax 0.5% pet	72. Steri-Strip Blend Tone Skin Closures (3M) as is, cut in thirds (2.0 × 2.5 cm)
30. Dibutyl thiourea 1.0% pet	73. Transpore Surgical Tape (3M) as is, 2.5 × 2.5 cm
31. Resorcinol 1.0% pet	74. Meditrace Pre-gelled Cardiac Snap Electrodes (Kendall) as is, cut in quarters, 2.5 × 2.5 cm
32. Methylene-bis-thiocyanate 1.0% pet	75. Curity Plastic Bandages-Latex Free (Kendall) as is, cut in half (2.0 × 3.5 cm)
33. Diethyl thiourea 1.0% pet	76. Nexcare™ Sheer Bandages (3M) as is, cut in half (2.0 × 1.5 cm)
34. Ethyl methacrylate 2.0% pet	77. Adhesive Bandage-Sheer (Curad) as is, cut in half (3.5 × 2.0 cm)
35. n-Butyl methacrylate 2.0% pet	78. Band-Aid Brand-Sheer Comfort Flex (Johnson & Johnson) as is, cut in half (3 × 1.5 cm)
36. 3-Methyl-thiazolidone-thione-2 1.0% pet	79. Curity Sheer Bandage Strips (Kendall) as is, cut in half (3.5 × 2.0 cm)
37. Dodecylmercaptan 0.1% pet	
38. Bisphenol F epoxy resin 1.0% pet	
39. 1,6-Hexamethylene diisocyanate 0.1% pet	
40. Trimethylol propane triglycidyl ether 0.25% pet	
41. Trimethylol propane triacrylate 0.1% pet	
42. 2-Phenylindone 2.0% pet	
43. Cyclohexanone resin 1.0% pet	

Keterangan: pet = *in petrolatum*;

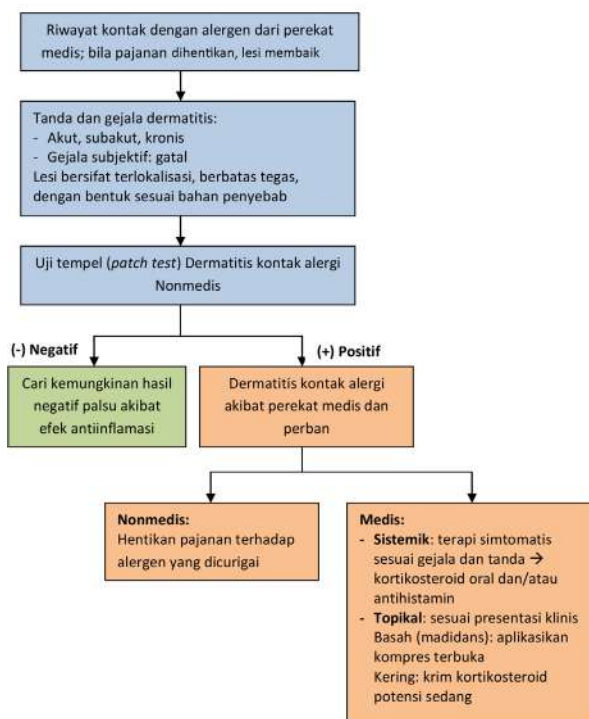
* Chemical present on the North American Contact Dermatitis Group Standard Allergen Tray.

Gambaran klinis dari dermatitis kontak alergi (DKA) bersifat polimorfik dan sangat bervariasi, bergantung pada stadium penyakit, sebagai berikut:

- Stadium akut: eritema, edema, dan vesikel.
- Stadium subakut: eritema, lesi eksudatif (*madidans*), dan krusta.
- Stadium kronik: likenifikasi, fisura, dan skuama.

Lesi dapat juga bersifat non-eksematosa, misalnya purpurik, likenoid, pigmented, dan limfomatoid. Gejala subjektif yang paling sering dikeluhkan berupa rasa gatal. Pada DKA yang terlokalisasi, lesi umumnya terbatas tegas dan berbentuk sesuai dengan bahan penyebab.⁷ Pada kasus yang disajikan ini, ditemukan gejala akut yang khas berupa eritema dengan papul hingga vesikel disertai skuama, yang tersebar difus mengikuti betuk plester penutup luka.

Terdapat enam metode diagnostik utama untuk menilai dermatitis kontak alergi, yaitu uji tempel, uji *fotopatch*, uji kulit untuk mendeteksi reaksi kontak langsung, pemeriksaan alergen secara *in vitro*, uji kualitatif dan kuantitatif terhadap alergen pada bahan yang diduga bersentuhan dengan pasien, dan uji tantangan. Uji tempel, baik menggunakan perban secara utuh maupun alergen individual, merupakan prosedur standar untuk menegakkan diagnosis jenis dermatitis kontak sekaligus mengidentifikasi alergen penyebab alergi. Lebih dari 70 alergen potensial tercakup dalam panel perekat dan sampel produk *patch*, termasuk Steri-Strip (3M), Tegaderm (3M), Micropore (3M), Transpore Surgical Tape (3M) dan Nexcare™ Sheer Bandage (3M). Standar North American Contact Dermatitis Group (NACDG) mencakup 104 bahan kimia yang secara rutin diuji pada pasien (**Tabel 1**).^{5,12,13} Namun, dalam kasus ini, uji tempel terhadap alergen perekat medis tidak dapat dilakukan karena keterbatasan fasilitas rumah sakit. Meskipun demikian, diagnosis DKA tetap dapat ditegakkan berdasarkan gambaran klinis yang khas, sehingga diagnosis banding lain dapat disingkirkan.



Gambar 6. Alur diagnosis dan penatalaksanaan DKA akibat perekat medis⁷

Penatalaksanaan akut pada kasus ini mencakup pelepasan pita perekat dari permukaan kulit, diikuti dengan pembersihan area yang terdampak secara hati-hati, serta penggunaan kortikosteroid topikal jangka pendek, bila diperlukan. Pasien dianjurkan untuk menghindari tindakan menggaruk. Perbaikan klinis umumnya terjadi dalam beberapa jam hingga beberapa hari setelah perekat dilepas. Terapi sistemik diberikan secara simptomatis; pada kasus dengan manifestasi klinis yang lebih berat dapat dipertimbangkan pemberian kortikosteroid sistemik setara *prednisone* 20 mg/hari dalam jangka pendek (± 3 hari), serta antihistamin untuk mengatasi pruritus. Terapi topikal tambahan dapat berupa pelembab yang dianjurkan untuk diberikan setelah fase akut mereda, terutama pelembab dengan kandungan lipid tinggi seperti Vaseline® (*petrolatum*). Pada lesi yang bersifat basah (*madidans*), dapat diberikan kompres terbuka menggunakan kasa steril berlapis (2–3 lapis) yang dibasahi dengan larutan NaCl 0,9%. Sebaliknya, pada lesi kering, digunakan kortikosteroid topikal dengan potensi sedang hingga tinggi, seperti *mometasone furoate*, *fluticasone propionate*, atau *clobetasone butyrate*.^{7,13} Skema alur diagnosis dan penatalaksanaan DKA akibat perekat medis ditampilkan pada **Gambar 6**.

Kesimpulan

Penggunaan perekat medis sebagai penutup luka dapat memicu sensitisasi serta menimbulkan dermatitis kontak alergi (DKA). Perekat medis yang mengandung akrilat berpotensi menyebabkan sensitisasi karena sifatnya sebagai hapten dengan berat molekul rendah yang mampu menembus *stratum corneum* dan mengaktifasi respons imun serta inflamasi kulit. Penatalaksanaan utama dari DKA akibat perekat medis meliputi pelepasan perekat medis dari permukaan kulit dan menghindari penggunaannya. Pada kasus dengan manifestasi klinis tertentu dapat diberikan kortikosteroid. Meskipun demikian, seluruh bahan perekat medis, baik sintetis maupun biologis, harus melalui pengujian untuk memastikan efikasi dan keamanan sebelum digunakan secara klinis.

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Peran *Mannitol* dalam Penanganan Peningkatan Tekanan Intrakranial pada Strok Nonhemoragik dengan Penyakit Jantung Bawaan: Laporan Kasus

Putu Indah Mahardika Putri, I Wayan Widyantara

Departement of Neurology, Faculty of Medicine, Udayana University/RSUP Prof. dr. I.G.N.G. Ngoerah, Denpasar, Bali, Indonesia

Abstrak

Latar belakang: Strok adalah suatu keadaan gangguan peredaran darah di otak yang menyebabkan terjadinya kematian jaringan otak. Strok merupakan penyebab kematian kedua terbesar di dunia setelah penyakit jantung. Strok nonhemoragik dapat disebabkan oleh adanya trombus ataupun penyumbatan emboli. Penyakit jantung bawaan (PJB) merupakan salah satu faktor risiko terjadinya strok, termasuk *tetralogy of Fallot* (TOF). Angka kejadian PJB dengan strok sebesar 1 dari 11 laki-laki dan 1 dari 15 perempuan. Salah satu komplikasi yang terjadi pada strok adalah peningkatan tekanan intrakranial (TIK). *Mannitol* merupakan salah satu terapi yang dapat digunakan untuk menurunkan tekanan intrakranial.

Laporan kasus: Laki-laki, 19 tahun, riwayat TOF datang dengan penurunan kesadaran dan kelemahan separuh tubuh kiri. Gambaran CT scan didapatkan hasil lesi hipodens mengarah ke strok iskemik. Tiga hari setelah perawatan, pasien mengalami perburukan kondisi dengan tanda peningkatan TIK. CT scan ulang didapatkan gambaran transformasi hemoragik disertai herniasi unkal. *Mannitol* digunakan sebagai penanganan peningkatan TIK selama 3 hari dengan hasil perbaikan klinis. Tiga hari setelah itu pasien dipulangkan dengan perbaikan klinis.

Kesimpulan: Penggunaan *mannitol* pada kasus strok dengan kelainan PJB atau TOF memiliki hasil yang baik tanpa menyebabkan efek samping atau gangguan pada kelainan jantung tersebut. *Mannitol* dapat digunakan pada pasien dengan gangguan jantung.

Kata kunci: *tetralogy of Fallot*, strok, emboli, *mannitol*, peningkatan tekanan intrakranial

Abstract

Background: Stroke is a condition of impaired cerebral circulation leading to brain tissue necrosis. It is the second leading cause of death worldwide after heart disease. Nonhemorrhagic stroke may result from thrombus formation or embolic occlusion. Congenital heart disease (CHD) is one of the risk factor for stroke, including tetralogy of Fallot (TOF). The incidence of stroke in CHD is approximately 1 in 11 males and 1 in 15 females. One of the complications of stroke is increased intracranial pressure (ICP). Mannitol is one of treatment that can be used to reduce elevated intracranial pressure (EICP).

Case report: A 19-year-old male with a history of TOF presented with decreased consciousness and left-sided hemiparesis. A CT scan revealed a hypodense lesion suggestive of ischemic stroke. On the third day of hospitalization, the patient's condition worsened, showing signs of increased ICP. A repeat CT scan showed hemorrhagic transformation accompanied by uncal herniation. Mannitol was administered for 3 days to manage the increased ICP, resulting in clinical improvement.

Three days later, the patient was discharged with improved condition.

Conclusion: The use of mannitol in stroke cases with CHD, such as TOF, showed favorable outcomes without causing adverse effects or worsening the underlying cardiac condition. Mannitol may be considered in patients with cardiac comorbidities.

Keywords: tetralogy of Fallot, stroke, embolism, mannitol, elevated intracranial pressure

Pendahuluan

Strok merupakan penyakit dengan angka kejadian terbanyak ketiga setelah penyakit jantung dan kanker, serta merupakan penyebab kecacatan tertinggi di dunia.¹ Menurut American Heart Association (AHA), pada tahun 2015 prevalensi strok di dunia mencapai angka 33 juta pasien. Strok adalah penyebab kematian ke-5 di Amerika dengan angka penderita sebanyak 795.000 pasien setiap tahun dan pasien yang meninggal sebanyak 129.000 jiwa. Berdasarkan hasil Riskesdas tahun 2013, prevalensi penyakit strok di Indonesia meningkat seiring bertambahnya usia. Kasus strok tertinggi yang terdiagnosis oleh tenaga kesehatan terjadi pada usia >75 tahun (43,1%) dan terendah pada kelompok usia 15–24 tahun (0,2%). Prevalensi berdasarkan jenis kelamin terjadi lebih banyak pada laki-laki (7,1%) dibandingkan dengan perempuan (6,8%). Kasus strok yang paling sering terjadi di dunia diperkirakan adalah strok nonhemoragik (SNH) dengan persentase 85–87% dari semua kasus strok.¹

Strok adalah terjadinya gangguan fungsional otak fokal maupun global secara mendadak dan akut yang berlangsung lebih dari 24 jam, akibat adanya gangguan aliran darah otak. Adanya gangguan peredaran darah di otak dapat menyebabkan terjadinya kematian jaringan otak sehingga mengakibatkan seseorang menderita kelumpuhan atau kematian. Setiap 7 orang yang meninggal di Indonesia, 1 diantaranya karena strok. Sebagian besar pasien strok dapat ditangani melalui unit gawat darurat (UGD) atau dengan perawatan di bangsal. Namun, sekitar 15–20% pasien strok membutuhkan penanganan di ruang perawatan intensif (*intensive care unit/ICU*).

Tekanan intrakranial (TIK) adalah tekanan di dalam ruang tengkorak yang dilindungi dari tekanan luar. Tekanan ini dinamik dan berfluktuatif secara ritmis mengikuti siklus jantung, respirasi, dan perubahan proses fisiologis tubuh; secara klinis bisa diukur dari tekanan intraventrikuler, intraparenkimal, ruang subdural, dan epidural. Pengukuran kontinu pada satu kompartemen intrakranial akan memperlihatkan perubahan fisiologis dan patologis ruang dalam tengkorak dari waktu ke waktu, yang diperlukan sebagai dasar tata laksana pasien dengan peningkatan tekanan intrakranial.²

Laporan Kasus

Pasien laki-laki usia 19 tahun, dikonsulkan oleh rekan sejawat dari bagian kardiologi pada tanggal 15 Agustus 2022, dengan keluhan penurunan kesadaran. Penurunan kesadaran terjadi sejak 2 hari sebelum masuk rumah sakit (SMRS). Dua hari sebelum terjadi penurunan kesadaran, pasien merasa lemas, dan ketika badan pasien akan dibersihkan oleh keluarga, tiba-tiba pasien pingsan. Kemudian pasien dibawa ke instalasi gawat darurat (IGD) dalam kondisi kesadaran sudah membaik namun masih merasa lemas. Satu hari SMRS pasien mulai tidak merespons saat diajak berkomunikasi dan hanya mengucapkan kata “aduh” bila diberikan stimulus nyeri. Pasien memiliki riwayat TOF (*tetralogy of Fallot*) yang baru diketahui sekitar 2 bulan yang lalu. Berdasarkan informasi dari ayah pasien, saat kecil pasien sering kesulitan dalam melakukan aktivitas berat seperti olahraga sehingga lebih banyak beristirahat. Keluarga pasien tidak mengetahui adanya sesak atau kebiruan pada pasien ketika kecil, namun beberapa bulan terakhir keluarga nampak mengamati adanya kebiruan yang hilang timbul pada pasien terutama pada bibir dan kuku pasien. Pasien memiliki berat badan 40 kg dan tinggi badan 160 cm. Saat dilakukan pemeriksaan fisik didapatkan tensi 90/60 mmHg, frekuensi nadi 45 kali per menit, frekuensi pernapasan 22 kali per menit, suhu 37,2°C, dan saturasi oksigen 76% dengan oksigen nasal kanul 3 liter per menit (lpm). Pada pemeriksaan umum didapatkan adanya *clubbing finger* dan suara murmur sistolik. Evaluasi pemeriksaan neurologis pasien didapatkan dengan GCS E3V3M5, menunjukkan adanya meningismus, kesan paresis nervus kranialis lateralisasi

tenaga tidak ditemukan, klonus didapatkan pada kedua kaki kanan dan kiri, sedangkan refleks patologis negatif. Hasil pemeriksaan rontgen didapatkan adanya gambaran *boot-shaped*. Kemudian dilakukan CT (*computed tomography*) scan kepala pasien pada tanggal 15 Agustus 2022, dengan hasil *leptomeningeal enhancement* pada regio parietal kanan dan oksipital kiri, mengesankan gambaran meningitis, *subacute cerebral infarction* pada lobus temporoparietal kanan (sesuai teritori M2, M3, M4, M5, M6 kanan), lobus parietal kiri (sesuai teritori M3, M6 kiri) dengan *luxury perfusion*, serta *cerebellum* hemisfer kiri, edema *cerebri*, kalsifikasi *falx cerebri* dan *tentorium cerebelli* kanan kiri, suspek *old infection process*.

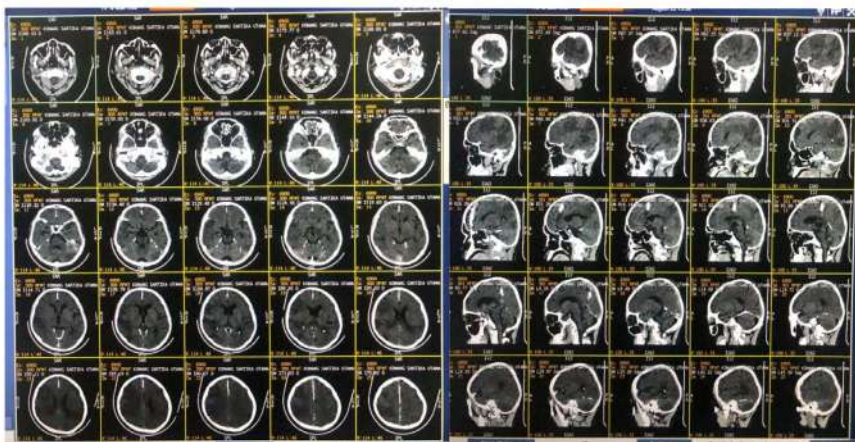
Pemeriksaan *echocardiography bedside* pada 12 Agustus 2022 menunjukkan gambaran *atrial septal defect* (ASD) dan *ventricular septal defect* (VSD), sehingga didapatkan kesimpulan adanya *classic tetralogy of Fallot* (TOF). Berdasarkan hasil pemeriksaan fisik dan penunjang, pasien didiagnosis dengan observasi penurunan kesadaran *et causa* suspek proses intrakranial, suspek *early cerebritis* dan strok nonhemoragik kardioemboli *et causa* suspek emboli septik. Terapi dilakukan dengan pemberian antibiotik *metronidazole* 3 x 500 mg intravena dan *ceftriaxone* 2 x 2 gram intravena untuk kecurigaan awal meningoensefalitis dari gambaran CT scan, serta pemberian *acetosal* 1 x 80 mg peroral. Disarankan untuk dilakukan kultur darah dan pemeriksaan *provider initiated testing and counseling* (PITC) serta MRI lebih lanjut pada pasien. Rekan sejawat dari bagian kardiologi mendiagnosis pasien dengan *cyanotic spell* dan *classic* TOF. Terapi dari rekan sejawat kardiologi adalah *propranolol* 3 x 30 mg peroral dan *morphine* 2 mg intravena selama 24 jam setiap kali pasien gelisah. Hasil pemeriksaan laboratorium darah pasien juga menunjukkan pasien mengalami anemia sehingga dilakukan transfusi *packed red cells* (PRC) 1 kolf per hari sampai dengan Hb >14 g/dl ditambah *ferrous sulfate* 3 x 200 mg dan *omeprazole* 2 x 20 mg per oral.



Gambar 1. CT scan kepala nonkontras (15 Agustus 2022)

Dari hasil pemeriksaan pasien tanggal 16 Agustus 2022 dilakukan *review* ke divisi vaskular dan divisi infeksi dengan hasil ditemukan adanya vaskulitis dengan infeksi intrakranial. Kemudian diusulkan untuk dilakukan pungsi lumbal serta pemberian *acetosal*. Hasil *review* divisi infeksi didapatkan adanya meningoensefalitis bakteri dengan suspek *early cerebritis*. Kemudian pasien diberikan tambahan terapi *dexamethasone* 4 x 10 mg intravena. Tidak dilakukan pungsi lumbal karena kondisi pasien saat itu tidak stabil di mana saturasi oksigen masih sama seperti pada saat awal dikonsulkan. Hasil pemeriksaaan pada tanggal 22 Agustus 2022 (3 hari perawatan di ruang biasa *nonintermediate*) pasien kembali

mengalami penurunan kesadaran dengan temuan GCS E2V2M5. Pasien tidak mau berbicara serta sulit dibangunkan dengan menggunakan suara panggilan, tetapi mampu bangun bila dirangsang dengan rangsangan nyeri kuat. Dari informasi yang disampaikan kakak pasien, sebelumnya pasien sempat mengalami perbaikan, yaitu mampu melakukan kontak dengan kakaknya. Nyeri kepala ataupun muntah proyektil disangkal oleh kakak pasien. Pemeriksaan fisik neurologis terbaru didapatkan adanya pupil yang anisokor, dengan hasil funduskopi didapatkan adanya papil edema, terkesan adanya lateralisasi sinistra *grade* >3. Berdasarkan evaluasi tersebut dilakukan CT scan ulang pada pasien dan dicurigai adanya peningkatan TIK dan tanda herniasi. Pasien juga diduga mengalami transformasi hemoragik serta dicurigai adanya herniasi unkal *et causa* transformasi hemoragik. Hasil evaluasi CT scan dibandingkan dengan CT scan kepala sebelumnya tanggal 15 Agustus 2022 sebagai berikut: *subacute cerebral infarction* pada *cortical, subcortical lobus temporo-parietal* kanan (sesuai teritori segmen M2, M3, M4 MCA (*middle cerebral artery*) kanan), dan di lobus parietal kiri (sesuai teritori segmen M3, M4 MCA kiri), disertai tanda-tanda transformasi hemoragik. *Subacute cerebellar infarction* di *hemisphere cerebellum* kanan kiri (sesuai teritori *superior cerebellar artery* (SCA) kanan kiri), kalsifikasi *falx cerebri* dan *tentorium cerebelli* kanan kiri. *Retention cyst* sinus *sphenoidalis* kiri serta hipertrofi konka nasi inferior kanan kiri.



Gambar 2. Evaluasi CT scan kepala nonkontras (22 Agustus 2022)

Berdasarkan evaluasi hasil CT scan, ditambahkan pemberian terapi *mannitol* 200 ml (setara dengan 40 mg) bolus untuk mengatasi peningkatan TIK, dan terapi pemeliharaan dengan dosis 100 ml (setara dengan 20 mg). Pemberian *acetosal* pada pasien tetap dilanjutkan. Pada tanggal 26 Agustus 2022, kesadaran pasien mulai membaik, dapat membuka mata dengan spontan, kontak pasien cukup, dapat mengeluarkan beberapa kata namun belum dapat mengeluarkan kata yang membentuk sebuah kalimat. Dari hasil pemeriksaan neurologis, didapatkan adanya perbaikan GCS dari E2V2M5 menjadi E4V3M5, serta perubahan pupil pasien menjadi isokor dengan besar 3 mm/2 mm. Selain itu, pemeriksaan motorik mengalami perbaikan menjadi *grade* 4+. Pada tanggal 28 Agustus 2022, pasien dirawat di poliklinik dan direncanakan untuk dilakukan pemeriksaan *magnetic resonance angiography* (MRA) melalui poliklinik. Dalam evaluasi pemberian *mannitol* selama tiga hari, pasien mengalami perbaikan klinis.

Diskusi

Tetralogy of Fallot (TOF) merupakan sebuah penyakit jantung bawaan yang secara anatomis malformasi terdiri dari stenosis katup pulmonal (umumnya stenosis subinfundibular), defek septum ventrikel, *overriding* aorta, dan hipertrofi ventrikel kanan.⁴ Kondisi ini melibatkan empat defek yang membuat tingkat oksigen dalam darah terlalu rendah:

1. Defek septum ventrikel. Terdapat sebuah lubang besar pada dinding antara kedua ventrikel yang memungkinkan darah yang rendah oksigen bercampur dengan darah yang kaya oksigen.
2. Terjadi penyempitan pada katup pulmonal. Penyempitan bisa terjadi tepat di bawah atau di atas katup sehingga dapat menghalangi aliran darah dari sisi kanan jantung ke paru-paru. Penyempitan ini biasanya terjadi pada ketiga wilayah sekaligus.
3. Hipertrofi ventrikel kanan.
4. *Overriding aorta*. Terjadi deviasi katup aorta ke kanan sehingga kedua ventrikel bermuara ke aorta. Aorta yang terletak langsung di atas ventrikel kanan, sehingga darah yang rendah oksigen juga mengalir ke aorta.

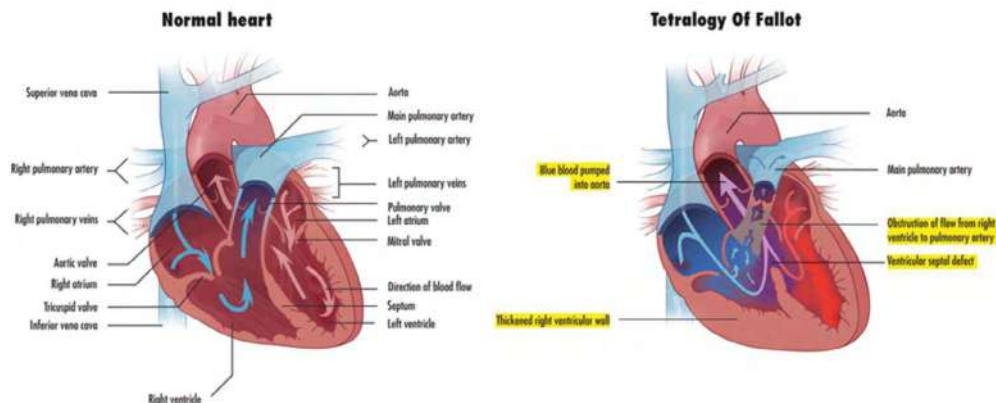
TOF dapat diketahui dengan mengukur kadar oksigen neonatus yang lebih rendah dibandingkan dengan kondisi normal atau neonatus tampak biru pada bagian bibir atau ujung kuku (sianosis). Pada pemeriksaan klinis seringkali didapatkan murmur jantung. Pemeriksaan ekokardiografi dilakukan untuk menegakkan diagnosis.^{3,4} Pada umumnya, neonatus dengan TOF mengalami asianotik saat lahir. Setelah 6 bulan, sianosis mulai muncul disertai hipoksia *spell* atau *tet spell*.⁴ *Tet spell* adalah munculnya sianosis saat bayi menangis atau menyusui. Gejala yang dapat muncul bervariasi tergantung dari beratnya obstruksi aliran darah ke paru-paru. Beberapa neonatus dengan obstruksi yang ringan seringkali tidak menjadi biru dan memiliki gejala napas cepat, tidak mau makan, dan pertumbuhan yang lambat karena terlalu banyak aliran darah ke paru-paru.³

Strok pada pasien dengan penyakit TOF yang mendasari merupakan kejadian yang tidak jarang ditemukan. Strok terjadi ketika aliran darah ke suatu bagian otak terganggu atau sangat berkurang, sehingga otak mengalami kekurangan oksigen dan nutrisi. Beberapa cacat jantung bawaan meningkatkan risiko terjadinya strok karena adanya kondisi abnormal pada jantung memungkinkan terjadinya gumpalan darah (trombus) di jantung yang akan sampai ke pembuluh darah otak. Aritmia jantung tertentu juga dapat meningkatkan kemungkinan terjadi pembentukan gumpalan darah yang bisa menyebabkan strok. Perubahan fisiologis yang terjadi tergantung dua variabel, derajat obstruksi pulmonal, dan resistansi vaskular sistemik. Sebagian besar pasien dengan TOF akan mengalami gangguan pertumbuhan, namun kadang terjadi sirkulasi kolateral ke paru sehingga dapat mempertahankan pertumbuhan.³ Sianosis yang terjadi simetris, akibat adanya parau dari ventrikel kanan ke kiri melalui defek besar yang nonrestriktif. Hipertrofi ventrikel kanan biasanya tidak terlalu berat, lain halnya pada hipoplasia arteri pulmonal, sehingga tidak sampai terjadi obliterasi pada rongga ventrikel kanan. Tindakan reparasi masih mungkin dilakukan pada kondisi ini. Bila obstruksi pulmonal tidak terlalu berat maka derajat sianosis juga ringan, yang dikenal sebagai *acyanotic Fallot* atau *pink tetralogy*, dan kadang-kadang ditemui pada dewasa muda.

Mayoritas strok yang terjadi adalah strok iskemik dan sekitar 20% di antaranya terkait dengan emboli serebral kardiogenik. Penyakit jantung bawaan seperti defek septum dan *patent foramen ovale* bisa menjadi potensi penyebab strok pada orang dewasa. *Tetralogy of Fallot* (TOF) adalah bentuk paling umum dari penyakit jantung bawaan sianotik dan terdiri dari *ventricular septal defect* (VSD), obstruksi saluran keluar ventrikel kanan, *overriding aorta*, dan hipertrofi ventrikel kanan.³ Meskipun biasanya didiagnosis dan diobati selama masa bayi, hanya 3% dari pasien mencapai usia 40 tahun tanpa koreksi bedah. Orang dewasa dengan kelainan jantung kongenital sianotik juga berisiko tinggi terkena strok dan tromboemboli. Strok merupakan salah satu komplikasi yang sering terjadi pada pasien dengan TOF, bentuk paling umum dari kelainan jantung kongenital sianotik. Malformasi jantung kongenital dewasa dapat menyebabkan pembentukan trombus intra-jantung (di ruang jantung kanan dan atrium kiri pada pasien dengan kelainan jantung kongenital dan ventrikel kiri pada pasien dengan kardiomiopati) serta memfasilitasi trombogenesis dalam pembuluh darah sistem saraf pusat.

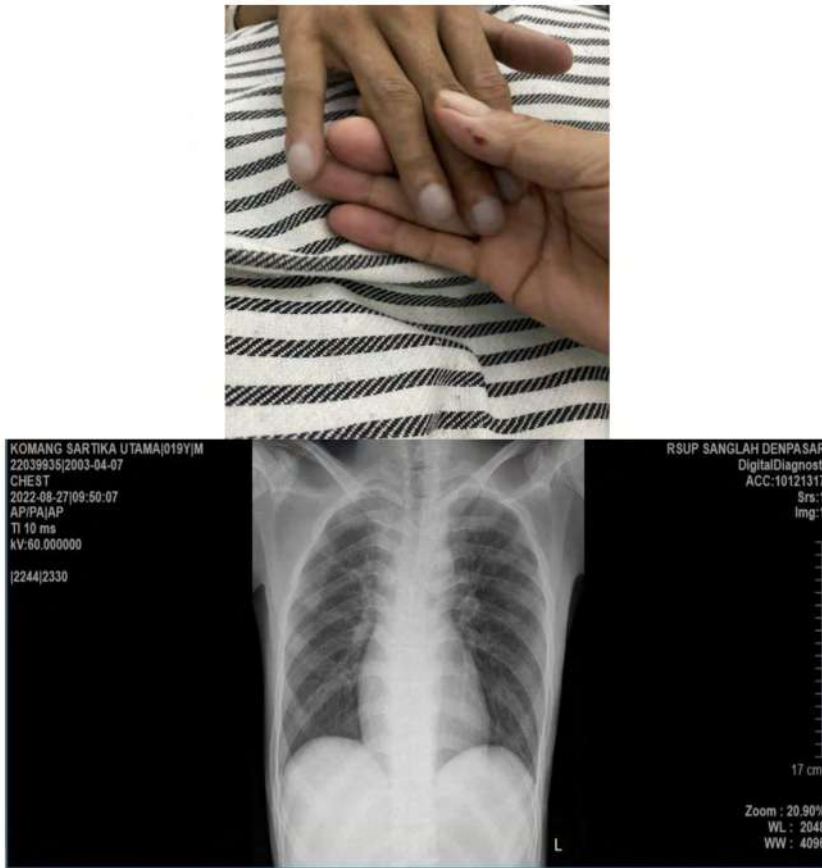
Ada beberapa faktor risiko yang terlibat dalam patogenesis trombosis pada pasien dengan penyakit jantung kongenital seperti eritrositosis, hipoksia/hipoksemia yang diinduksi aktivasi sekunder dari jalur prokoagulan, asidosis kronik, peningkatan deposisi fibrin, peningkatan ekspresi faktor jaringan, dan gangguan fibrinolisis. Orang dewasa dengan kelainan jantung

kongenital sianotik memiliki peningkatan massa sel darah merah. Eritrositosis sekunder ini dapat meningkatkan viskositas darah sehingga dapat mengurangi aliran darah otak. Meskipun terdapat gangguan koagulasi signifikan dan meningkatkan kecenderungan trombotik pada pasien dengan kelainan jantung kongenital sianotik, pemberian antikoagulan tidak rutin dianjurkan jika tidak ada indikasi lain (katup mekanik, atrial fibrilasi, dan lain-lain). Flebotomi mungkin efektif dalam meningkatkan hiperviskositas tapi kemampuannya untuk mencegah emboli masih kontroversial.



Gambar 3. Gambar jantung normal dan *tetralogy of Fallot*

Dikaitkan dengan kasus yang dipaparkan, pasien merupakan laki-laki berusia 19 tahun, yang baru diketahui mengalami penyakit TOF 2 bulan sebelum rawat inap. Namun dari keterangan keluarga pasien, sejak kecil pasien sering mengalami kebiruan di sekujur tubuh dan area kuku, dan pasien tidak pernah mengikuti pelajaran olahraga karena sering atau mudah merasakan kelelahan. Saat itu pihak keluarga belum memiliki kecurigaan mendasar yang mengarah ke penyakit jantung bawaan, hingga akhirnya 2 bulan sebelum dirawat inap di RSUP Prof. dr. I.G.N.G. Ngoerah, Denpasar. Awalnya pasien dirawat inap di RSUD Buleleng dan dilakukan evaluasi lebih lanjut, yang kemudian baru diketahui pasien mengalami penyakit jantung bawaan. Pasien dirujuk untuk penanganan lebih lanjut di pusat jantung terpadu (PJT) RSUP Prof. dr. I.G.N.G. Ngoerah, Denpasar. Dari data objektif yang ditemukan, secara klinis pasien memiliki *clubbing finger* dengan warna kebiruan di sekitarnya. Hasil pemeriksaan fisik didapatkan adanya murmur sistolik kemudian didukung dengan gambaran EKG pada tanggal 12 Agustus 2022, yang mengarah ke diagnosis *classic tetralogy of Fallot*. Berdasarkan hasil pemeriksaan radiologi, didapatkan adanya suatu gambaran *boot-shaped appearance* yang mendukung gambaran TOF.



Gambar 4. Gambaran *clubbing finger* dan *boot-shaped appearance*

Strok didefinisikan sebagai adanya defisit neurologis fokal atau gangguan global dari fungsi serebral yang cepat, bertahan hingga lebih dari 24 jam atau menyebabkan kematian, dengan tidak ada penyebab pasti selain dari gangguan vaskular. Strok merupakan penyebab mortalitas dan disabilitas jangka panjang tertinggi di dunia. Salah satu penyebab kematian pada kasus strok adalah timbulnya peningkatan TIK ataupun adanya herniasi unkal yang menyebabkan adanya kompresi pada batang otak. Pada strok iskemik berkaitan dengan terjadinya edema sitotoksik (intraseluler) dan vasogenik (ekstraseluler, interstisial). Edema sitotoksik terbentuk dalam 1 jam setelah terjadinya serangan, kemudian setelah 3–4 hari dapat berubah menjadi edema vasogenik. Pada strok iskemik yang luas, peningkatan TIK seringkali terjadi antara hari ke-1 dan ke-3. Sedangkan pada strok hemoragik, edema yang terbentuk dari hari ke-4 hingga hari ke-14 dapat menyebabkan tekanan tinggi intrakranial (TTIK).

Dalam kasus ini, adanya defisit global, yaitu penurunan kesadaran secara gradual selama dua hari sebelum kondisi semakin memburuk, disertai adanya kesan hemiparesis pada salah satu sisi tubuh (defisit fokal) menimbulkan kecurigaan terjadinya strok iskemik akut. Riwayat TOF pada pasien diduga sebagai salah satu faktor risiko dalam terjadinya serangan strok ini. Hasil CT scan memperkuat diagnosis strok iskemik akut pada pasien ini. Setelah beberapa hari masa perawatan, pasien nampak mengalami penurunan kesadaran kembali dengan ditemukan pupil anisokor disertai dengan hasil funduskopi didapatkan adanya edema papil yang membuat dugaan terjadinya peningkatan TIK semakin kuat. Hasil CT scan ulang

memperkuat dugaan terjadinya peningkatan TIK dan juga herniasi pada kasus ini. Beberapa gejala TTIK yang sering terjadi adalah nyeri kepala, muntah, kejang, ataupun perubahan status mental dan penurunan kesadaran. Patofisiologi terjadinya TTIK antara lain adalah edema serebri, obstruksi aliran cairan serebrospinal (*cerebral spinal fluid/CSF*), peningkatan volume darah otak (*cerebral blood volume/CBV*), dan perluasan massa otak. Edema serebri merupakan salah satu komplikasi semua tipe stroke. Waktunya bervariasi mulai dari 24 jam pertama sampai sekitar 72 jam setelah onset.

Edema serebri yang terjadi adalah edema serebri tipe sitotoksik. Proses terbentuknya edema sitotoksik pada stroke iskemik akut adalah akibat penurunan *cerebral blood flow* (CBF) regional otak yang terisolasi dari aliran darah sehingga akan terjadi daerah yang iskemik. Autoregulasi dan vasomotor di daerah tersebut bekerja sama untuk menanggulangi keadaan iskemik dengan mengadakan vasodilatasi maksimal. Pada bagian yang mengalami iskemik berat, autoregulasi akan terganggu. Saat proses iskemik menjadi infark, fungsi homeostatik yang mengontrol volume sel dan permeabilitas sawar darah otak terganggu karena pompa ATP-dependent Na^+/K^+ ATP-ase tidak bisa berfungsi tanpa ATP. Hal ini berakibat masuknya Na^+ ke dalam sel, diikuti oleh masuknya Cl^- dan air, sehingga mengakibatkan edema. Kaskade inilah yang mengganggu mekanisme kontrol volume sel dan menyebabkan edema sitotoksik. Seperti pada edema sitotoksik yang mendahuluinya, edema vasogenik juga berkembang sebagai konsekuensi kegagalan energi, pelepasan glutamat, dan peningkatan konsentrasi kalsium intraseluler. Radikal bebas juga berperan dalam pembentukan edema vasogenik iskemik. Proses edema ini akan meningkatkan tekanan intrakranial pada stroke infark yang luas. Edema sitotoksik terjadi pada jam-jam pertama setelah onset stroke iskemik dan dapat dideteksi sebagai penurunan *apparent diffusion coefficient* (ADC) air. Penurunan ADC juga ditunjukkan pada stroke hemoragik akut, tapi berbeda dengan stroke iskemik di mana ADC tetap menurun sampai 100 hari setelah onset. Emboli dari jantung ke otak dapat disebabkan oleh 3 mekanisme: adanya stasis dalam pembuluh darah dan formasi trombus pada pembesaran ventrikel kiri, pelepasan material dari permukaan valvular yang abnormal; dan adanya aliran yang abnormal dari vena ke sirkulasi arteri. Infark karena kardioemboli merupakan jenis stroke yang paling berat.

Stroke kardioemboli seringkali muncul dengan manifestasi defisit neurologi yang mendadak dan maksimal. Kardioemboli seringkali menyumbat di bagian arteri distal yang menyuplai korteks serebral, di mana oklusi pembuluh darah mengenai jaringan subkortikal. Stroke kardioemboli dapat dibedakan dari stroke *lacunar*, yaitu dari adanya gejala kortikal seperti afasia atau gangguan lapang pandang. Emboli yang menyumbat pembuluh darah dapat menyebabkan penurunan perfusi darah ke otak sehingga menyebabkan adanya iskemia pada otak. Iskemia pada otak menyebabkan gangguan pada pompa Na^+/K^+ sehingga terjadi edema sitotoksik.

Terjadinya peningkatan TIK tidak lepas dari adanya hukum Monroe–Kellie yaitu kompartemen intrakranial merupakan sistem tertutup yang *nonexpandable*, tertutup oleh tulang kepala yang rigid (kranium), dan terdiri dari 3 elemen yaitu jaringan, darah, dan cairan serebrospinal (CSF). Kranium terdiri dari beberapa artikulasi tulang-tulang multipel yang didasari sutura kartilaginosa dalam membentuk kalvaria. Ruang kranial dan spinal dihubungkan melalui foramen magnum. Kavitas tengkorak dibagi dua kompartemen oleh tentorium serebelum, yaitu kompartemen supratentorial dan infratentorial. Kedua ruang ini berhubungan melalui insisura tentorial atau *tentorial notch*. Daerah supratentorial terdiri dari fosa anterior dan fosa media. Daerah infratentorial terdiri dari fosa posterior. *Falks serebri* yang merupakan struktur sagital membagi kompartemen supratentorial menjadi dua bagian.

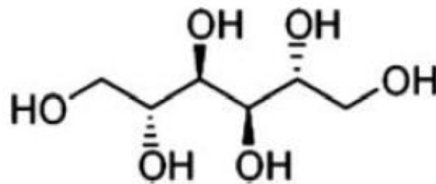
Tekanan intrakranial adalah tekanan yang terdapat pada otak dan cairan serebrospinal. Tubuh memiliki berbagai mekanisme melalui pergeseran dalam produksi dan penyerapan CSF yang membuat tekanan intrakranial stabil, bervariasi sekitar 1 mmHg pada orang dewasa normal. Tekanan CSF telah terbukti dipengaruhi oleh perubahan mendadak tekanan intratoraks selama batuk (tekanan intraabdominal), manuver Valsalva, dan komunikasi dengan pembuluh darah (sistem vena dan arteri). TIK diukur pada saat istirahat, biasanya 7–15 mmHg untuk dewasa saat posisi telentang. Perubahan TIK dikaitkan

dengan perubahan volume dalam satu atau lebih konstituen di dalam tempurung kepala. Tengkorak dan kanal tulang belakang, bersama dengan dura relatif inelastis, membentuk sebuah wadah yang kaku, sehingga peningkatan apapun dari otak, darah, atau CSF akan cenderung meningkatkan tekanan intrakranial (TIK). Selain itu, setiap peningkatan salah satu komponen harus dengan mengorbankan dua komponen lainnya (hukum Monro-Kellie). Peningkatan kecil volume otak tidak menyebabkan peningkatan TIK secara langsung, karena CSF akan dipindahkan ke kanal tulang belakang, serta sedikit meregangkan *falks cerebri*. Namun, setelah TIK sudah mencapai sekitar 25 mmHg, peningkatan kecil volume otak sudah dapat menyebabkan peningkatan TIK.

Prinsip tata laksana pada peningkatan TIK atau herniasi adalah meningkatkan aliran darah serebral dan memulihkan herniasi yang terjadi, dapat berupa tindakan umum, terapi farmakologis, dan tindakan bedah. Terdapat beberapa terapi yang dapat digunakan untuk menurunkan peningkatan TIK yaitu dengan:

1. Sedasi, digunakan pada kasus strok iskemik dengan adanya peningkatan TIK karena dapat menurunkan peningkatan TIK dan kebutuhan metabolik.
2. Diuretik, penggunaan *acetazolamide* atau *furosemide* akan menekan produksi CSS. *Acetazolamide* merupakan inhibitor karbonik anhidrase yang diketahui dapat mengurangi pembentukan cairan serebrospinal di dalam ventrikel sampai 50%.
3. Steroid, mekanismenya masih belum jelas. Steroid dikatakan mengurangi produksi CSS dan mempunyai efek langsung pada sel endotel.
4. Hiperventilasi, merupakan salah satu cara efektif untuk mengontrol peningkatan tekanan intrakranial dalam 24 jam pertama. Target PaCO_2 harus diturunkan menjadi 26–30 mmHg untuk menghasilkan dilatasi serebral maksimal.
5. Terapi hipotermi, penurunan suhu tubuh sampai 30–34°C akan menurunkan tekanan darah dan metabolisme otak, mencegah dan mengurangi edema otak, serta menurunkan tekanan intrakranial sampai hampir 50%.
6. Tindakan bedah, tergantung penyebabnya, perlu dipertimbangkan tindakan dekompresi berupa kraniotomi atau *shunting*.
7. Terapi osmosis, seperti pemberian *mannitol* atau cairan salin hipertonis yang diduga bekerja dengan cara menarik cairan dari ruang interstisial ke ruang intravaskuler dengan menciptakan gradien osmosis pada jaringan semipermeabel sawar darah otak. Terdapat dugaan bahwa terapi osmosis menurunkan viskositas darah sehingga meningkatkan aliran mikrovaskuler dan menurunkan volume darah serebral dengan cara vasokonstriksi. Efek maksimal dari terapi ini adalah pada saat akhir dari pemberian secara bolus dan bertahan hingga 4 jam. *Mannitol* (1,2,3,4,5,6-*hexanehexol* ($\text{C}_6\text{H}_8(\text{OH})_6$)) secara kimia adalah suatu *polyol* yang seringkali digunakan dalam industri makanan dan farmasi.⁵ Pada umumnya *mannitol* adalah sejenis gula dan dapat ditemukan pada jamur, rumput laut, dan eksudat tumbuhan. *Mannitol* juga digunakan sebagai obat karena memiliki efek osmosis. Sediaan yang sering digunakan adalah larutan steril *mannitol* 10% dan 20% dalam 500 ml larutan yang mengandung 50 g dan 100 g *mannitol*. *Mannitol* dapat menjadi kristal bila disimpan dalam suhu ruang.⁵

Mannitol memiliki berat molekul yang rendah sehingga dapat difiltrasi melalui tubulus renal.⁵ *Mannitol* tidak mengalami reabsorpsi tetapi secara aktif berperan dalam proses osmosis di dalam tubulus, sehingga memiliki efek diuresis osmosis. *Mannitol* juga dapat melepaskan prostaglandin renal yang menyebabkan vasodilatasi renal dan meningkatkan aliran urine tubular, di mana dapat memberikan efek proteksi dari cedera ginjal.



Gambar 5. Struktur *mannitol*

Mannitol seringkali digunakan untuk mengatasi peningkatan TIK, peningkatan tekanan intraokular, mengekskresikan zat toksik, mencegah hipotensi intradialis, dan sebagai diuresis pada gagal ginjal akut.⁵ *Mannitol* menurunkan tekanan intrakranial dengan menurunkan cairan di otak dan volume CSF, serta menurunkan tekanan darah melalui vasokonstriksi. *Mannitol* dapat meningkatkan perfusi serebral dengan menurunkan viskositas darah, atau dengan mengubah bentuk sel darah merah. Komplikasi yang paling sering terjadi dengan penggunaan *mannitol* adalah adanya gangguan cairan dan elektrolit, edema kardiopulmonari, dan *rebound* edema serebri. Selain itu *mannitol* diduga dapat menyebabkan adanya gangguan ginjal dan reaksi hipersensitivitas. Cairan hipertonis biasa diberikan jika terjadi peningkatan tekanan intrakranial akut tanpa kerusakan sawar darah otak. *Mannitol* 20% per infus dengan dosis 1–1,5 g/kgBB pada dewasa atau 1–3 g/kgBB pada anak-anak diberikan dalam 30–60 menit.

Guideline ESO (European Stroke Organization) tidak merekomendasikan penggunaan terapi osmosis sebagai terapi rutin.⁹ Penggunaan terapi *mannitol* secara bolus lebih dianjurkan dibandingkan infus *drip*. Pemilihan *mannitol* ataupun cairan salin hipertonis tergantung dari guideline ataupun ekspertis di tiap daerah. Pada guideline Neurocritical Care Society, walaupun pemberian terapi osmosis efektif dalam mengatasi peningkatan TIK, tidak cukup banyak bukti klinis yang kuat untuk merekomendasikan terapi osmosis untuk mengatasi peningkatan TIK pada kasus stroke iskemik akut.⁸ Namun demikian, dosis tunggal atau dosis kecil terapi osmosis masih dapat dipertimbangkan sebagai terapi emergensi pada pasien dengan adanya tanda peningkatan TIK atau *impending* herniasi. Terdapat beberapa masalah dalam penggunaan *mannitol* seperti gangguan kardiovaskular, asidosis metabolik, gangguan elektrolit, dan gangguan pada ginjal. Namun beberapa penelitian menunjukkan bahwa *mannitol* dapat digunakan pada kasus-kasus kardiovaskular.⁶ Penelitian dengan penggunaan *mannitol* terhadap kasus peningkatan tekanan intraokular menunjukkan bahwa tidak ada efek samping kardiovaskular terkait penggunaan *mannitol*.⁷ Sedangkan pada penelitian ekperimental terhadap hewan uji tikus, menunjukkan bahwa *mannitol* memiliki efek sebagai kardioproteksi dengan cara mengaktivasi *mitochondrial ATP-sensitive potassium (mKATP) channels*.

Pada kasus ini, dilakukan CT scan ulang ketika terjadi penurunan kesadaran disertai adanya pupil anisokor sebagai tanda dari adanya peningkatan TIK dan herniasi. Setelah itu diberikan terapi osmosis dengan menggunakan *mannitol* untuk menurunkan TIK. Adanya perbaikan klinis tanpa efek samping terhadap kelainan kardiovaskular menunjukkan bahwa *mannitol* dapat dipertimbangkan untuk digunakan dalam mengatasi peningkatan TIK pada kelainan kardiovaskular.



Gambar 6. Evaluasi CT scan kepala

Kesimpulan

Peningkatan tekanan intrakranial (TIK) pada stroke sangat penting dan menjadi faktor penentu fungsi otak selanjutnya. Peningkatan TIK dapat menurunkan aliran darah serebral dan/atau herniasi otak yang mengakibatkan kompresi dan iskemi batang otak. Gejala umum TTIK adalah nyeri kepala, muntah proyektil, kejang, dan perubahan status mental. Tanda fisik yang terpercaya adalah adanya edema papil. Penanganan TTIK bertujuan untuk menurunkan tekanan intrakranial dan meningkatkan aliran darah serebral, serta memulihkan herniasi. Penggunaan *mannitol* pada kasus stroke disertai riwayat kelainan penyakit jantung bawaan (PJB) atau TOF memiliki hasil yang baik tanpa menyebabkan efek samping atau gangguan pada kelainan PJB tersebut. *Mannitol* dapat digunakan pada pasien dengan gangguan jantung.

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Hepatic Encephalopathy in a Postpartum Patient with Chronic Hepatitis B: A Case Report

Priska Harsanti Devi, I Ketut Mariadi

Department of Internal Medicine, Faculty of Medicine, Udayana University/RSUP Prof. dr. I.G.N.G. Ngoerah, Denpasar, Bali, Indonesia

Abstract

Decompensated liver cirrhosis in the postpartum period is rarely reported, particularly in association with chronic hepatitis B infection. We presented the case of a 33-year-old woman who developed decreased level of consciousness one day after delivery. She had no prior history of chronic illness, although her father had passed away from complications of hepatitis B. Clinical findings included jaundice, ascites, and hepatic encephalopathy. Laboratory results revealed reactive HBsAg, hypoalbuminemia, elevated liver enzymes, hyponatremia, hypokalemia, and markedly elevated total bilirubin. Abdominal ultrasound demonstrated cirrhosis with splenomegaly and ascites. The patient was diagnosed with Child-Turcotte-Pugh class C cirrhosis with grade II ascites, grade II hepatic encephalopathy, chronic hepatitis B, and esophageal varices. She received supportive treatment including lactulose, albumin transfusion, and antiviral therapy with tenofovir, resulting in clinical and biochemical improvement after one month. This case highlighted the importance of early screening for hepatitis B during pregnancy to prevent potentially fatal postpartum hepatic decompensation.

Keywords: liver cirrhosis, chronic hepatitis B, hepatic encephalopathy, postpartum period, esophageal varices

Abstrak

Sirosis hepatis dekompensata pada periode *postpartum* merupakan kondisi yang jarang dilaporkan, khususnya bila berhubungan dengan infeksi hepatitis B kronis. Kami melaporkan seorang wanita berusia 33 tahun yang datang dengan penurunan kesadaran satu hari setelah melahirkan. Pasien sebelumnya tidak memiliki riwayat penyakit kronis, namun terdapat riwayat keluarga, yaitu ayahnya meninggal akibat komplikasi hepatitis B. Pemeriksaan klinis menunjukkan ikterus, asites, dan ensefalopati hepatikum. Pemeriksaan laboratorium menunjukkan HBsAg reaktif, hypoalbuminemia, peningkatan enzim hati, hiponatremia, hipokalemia, serta bilirubin total tinggi. USG abdomen menunjukkan sirosis hepatis dengan splenomegali dan asites. Diagnosis ditegakkan sebagai sirosis hepatis Child-Turcotte-Pugh kelas C dengan asites *grade* II, ensefalopati hepatikum *grade* II, hepatitis B kronis, dan varises esofagus. Pasien mendapatkan terapi suportif, laktulosa, transfusi albumin, dan antivirus *tenofovir*, dengan perbaikan klinis dan laboratorium setelah satu bulan. Kasus ini menekankan pentingnya deteksi dini infeksi hepatitis B pada kehamilan untuk mencegah dekompensasi *postpartum* yang berpotensi fatal.

Kata kunci: sirosis hepatis, hepatitis B kronis, ensefalopati hepatikum, periode *postpartum*, varises esofagus

Introduction

Chronic hepatitis B remains a global health problem with a high prevalence in developing countries, including Indonesia.¹ This infection carries the risk of long-term complications such as liver cirrhosis and hepatocellular carcinoma. The disease course is often asymptomatic until hepatic decompensation occurs, which may present with ascites, jaundice, hepatic

encephalopathy, or esophageal variceal bleeding.^{2,3} Pregnancy and the postpartum period are known to exacerbate the condition in patients with chronic hepatitis B due to physiological and immunological changes in the maternal body.^{4,5}

The postpartum period is considered a critical phase for patients with hepatitis B infection. Following delivery, the maternal immune system shifts from a tolerant state during pregnancy to a hyperimmune state, which can trigger hepatitis B virus (HBV) reactivation. This reactivation may aggravate liver injury and increase the risk of decompensation, potentially leading to life-threatening acute liver failure.⁶ Reports of hepatic decompensation during the postpartum period remain relatively scarce, particularly in Indonesia.

Decompensated cirrhosis in postpartum mothers presents both diagnostic and therapeutic challenges. Its clinical manifestations may resemble obstetric complications or other infections, which can delay diagnosis. Appropriate management requires early identification, careful assessment of liver status, and timely initiation of antiviral therapy.^{4,5} Tenofovir disoproxil fumarate is recommended as the first-line antiviral treatment for hepatitis B during pregnancy and postpartum due to its favorable safety profile.⁷

In this case report, we presented a postpartum patient with chronic hepatitis B who developed decompensated cirrhosis with hepatic encephalopathy. This report aims to emphasize the importance of early detection of hepatitis B during pregnancy and vigilance regarding the risk of hepatic decompensation in the postpartum period, which can be fatal if not managed promptly and appropriately.

Case Report

A 33-year-old woman presented with decreased consciousness that had occurred 11 days prior to hospital admission. The complaint appeared suddenly, one day after she delivered with the assistance of a midwife. The decreased level of consciousness was accompanied by jaundice of the eyes and skin. The patient also reported persistent abdominal enlargement after delivery, along with fever unresponsive to antipyretics. Shortness of breath developed in the last five days, relieved in the sitting position. She had previously been hospitalized at private hospital for 10 days, where an ultrasound revealed liver cirrhosis, after which she was referred to RSUP Prof. dr. I.G.N.G. Ngoerah in Denpasar. On admission, the patient's orientation to time and place was impaired, and she was unable to recall long-term memories such as the names of her school friends.

Since her last pregnancy, the patient had complained of insomnia at night and hypersomnolence during the day. From early pregnancy, her urine appeared tea-colored, while bowel habits were normal. Three months before delivery, she experienced bilateral leg edema, more severe on the left, accompanied by significant hair loss (about one handful each time she combed). Obstetric history revealed this was her fourth pregnancy. The first pregnancy resulted in a normal delivery without antenatal care (ANC) under the care of a midwife, the second ended in miscarriage, the third resulted in a normal delivery at a primary health center but the infant died two hours after birth, and the fourth pregnancy (current) resulted in a normal delivery at home without medical assistance, with ANC only once at three months of gestation. She denied a history of jaundice in all of the previous pregnancies. There was no history of heart disease, diabetes, or kidney disease. Her father had hepatitis B and died from its complications, while her mother had never been tested for hepatitis B, and her husband's HBV status was unknown.

Initial physical examination revealed decreased consciousness, normal blood pressure, and tachycardia. Sclerae were icteric without conjunctival anemia. Thoracic examination showed no spider nevi, cardiac findings were normal, while the lungs revealed bilateral basal rales. The abdomen was distended with a flat umbilicus, shifting dullness was positive, while the liver and spleen were difficult to assess. No lymphadenopathy was found. Extremities showed edema of the hands and legs, without flapping tremor or palmar erythema. Physiological reflexes were normal and no pathological reflexes were

noted.

Laboratory tests revealed mild normocytic normochromic anemia with lymphopenia and thrombocytopenia. Liver biochemistry showed SGOT 144.0 mmol/l, SGPT 63.9 mmol/l, albumin 2 g/dl, globulin 3.10 g/dl, gamma GT 38 U/l, and ALP 143 U/l. HBsAg was positive, anti-HCV was nonreactive. Renal function was within normal limits (BUN 11.0 mg/dl, serum creatinine (SC) 0.60 mg/dl, eGFR 120 ml/minute/1.73 m²). Total bilirubin was 15.28 mg/dl. Electrolytes revealed hyponatremia (127 mmol/l) and hypokalemia (2.75 mmol/l). Ascitic fluid analysis showed total protein 0.3 g/dl, cell count 60/mm³ with 90% mononuclear cells, and serum-ascites albumin gradient (SAAG) 1.7 g/dl, consistent with portal hypertension. Chest radiograph showed cardiomegaly, while abdominal ultrasound demonstrated liver cirrhosis with splenomegaly and moderate ascites.

The initial diagnosis was established as liver cirrhosis Child-Turcotte-Pugh class C (CTP-C) with grade III ascites, grade II hepatic encephalopathy, and chronic hepatitis B. Additional diagnoses included P3012 postpartum day-12, mild normochromic normocytic anemia (suspected anemia of chronic disease), chronic asymptomatic hypervolemic hyposmolar hyponatremia (suspected dilutional), and hypokalemia (suspected shift). Initial treatment included oral tenofovir 300 mg every 24 hours, high branched-chain amino acid (BCAA) diet, lactulose 15 ml orally every 8 hours, daily lavement, and albumin transfusion. During hospitalization, transaminase levels increased. Esophagogastroduodenoscopy revealed gastroesophageal varices type 1 (Sarin classification) with severe portal hypertensive gastropathy.

The final diagnosis was liver cirrhosis CTP-C with grade II ascites, grade II hepatic encephalopathy, hypoalbuminemia, chronic hepatitis B, and esophageal varices GOV-1. The patient was also recorded as P3012 postpartum day-24. She was subsequently followed up at the Gastroenterology Clinic at RSUP Prof. dr. I.G.N.G. Ngoerah and continued tenofovir therapy. HBV-DNA testing showed 3.81×10^3 IU/ml (1.58 log IU/ml). Liver function tests one month after therapy demonstrated improvement with SGOT 68 U/l, SGPT 24 U/l, gamma GT 44 U/l, ALP 164 U/l, total bilirubin 3.10 mg/dl, direct bilirubin 2.48 mg/dl, indirect bilirubin 0.62 mg/dl, and nonreactive HBeAg.

Discussion

This patient was diagnosed with chronic hepatitis B, confirmed by a positive HBsAg result. Chronic HBV infection is a leading cause of liver cirrhosis worldwide. Hepatitis B virus causes persistent hepatic inflammation, which, if untreated or not cleared by the immune system, leads to progressive scarring (fibrosis). Over time, this accumulation of fibrosis replaces healthy hepatocytes, altering the normal liver architecture into cirrhosis.⁸

The patient's family history is highly relevant in this case. Her father suffered from hepatitis B and died from its complications. Although hepatitis B is not a genetic disease that inherited directly from parents, the virus is highly contagious through body fluids, including vertical transmission from mother to child during delivery or horizontal transmission through close household contact. Therefore, the father's positive HBV status increases the likelihood that this patient was exposed to the virus early in life, either horizontally from her father or other family members, or vertically if her mother was also infected (her mother's infection status remains unknown).^{9,10} Early exposure often leads to chronic infection, as the infant's immune system is not yet fully developed to clear the virus effectively. The asymptomatic nature of chronic hepatitis B over many years explains why the patient had no history of jaundice during her previous pregnancy, and why cirrhosis is often only diagnosed once advanced liver damage results in decompensation symptoms.¹¹ This highlights the importance of universal HBV screening, particularly in individuals with a positive family history, to enable early detection and intervention before severe hepatic injury occurs.¹²

The sudden onset of impaired consciousness and severe symptoms one day after delivery underscores the significant

role of pregnancy and postpartum physiological changes as triggers of acute hepatic decompensation in patients with preexisting cirrhosis.⁵ Pregnancy induces substantial hemodynamic adaptations, including up to 50% plasma volume expansion and a 40% increase in cardiac output by the third trimester.^{13,14} While these changes meet maternal and fetal metabolic demands, in cirrhotic patients the additional circulatory load can worsen existing portal hypertension, increase portal venous pressure, and precipitate complications such as variceal bleeding or ascites.^{14,15}

The postpartum period is characterized by rapid hemodynamic shifts. After delivery, “autotransfusion” of up to 500 ml of blood from the uteroplacental unit back into maternal circulation occurs. This sudden increase in circulating volume, combined with abrupt hemodynamic changes, places acute stress on the diseased liver and already strained cardiovascular system. The patient’s cirrhotic liver, which had been compensating throughout pregnancy, was likely pushed into decompensation by this physiological stress. Clinical manifestations such as hepatic encephalopathy, ascites, and jaundice emerging acutely after delivery illustrate how childbirth, though physiological, can serve as an extreme “stress test” for compromised organ systems, triggering acute crises in patients with limited hepatic reserve.^{16,17}

The patient presented with the classic clinical features of decompensated cirrhosis, reflecting failure of the liver to perform its vital functions. The main complaint was decreased consciousness accompanied by spatial and temporal disorientation and long-term memory impairment, such as the inability to recall the names of former schoolmates. These manifestations are consistent with hepatic encephalopathy (HE) grade II, a serious neurological complication of end-stage liver disease that occurs due to the accumulation of neurotoxic substances, particularly ammonia, in the brain. In cirrhotic patients, HE is often precipitated by gastrointestinal bleeding from esophageal varices, infection with associated fever, and electrolyte disturbances such as hyponatremia and hypokalemia.¹⁸ In addition, the patient demonstrated jaundice of the sclera and skin, a clinical manifestation of hyperbilirubinemia caused by impaired hepatic processing and excretion of bilirubin.

Postpartum abdominal distension with positive shifting dullness confirmed the presence of ascites. Ascites is the most frequent complication of decompensated cirrhosis, caused by a combination of portal hypertension and hypoalbuminemia leading to abnormal accumulation of fluid in the peritoneal cavity.¹⁹ Furthermore, fever unresponsive to antipyretic therapy raised suspicion of infection, such as spontaneous bacterial peritonitis, which is one of the most common precipitants of decompensation in cirrhosis.²⁰

The patient also experienced worsening shortness of breath in the supine position, which improved when sitting upright (orthopnea). This symptom may be explained by several mechanisms, including massive ascites compressing the diaphragm and limiting lung expansion, or pleural effusion resulting from ascitic fluid shifting into the pleural cavity through diaphragmatic defects (hepatic hydrothorax). Additionally, cardiomegaly on chest X-ray supported the possibility of pulmonary congestion due to cirrhotic cardiomyopathy or volume overload. Overall, these clinical manifestations indicated advanced liver injury with serious multisystem complications.²¹

Physical examination and laboratory results provided objective evidence of the severity of liver disease and its complications. Physical findings included tachycardia, suggestive of a hyperdynamic response, and peripheral edema, indicating fluid retention and hypoalbuminemia. The absence of flapping tremor in grade II encephalopathy highlighted the variability of clinical presentation. Liver function tests demonstrated elevated SGOT (144.0 mmol/l) and SGPT (63.9 mmol/l), signifying hepatocellular injury, although in advanced cirrhosis transaminase elevations tend to be lower than in acute hepatitis due to reduced functional hepatocyte mass. Severe hypoalbuminemia (2 g/dl) reflected impaired hepatic synthetic function, while hyperbilirubinemia (15.28 mg/dl) indicated defective bilirubin excretion. Positive HBsAg confirmed chronic hepatitis B infection as the underlying cause of cirrhosis. This laboratory pattern is consistent with decompensated cirrhosis, differing from acute hepatitis, which is typically marked by much higher transaminase elevations.^{22,23}

Additional laboratory findings included mild normocytic normochromic anemia, lymphopenia, and thrombocytopenia, likely attributable to hypersplenism or bone marrow suppression. Renal function remained preserved, which is important for antiviral therapy selection and long-term prognosis. Electrolyte disturbances included hyponatremia (127 mmol/l) and hypokalemia (2.75 mmol/l), consistent with decompensated cirrhosis and related to fluid retention and secondary hyperaldosteronism. Abdominal ultrasonography demonstrated cirrhosis with splenomegaly and moderate ascites, while chest radiography revealed cardiomegaly, suggesting cirrhotic cardiomyopathy or volume overload due to fluid retention.^{24,25}

Assessment using the Child–Turcotte–Pugh (CTP) system classified the patient as CTP-C, with a total score of 12–14 based on high bilirubin, low albumin, moderate-to-severe ascites, grade II hepatic encephalopathy, and likely markedly elevated INR. This classification reflects advanced liver disease with poor prognosis and high one-year mortality. Patients with CTP-C cirrhosis have an estimated survival of approximately one year without liver transplantation, making this score crucial for guiding therapy, assessing procedural risk, and considering transplantation as the only long-term definitive treatment.²⁶

This patient presented with multiple complications of decompensated cirrhosis requiring aggressive management. Hepatic encephalopathy manifested as impaired consciousness, disorientation, and memory disturbance caused by ammonia accumulation that could not be detoxified by the failing liver. Likely precipitating factors included gastrointestinal bleeding, infection, and electrolyte imbalance.¹⁸ Management included lactulose to reduce ammonia levels and a branched-chain amino acid (BCAA)-rich diet to correct amino acid imbalance and reduce HE symptoms.^{18,27} Ascites was confirmed clinically and by ultrasound, with a serum-ascites albumin gradient (SAAG) of 1.7 g/dl, indicating portal hypertension as the underlying cause. Management included sodium restriction, diuretics, and albumin infusion, particularly after large-volume paracentesis.²⁸

Esophagogastroduodenoscopy (EGD) revealed gastroesophageal varices type 1 with severe portal hypertensive gastropathy, carrying a high risk of rupture and massive gastrointestinal bleeding. EGD served both diagnostic and therapeutic purposes through variceal ligation or sclerotherapy.²⁹ The patient also demonstrated severe hypoalbuminemia (2 g/dl) as a marker of impaired hepatic protein synthesis, managed with albumin transfusion to maintain oncotic pressure, reduce ascites and edema, and support plasma transport functions.

Electrolyte disturbances, namely hyponatremia (127 mmol/l) and hypokalemia (2.75 mmol/l), were also present. Hyponatremia resulted from splanchnic vasodilation leading to ADH release and water retention, whereas hypokalemia was mainly due to secondary hyperaldosteronism, causing increased urinary excretion of potassium and hydrogen ions. Both conditions exacerbate organ dysfunction and must be corrected as an integral part of decompensated cirrhosis management.^{24,28}

Radiological findings of cardiomegaly suggested cirrhotic cardiomyopathy (CCM), a cardiac dysfunction characteristic of cirrhosis. The presence of bilateral basal rhonchi could be explained by pulmonary congestion, hepatic hydrothorax, or cardiac dysfunction secondary to CCM. These conditions complicate management, as they affect fluid and diuretic strategies, and carry important prognostic implications, particularly in patients being evaluated for liver transplantation.²¹

The patient received antiviral therapy with oral tenofovir 300 mg daily, indicating the use of tenofovir disoproxil fumarate (TDF). TDF is one of the widely recommended first-line therapies for chronic hepatitis B infection, including in cirrhotic patients. It acts as a nucleotide reverse transcriptase inhibitor, effectively suppressing HBV replication. Unlike tenofovir alafenamide (TAF, 25 mg), which has a more favorable bone and renal safety profile but is not recommended in moderate-

to-severe liver impairment (Child–Pugh B or C), TDF can still be used in decompensated cirrhosis with close monitoring of renal function and risk of lactic acidosis. In this case, baseline renal function was preserved (eGFR 120 ml/minute/1.73 m²), making TDF an appropriate choice consistent with current guidelines. The rationale for TDF use reflects accurate clinical application of HBV treatment recommendations, with the main goal of suppressing viral replication, slowing liver disease progression, and reducing complications.³⁰

During the early phase of therapy, the patient experienced an increase in transaminase levels, followed by significant improvement at one-month evaluation. This increase may represent a “flare” of hepatitis B, which often occurs spontaneously or during antiviral therapy. Such flares usually reflect an effective immune response against the virus, characterized by clearance of infected hepatocytes, provided there are no signs of fulminant liver failure or worsening acute decompensation. In this case, the transaminase elevation was followed by reduction in HBV DNA levels and HBeAg seroconversion, suggesting a favorable flare indicative of successful viral suppression and recovery of hepatic function.^{31–33}

Therapeutic response in this patient was promising. HBV DNA decreased to 3.81×10^1 IU/ml (1.58 log IU/ml), reflecting effective viral suppression associated with slower disease progression, reduced hepatic inflammation, and lower risk of further complications. Moreover, HBeAg became nonreactive, indicating seroconversion, which is an important marker of therapeutic success in HBeAg-positive patients. HBeAg seroconversion is associated with a reduced risk of advanced cirrhosis and hepatocellular carcinoma, as well as improved survival.³³ Improvement in liver function tests, with SGOT 68 U/l, SGPT 24 U/l, and total bilirubin 3.10 mg/dl after one month of therapy, further confirmed a favorable clinical and biochemical response, suggesting early signs of hepatic functional recovery.³⁴

Patients with CTP-C cirrhosis generally have poor prognosis, with high mortality and a median survival of about one year without transplantation.²⁶ However, this patient’s positive response to antiviral therapy, demonstrated by HBV DNA suppression, HBeAg seroconversion, and improvement in liver function parameters, offers a more optimistic outlook.^{33,35} These findings indicate successful viral suppression and evidence of hepatic recovery, which may ultimately improve quality of life and extend survival.

For long-term management, tenofovir therapy must be continued to ensure sustained viral suppression and prevent HBV reactivation, which could worsen decompensation.^{36,37} Close monitoring of cirrhosis complications is also essential, including periodic endoscopy for esophageal varices, hepatocellular carcinoma (HCC) screening with abdominal ultrasound and AFP every six months, as well as regular evaluation of ascites, electrolyte balance, and hepatic encephalopathy with adjustment of lactulose and BCAA diet. Cardiopulmonary assessment is also required to detect cirrhotic cardiomyopathy or hepatic hydrothorax, with additional interventions as needed.^{21,24,25,28,29}

Given the severity of disease, this patient should also be evaluated for liver transplantation as definitive therapy. The MELD-Na score should be used to determine transplant priority, and early discussion of transplantation is necessary to maximize survival opportunities.^{26,38,39}

Conclusions

This case illustrates a postpartum woman with a history of chronic hepatitis B who progressed to decompensated liver cirrhosis accompanied by hepatic encephalopathy and esophageal varices. Physiological and immunological changes during the postpartum period are presumed to have contributed to the worsening of hepatic function, leading to decompensation. Administration of antiviral therapy with tenofovir, along with supportive management, proved effective in improving liver function and stabilizing the patient’s clinical condition. This report highlights the importance

of early detection of hepatitis B in pregnant women, close monitoring during pregnancy and the postpartum period, and comprehensive management to prevent life-threatening complications.

Conflict of interest

The authors have no conflict of interest in the preparation of this case report.

Ethical consideration

This case report has obtained informed consent from the patient and their family and has followed the COPE guidelines on ethics in scientific publication.

Funding

The preparation of this case report did not involve any sponsorship or other funding sources.

Author contributions

All authors contributed to the writing of this manuscript, starting from the patient examination, data collection, and the writing of the report.

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A Rare Case of Eisenmenger Syndrome Complicated by Dengue Hemorrhagic Fever

Felly Moelyadi¹, Hendrata Erry Andisari^{1,2}

¹Faculty of Medicine, Hang Tuah University, Surabaya, East Java, Indonesia

²Department of Internal Medicine, dr. Ramelan Naval Central Hospital, Surabaya, East Java, Indonesia

Abstract

Background: Eisenmenger syndrome (ES) is a rare complication of congenital heart disease characterized by pulmonary hypertension and bidirectional or reversed shunt. Patients with ES are vulnerable to infections, including dengue virus (DENV), which can further aggravate cardiovascular compromise. **Case:** A 32-year-old woman with a history of congenital heart disease was admitted with shortness of breath, cyanosis, palpitations, and vomiting. During hospitalization, patients developed fever, rash, petechiae, and thrombocytopenia. Echocardiography demonstrated an atrial septal defect with bidirectional shunt and pulmonary hypertension, consistent with ES. Laboratory results confirmed dengue hemorrhagic fever (DHF) with hemoconcentration and severe thrombocytopenia. Management included cautious fluid resuscitation, platelet transfusion, corticosteroids, and supportive therapy with sildenafil citrate for pulmonary hypertension. Clinical improvement was achieved, and the patient was discharged after nine days of hospitalization. **Conclusion:** This case illustrates the complex interaction between ES and DHF, in which increased vascular permeability, coagulation abnormalities, and chronic hypoxemia exacerbate hemodynamic instability. Currently, there are no standardized guidelines for managing dengue in patients with ES; therefore, therapy must be individualized with vigilant monitoring. Recognition of this rare comorbidity is important to prevent complications, optimize treatment, and improve survival.

Keywords: Eisenmenger syndrome, pulmonary hypertension, dengue hemorrhagic fever, heart defects

Abstrak

Latar Belakang: Sindrom Eisenmenger (SE) merupakan komplikasi langka dari penyakit jantung bawaan yang ditandai dengan hipertensi pulmonal serta pirau dua arah atau terbalik. Pasien dengan SE rentan terhadap infeksi, termasuk infeksi virus dengue (DENV), yang dapat memperburuk gangguan kardiovaskular. **Kasus:** Seorang wanita berusia 32 tahun dengan riwayat penyakit jantung bawaan datang dengan keluhan sesak napas, sianosis, palpitasi, dan muntah. Selama perawatan, pasien mengalami demam, ruam, petekie, serta trombositopenia. Ekokardiografi menunjukkan adanya kelainan septum atrium dengan pirau dua arah dan hipertensi pulmonal, sesuai dengan diagnosis SE. Pemeriksaan laboratorium mengonfirmasi diagnosis demam berdarah dengue (DBD) dengan hemokonsentrasi dan trombositopenia berat. Terapi yang diberikan meliputi resusitasi cairan secara hati-hati, transfusi trombosit, kortikosteroid, serta terapi suportif *sildenafil citrate* untuk hipertensi pulmonal. Kondisi klinis pasien membaik dan pasien dipulangkan setelah sembilan hari perawatan. **Kesimpulan:** Kasus ini menggambarkan interaksi kompleks antara SE dan DBD, di mana peningkatan permeabilitas vaskular, kelainan koagulasi, dan hipoksemia kronis memperberat ketidakstabilan hemodinamik. Hingga saat ini, belum terdapat pedoman standar untuk penatalaksanaan DBD pada pasien SE, sehingga terapi perlu disesuaikan secara individual dengan pemantauan ketat. Pengenalan komorbiditas langka ini penting untuk mencegah komplikasi, mengoptimalkan terapi, serta meningkatkan kelangsungan hidup pasien.

Kata Kunci: sindrom Eisenmenger, hipertensi pulmonal, demam berdarah dengue, kelainan jantung

Introduction

Eisenmenger syndrome (ES) is a clinical condition related to congenital heart defects. It occurs when a long-standing left-to-right anatomic cardiac shunt leads to increased pulmonary vascular resistance (PVR) and eventually reverses into a cyanotic right-to-left shunt or a balanced flow (bidirectional shunt), typically manifesting in early life.^{1,2} ES is a rare condition that can affect individuals of all ages and genders. The estimated prevalence in adults is approximately 1–6%, with survival rates of about 80% at 10 years and 42% at 25 years after diagnosis.¹

Complications contribute to increased morbidity and mortality, as well as reduced quality of life in patients with ES.¹ Cardiovascular disease is frequently complicated by viral illnesses such as dengue.³ In contrast to the rarity nature of ES, dengue virus (DENV) infection is a common mosquito-borne tropical infectious disease.⁴ DENV infection is caused by a positive-strand RNA flavivirus, and is predominantly transmitted through bites of *Aedes spp.* mosquitoes. The incidence of this endemic disease results in 100–400 million infections each year.^{5,6}

In DENV infection, the complex interplay between pro-inflammatory cytokines and vascular injury increases vessel wall permeability, leading to capillary leakage.⁷ Cardiac manifestations of DENV infection range from mildly elevated cardiac enzyme (7.4–40%) and cardiac dysfunction (22–64%) to severe myocarditis, which can lead to congestive heart failure, cardiogenic shock, and death.^{2,4,7}

Patient with complicated ES may need corrective surgery or heart transplantation; however, some conditions are irreversible, requiring lifelong palliative care.¹ These complications also increase length of stay (LOS) and mortality.³ Thus, delivering adequate and timely management for patient with cardiovascular disease complicated by DENV infection is crucial. Unfortunately, the available literature on this condition remains limited. Here, we present the case of a 32-year-old female diagnosed with ES complicated by dengue hemorrhagic fever (DHF).

Case Illustration

A 32-year-old female patient was admitted to dr. Ramelan Naval Central Hospital, Surabaya, on April 28, 2025, with a chief complaint of shortness of breath for the past day. The symptoms worsened with activity or walking a few meters. The patient reported occasionally cyanosis (bluish) due to shortness of breath. Patient also complained of palpitations accompanied by cold sweat. Prior to arrival at the emergency department, the patient had vomited four times. Her past medical history revealed uncontrolled valvular heart disease since elementary school.

On physical examination, the patient appeared moderately ill. Blood pressure was 124/74 mmHg; respiratory rate 30 breaths/minute; heart rate 106 bpm; temperature 37.3°C; and SpO₂ 78% on room air. Clubbing of the fingers was noted.

During hospitalization, the patient developed fever starting on April 30, 2025. A red rash all over the body appeared on May 5, 2025. Physical examination revealed petechiae and purpura across the body. Serial complete blood counts were performed (**Table 1**). Additional supporting examination are presented below.

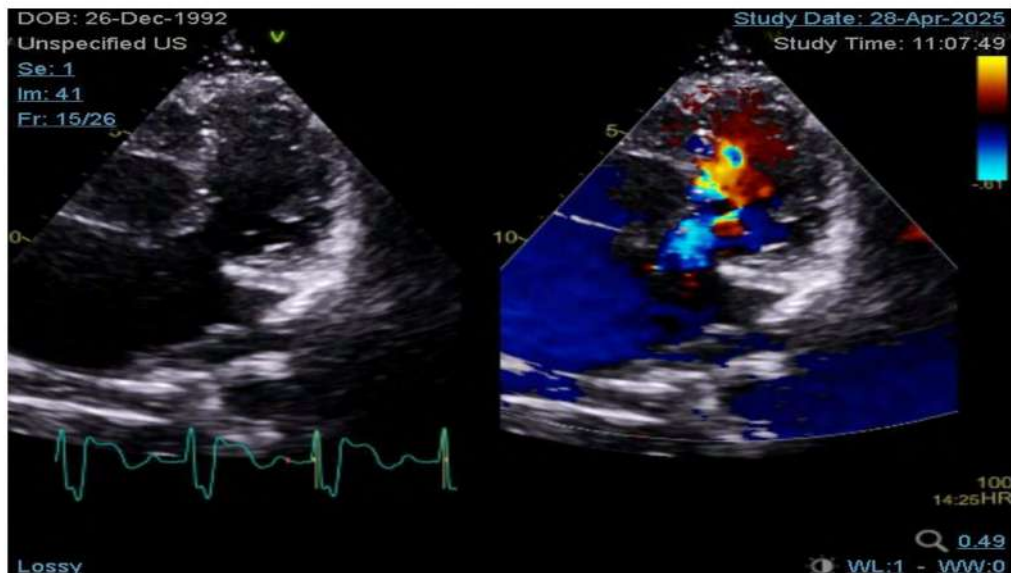


Figure 1. Echocardiography performed on April 28, 2025

Quality of the study is adequate. The left atrium (LA) & left ventricle (LV) dimensions were within normal limits (LA dimension 2.6 cm). Concentric remodelling LV. Global normokinetic. Normal LV systolic function ejection fraction (EF) biplane 66%. Right atrium (RA) and right ventricle (RV) were dilated. Normal RV systolic function, tricuspid annular plane systolic excursion (TAPSE) 29 mm. Valves: mitral mild regurgitation; tricuspid: mild regurgitation (V_{max} 3.3 m/s). Normal pericardium. Intact interventricular septum (IVS). There is a gap at interatrial septum (IAS) approximately 3.9 cm, bidirectional shunt. Mitral and tricuspid valve in one level. Conclusion: Suspected atrial septal defect (ASD) primum, bidirectional shunt; mild mitral regurgitation (MR); mild tricuspid regurgitation (TR); high probability pulmonary hypertension (PH); normal LV systolic function EF 66%.

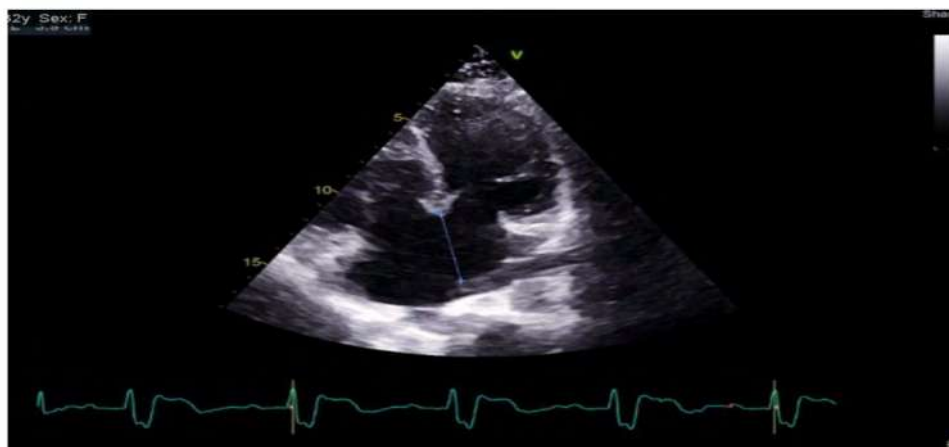


Figure 2. Echocardiography on April 30, 2025

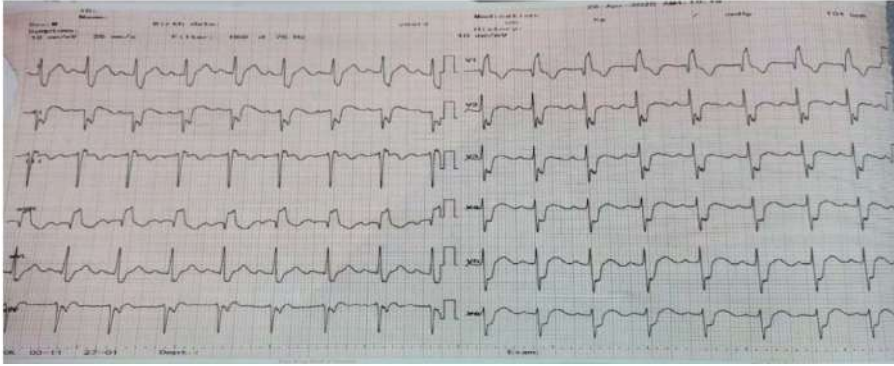


Figure 3. Electrocardiography (ECG) performed on April 28, 2025
Normal sinus rhythm, left axis deviation, and an incomplete right bundle branch block.

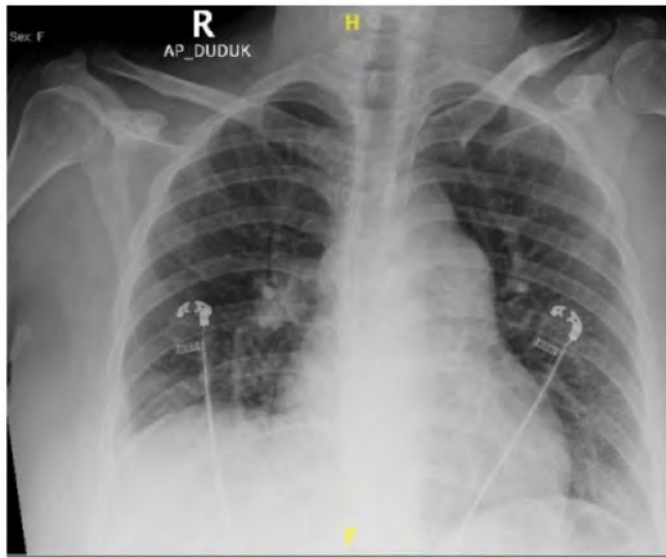


Figure 4. Thorax X-ray AP on April 28, 2025

Cor: prominent with concave heart waist & apex rounded, double contour (+). Pulmo: cephalisation (+), bronchovascular patterns (BVP) increased. Right diaphragm high positioned, left appeared normal. Conclusion: Cor prominent with congestive pulmunum (suspect mitral heart configuration/mitral stenosis).

Table 1. Serial complete blood count

Examination	Results (2025)						Unit	Reference
	28/4	30/4	02/5	04/5	06/5	07/5		
Leukocytes	7.55	2.89	4.06	3.93	5.04	7.62	10 ⁹ /μl	4.0–10.0
Hemoglobin	18.5	17.2	18.9	18.2	17.7	18.2	g/dl	12–15
Hematocrit	54.9	51.0	55.6	53.4	50.8	53.2	%	37.0–47
Platelets	228	87.0	20.0	15.0	85.0	169	10 ⁹ /μl	150–450

Table 2. Other laboratory parameters

Examination	Results (2025)					Unit	Reference
	28/4	29/4	01/5	02/5	04/5		
RBG	104					mg/dl	<200
Creatinine	0.6					mg/dl	0.6–1.5
BUN	8.6					mg/dl	10–24
Natrium serum	133					mEq/l	135–147
Potassium serum	3.90					mmol/l	3.5–5.2
FBG		90				mg/dl	70–99
Uric acid		5.3				mg/dl	2–7
SGOT				123		U/l	0–35
SGPT				27		U/l	0–37
Quantitative CRP					<2.0	mg/dl	<10
Procalcitonin					0.14	ng/ml	<0.5
Albumin					3.08	mg/dl	3.5–5.2
IgM anti-DHF			positive				
IgG anti-DHF			positive				

Note: RBG= random blood glucose, FBG= fasting blood glucose, BUN= blood urea nitrogen, CRP= C-reactive protein, DHF= dengue hemorrhagic fever

Table 3. Arterial blood gas analysis results on April 28, 2025

Examination	Results	Unit	Reference
pH	7.484		7.350–7.450
PCO ₂	29.0	mmHg	35–45
PO ₂	62.2	mmHg	80.0–100.0
HCO ₃ Std	23.8	mEq/l	22–26
BE (ecf)	-2.2	mmol/l	-2 s/d +2
O ₂ SAT	94.5	%	>95%
FIO ₂	61.0	%	

A peripheral blood smear performed on April 29, 2025, showed findings suggestive of thrombocytopenia and monocytosis, with a recommendation for reevaluation in one month. The patient was subsequently diagnosed with Eisenmenger syndrome (pulmonary hypertension with atrial septal defect), dengue hemorrhagic fever, dengue rash, hemoconcentration, and idiopathic thrombocytopenic purpura.

Management included rehydration therapy with PZ infusion, methylprednisolone 62.5 mg IV once daily (1-0-0), lansoprazole 2 x 30 mg IV, antacid 3 x 1, transfusion of TC (thrombocyte concentrate) with a total of six bags, sucralfate suspension 100 ml 3 x 10 cc per oral (PO), cetirizine 1 x 10 mg PO, paracetamol 3 x 500 mg PO, Neurohax® 1 x 1 PO, sildenafil citrate 3 x 20 mg PO, bisoprolol 1 x 2.5 mg PO, Kalk® 1 x 1 PO, and a porridge diet providing 2,100 kcal/day. The patient was

hospitalized for a total of nine days and was discharge on May 9, 2025.

Discussion

The overall incidence of ES is estimated to range from 1% to 5.6% based on European cohorts evaluating congenital heart disease (CHD). Early diagnosis and timely repair of CHD have been associated with a decrease number of ES in patients with simple defects. However, this association has been reported only in high-income countries (HICs). Studies in low- and middle-income countries (LMICs) continue to demonstrate ES in patients with unrepaired lesions, often presenting late in adulthood.^{8,9} There is no gender predominance in ES. Our case involves a 32-year-old female diagnosed with ES since elementary school. This finding indicates that ES remains prevalent in LMIC settings and underscores the need for earlier diagnosis and intervention to prevent disease progression..

The complex pathophysiology underlying ES involve a large, chronic, left-to-right cardiac shunt. Increased right ventricular blood volume leads to increased pulmonary blood flow, resulting in elevated shear stress on the pulmonary endothelium. This process causes endothelial dysfunction and pulmonary vascular remodeling. The release of vasoconstrictive substances (such as endothelin), growth factors, and cytokines ultimately increases pulmonary vascular resistance (PVR) and pulmonary arterial pressure, leading to pulmonary arterial hypertension (PAH).¹⁰ When these triggering factors persist, arterial hypertrophy and intimal proliferation cause the progression of PAH. In advanced stages, fibrosis, development of plexiform lesions, and arteritis results in obstruction of the vessel lumen. This leads to a substantial reduction in total pulmonary arterial diameter, further increasing mean pulmonary arterial pressure (mPAP) and PVR. Consequently, right ventricular hypertrophy develops and clinically manifests as central cyanosis.^{1,10} Similar findings were observed in this patient, who occasionally developed bluish discoloration during episodes of shortness of breath, consistent with central cyanosis. Echocardiography examination confirmed the presence of a bidirectional shunt.

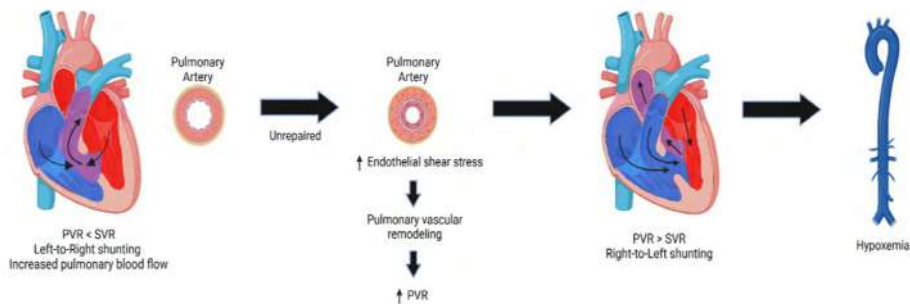


Figure 5. Developmental pathophysiology of Eisenmenger syndrome⁸

Eisenmenger syndrome can be classified as simple or complex based on the underlying lesion or congenital abnormality. Simple ES includes atrial septal defect (ASD), ventricular septal defect (VSD), patent ductus arteriosus (PDA), and aortopulmonary window. Complex lesions include pulmonary atresia with VSD, tricuspid atresia, atrioventricular septal defect, and tetralogy of Fallot (TOF).¹ Based on this classification, our patient was categorized as having simple ES, as the underlying lesion was pulmonary hypertension with ASD.

The clinical manifestations of ES vary depending on the underlying cardiac defect and the presence of end-organ complications. Some patients may be oligosymptomatic. Common symptoms include fatigue, syncope, exercise intolerance, and palpitations.¹¹ Patients with ES represent the most symptomatic subgroup of adults with congenital heart

disease (CHD) and also the group with the lowest average exercise capacity. Due to their predisposition to infections, patients may present with pneumonia, bacterial endocarditis, or other infectious diseases.¹¹ Our findings are consistent with the literature. The patient in this case developed exercise intolerance, as symptoms worsened with activity or walking a few meters. Exercise intolerance is attributed to exercise-induced hypoxemia, which often leads patients to adapt to lower levels of physical activity, thereby underestimating their symptoms.¹⁰

Physical examination findings in ES vary according to the underlying pathophysiology. Chronic hypoxemia manifests as cyanosis, with patient demonstrating bluish discoloration of the skin and mucous membranes. Cyanosis may be less apparent in individuals with low hemoglobin levels.⁹ Arrhythmias are common and related with malignant arrhythmias (mainly supraventricular arrhythmias), heart failure (HF), and sudden cardiac death.¹⁰ Hemorrhagic diathesis often initially appears as mucosal bleeding.¹ Other systemic manifestation include digital clubbing.^{10,11} Digital clubbing results from the shunting of megakaryocytes into the systemic circulation induced by chronic hypoxemia.^{9,12} Our patient exhibited several characteristic physical findings, such as bluish skin discoloration and digital clubbing. Chronic cyanosis leads to multisystem involvement, resulting in increased morbidity and hospitalization, which negatively affect quality of life. Overall, quality of life is significantly more impaired in patients with ES compared with those who have other forms of CHD or PAH of different etiologies.^{9,13}

Supporting examination in ES patients must consider multiorgan involvement, which is strongly associated with chronic hypoxemia. Characteristics of laboratory findings include secondary erythrocytosis, increased thrombotic and bleeding diathesis, hyperviscosity syndrome, renal disease, and coagulopathy.⁹ Some patients present with in situ pulmonary artery thrombosis. Mean platelet volume (MPV) >9.5 fl and hemoglobin (Hb) levels >220 g/l or <130 g/l have been identified as independent predictors of thrombotic events. Immune deficiency attributed to leukopenia further increases the risk of infections.¹⁰ Impaired renal function in patients with ES are associated with poorer prognosis. In patients with moderate to severe renal dysfunction, dose adjustment of some diuretic agents, anticoagulants, and advanced PAH therapies should be considered.⁹ Heart failure resulting from biventricular dysfunction is often atypical and manifests as low cardiac output and cyanosis at late stages of disease. Advanced HF has been reported to be the most common cause of death among ES patients, followed by infections.¹⁰

In our patient, initial laboratory parameters showed increased hemoglobin and hematocrit levels. These findings are consistent with the literatures, reflecting erythrocytosis and hemoconcentration associated with chronic hypoxemia in Eisenmenger syndrome. As discussed earlier, ES patients are at increased risk of infections, including dengue.^{5,14} The relationship between cardiovascular disease (CVD) and DHF is complex, as each condition can influence and exacerbate the other. In DHF, increased vascular permeability can result in pleural effusion and ascites.¹⁵ An intense immune response to DENV, especially in CVD patients, increases the risk of severe complications. Coagulation abnormalities observed in patients with DHF may also overlap with those encountered in CVD.^{16,17} Our patient represent a rare case of ES complicated by DHF.

The proposed mechanisms by which dengue hemorrhagic fever (DHF) complicates DENV infection include both direct and indirect pathways.⁵ In direct injury, the virus invades myocardial tissue, cardiomyocytes, and the endothelial cells of blood vessels. This invasion triggers a host immune response characterized by the release of proinflammatory cytokines, interleukins, and tumor necrosis factors. These inflammatory mediators increase vascular permeability causing plasma leakage and fluid extravasation, which may result in hemorrhage, hypotension, and circulatory shock.^{17,18} Increased vascular permeability further reduces preload and exacerbates hypovolemic shock, leading to acute HF during DENV infection in patients with underlying CVD. Collectively, these processes aggravate cardiovascular injury.⁴

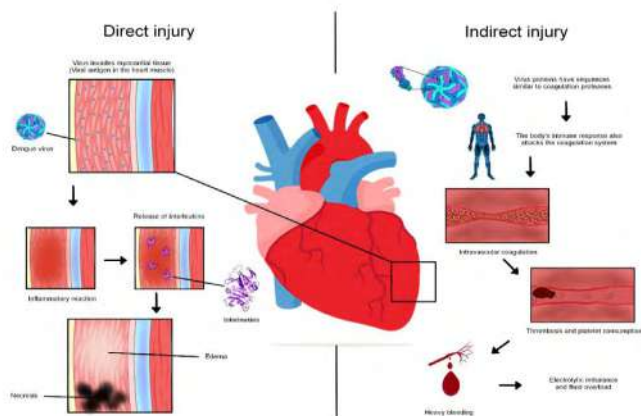


Figure 6. Proposed mechanisms of cardiac repercussions from DENV infection¹⁷

In indirect injury, DENV proteins dysregulate the immune system, leading to activation of coagulation factors and thrombosis, as well as platelet consumption. This process results in intravascular coagulation and severe bleeding, which may cause fluid overload.⁵ The changes in calcium storage within infected cells contribute as a secondary mechanism in the development of myocarditis.¹⁷ The patient in our case diagnosed with ES complicated by DHF. Understanding the pathophysiological mechanism of both conditions will help physicians to make clinical decisions and deliver adequate management.

The clinical manifestations of DENV infection range from mild, asymptomatic cases to severe manifestations with high mortality risk. DENV infection is divided into three distinct phases, although not all phases are observed in every patient. The initial phase includes classic symptoms such as fever, myalgia, retro-orbital pain, vomiting, diarrhea, and rash. The critical phase carries the potential for hemorrhagic abnormalities and circulatory shock.¹⁸ Some cases may exhibit transient cardiac involvement, but dengue can also lead to chronic cardiac complications.¹⁹ Cardiovascular manifestations include chest pain, palpitations, pulse irregularities, pulmonary edema, and shock.⁵ Electrocardiographic (ECG) abnormalities have also been reported. The recovery (convalescent) phase is marked by the resolution of skin rash and petechiae.^{17,19,20} Our patient has clinical features consistent with those described in the literatures, including classical dengue manifestations such as fever, skin rash, petechiae, and history of vomiting. Cardiovascular complications were not observed. This may be attributable to the classification of the patient's Eisenmenger syndrome as simple ES, which is associated with longer survival and a more favorable prognosis compared with complex ES. Additionally, asymptomatic ECG changes represent the most common cardiovascular manifestation of dengue infection, with sinus tachycardia reported most frequently.⁵ Physical examination and ECG of our patient reveal asymptomatic ECG change with sinus tachycardia.

The gold standard for diagnosing dengue infection is the detection of viral RNA fragments using real-time polymerase chain reaction (RT-PCR). This test is limited to the acute viremic phase and by its availability. The acute phase is difficult to identify because it lasts only a few days. In the convalescent phase, or in cases with negative RT-PCR results but high clinical suspicion, the presence of dengue-specific immunoglobulin M (IgM) is considered diagnostic.⁵ The identification of CV involvement due to dengue is challenging because of (1) the absence of universal diagnostic criteria, (2) varied clinical manifestations, and (3) other diseases that alter or mimic findings.^{5,21} Patients with ECG abnormalities and clinical characteristics of heart failure should undergo echocardiography.⁵

In our patient, the diagnosis of dengue hemorrhagic fever complicating Eisenmenger syndrome was established based on clinical manifestations and supportive investigations. Dengue IgM serology was positive. To support ongoing monitoring and management, serial complete blood counts and follow-up echocardiographic examinations were performed. Currently, no specific antiviral agents exist for the treatment of dengue infection. There are also no established guidelines for the management of DHF in patients with ES. Management of DHF in patients with CHD generally follows standard DHF protocols. During the febrile phase, fluid replacement is delivered through liberal oral fluid intake, and antipyretics are recommended. For DHF, the mainstay of treatment is intravenous fluid therapy. In cases of asymptomatic myocardial damage, specific treatment is unnecessary.²²

However, in patients who show inadequate response to fluid treatment, dobutamine or levosimendan may be considered. Diuretics and additional inotropic support may be indicated when necessary.¹⁷ Previous studies have reported conflicting outcomes regarding diuretics; therefore, drug choice should be individualized.¹⁴ Correction of electrolyte imbalances must be considered to reduce cardiovascular complications.^{5,14} In cases of symptomatic bradyarrhythmia or complete heart block, atropine and pacemakers are effective.⁵ Prevention of severe dengue to reduce complications is essential.⁸ Dengue vaccination may be useful to decrease disease severity and prevent CV manifestations.²³ Appropriate management with intravenous rehydration can reduce dengue mortality to less than 1%.^{5,22}

Patients with ES should be periodically assessed, and counseling on all aspects of care is important.^{10,24} Treatment options include pharmacological therapy, corrective surgeries, and rehabilitation. Timely diagnosis, multidisciplinary care, and access to CHD specialists may improve outcomes.⁹ PAH-specific therapies target three major pathways: the endothelin pathway, phosphodiesterase-5 (PDE-5) pathway, and prostacyclin pathway.¹⁰ Current European Society of Cardiology/European Respiratory Society (ESC/ERS) guidelines recommend bosentan as first-line therapy in symptomatic patients with ES followed by PDE-5 inhibitors.²⁶ Limited evidence is available regarding optimal management strategies for patients with ES. A recent study reported triple combination therapy and assessment for transplantation may be recommended in selected patients.²⁶ Guideline-recommended therapy for ES is largely determined by symptoms severity, as assessed using the WHO functional class (FC).²⁵ Corrective surgery with defect closure is contraindicated in established ES, as it is associated with high perioperative risk and poor clinical outcomes.¹⁰ In this case, the patient with DHF complicating ES was managed adequately with intravenous fluid administration and thrombocyte concentrate (TC) transfusion for severe thrombocytopenia. The primary treatment for DHF did not result in cardiovascular worsening. Additional supportive treatments also administered appropriately. For ES therapy, the patient received first-line treatment with sildenafil citrate, a PDE-5 inhibitor.

Survival outcomes among patients with ES exhibit considerable variability and predicting prognosis, especially in complicated cases, is challenging. Although PAH is present, survival can be relatively preserved depending on the disease severity.¹¹ For dengue infection, predictors of adverse outcomes include extremes of age, hypertension, diabetes mellitus, nutritional status, superimposed infections, dyspnea at rest, and altered mental status. Survival or prognostic data for patients with ES complicated by DHF remain unknown.³ Recent evidence suggests, that untreated ES patients have significantly reduced life expectancy, especially in complex lesions. Risk factors for mortality in ES patients include older age, lower oxygen saturation, complexity of the underlying heart defect, HF, elevated brain natriuretic peptides, low six-minute walk test (6MWT) distance, New York Heart Association (NYHA) functional class, absence of sinus rhythm, presence of arrhythmias or pre-tricuspid shunt, impaired right ventricular function (especially lower TAPSE), lower albumin levels, and increased C-reactive protein.^{11,27} Survival outcomes in our patient demonstrated tendency toward favorable conditions. The patient's clinical condition improved during hospitalization. This favorable outcome was likely due to the absence of established risk factors associated with poor outcomes or mortality in either ES or DHF.

Conclusion

Eisenmenger syndrome (ES) is defined as pulmonary hypertension due to elevated PVR with reversed or bidirectional shunt. ES patients are at higher risk of infections, including DENV-related viral illnesses. The mechanisms by which DENV infection affect cardiovascular function in ES are not fully understood. Uncontrolled inflammation, increased vascular permeability, and coagulation pathway disruption are proposed affect both conditions. To date, there are no standardized protocols available for the diagnosis and tailored treatment of dengue in ES patients. Prognosis varies depending on the clinical setting, and further studies are needed to improve outcomes.

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Preeclampsia in the Modern Era: New Insights from Global Research and Implications for Practice in Indonesia

Arya Ady Nugroho¹, Yudianto Budi Saroyo², Allan Taufiq Rivai³

¹Departement of Obstetrics & Gynecologic, Faculty of Medicine, University of Indonesia, Jakarta, Indonesia

²Division of Maternal-Fetal Medicine, Department of Obstetrics & Gynecologic, Faculty of Medicine, University of Indonesia, Jakarta, Indonesia

³Division of Maternal-Fetal Medicine, Department of Obstetrics & Gynecologic, University of Indonesia Hospital, Depok, West Java, Indonesia

Abstract

Preeclampsia (PE) remains a leading cause of maternal and neonatal morbidity and mortality worldwide, affecting 2–15% of pregnancies. This review synthesizes recent advancements in the understanding of PE pathophysiology, including placental dysfunction, endothelial impairment, and novel biomarkers such as angiogenic factors. Drawing on global studies published up to 2025, we explore predictive models for early detection before 11 weeks of gestation, innovative management strategies including aspirin prophylaxis, and disparities in maternal and neonatal outcomes. In Indonesia, where PE contributes to 26–30% of maternal deaths, we highlight local epidemiology, risk factors such as anemia and obesity, and tailored interventions to improve screening and care in resource-limited settings. By emphasizing evidence-based practices, this article underscores the need for integrated approaches to reduce the burden of PE and provides actionable insights for clinicians in both global and Indonesian contexts.

Keywords: preeclampsia, hypertensive disorders of pregnancy, placental dysfunction, angiogenic biomarkers, aspirin prophylaxis, maternal health in Indonesia

Abstrak

Preeklampsia (PE) masih menjadi penyebab utama morbiditas dan mortalitas maternal serta neonatal di seluruh dunia, yang memengaruhi 2–15% kehamilan. Tinjauan ini menyajikan sintesis kemajuan terkini dalam memahami patofisiologi PE, termasuk disfungsi plasenta, gangguan endotel, dan *biomarker* baru seperti faktor angiogenik. Berdasarkan studi global yang diterbitkan hingga tahun 2025, kami mengeksplorasi model prediksi untuk deteksi dini sebelum usia kehamilan 11 minggu, strategi manajemen inovatif seperti profilaksis aspirin, dan disparitas luaran maternal dan neonatal. Di Indonesia, di mana PE berkontribusi terhadap 26–30% kematian maternal, kami menyoroti epidemiologi lokal, faktor risiko seperti anemia dan obesitas, serta intervensi yang disesuaikan untuk meningkatkan skrining dan perawatan di layanan dengan sumber daya terbatas. Dengan menekankan praktik berbasis bukti, artikel ini menegaskan perlunya pendekatan terintegrasi untuk mengurangi beban PE serta memberikan wawasan yang dapat ditindaklanjuti bagi klinisi dalam konteks Indonesia maupun global.

Kata kunci: preeklampsia, gangguan hipertensi kehamilan, disfungsi plasenta, *biomarker* angiogenik, profilaksis aspirin, kesehatan maternal di Indonesia

Introduction

Preeclampsia (PE), a multisystem disorder characterized by new-onset hypertension after 20 weeks of gestation, often accompanied by proteinuria or end-organ dysfunction, continues to pose significant challenges in maternal-fetal medicine. Globally, it affects 5–10% of pregnancies and accounts for approximately 15% of maternal deaths, with higher rates observed in low- and middle-income countries (LMICs).^{1–3} Recent research published between 2024 and 2025 has shifted the focus toward early prediction, molecular mechanisms, and equitable management strategies, addressing the limitations of traditional approaches. In Indonesia, PE is the second leading cause of maternal mortality, contributing to 26.47% of cases per 100,000 live births, a burden exacerbated by socioeconomic factors and limited access to antenatal care.^{4,5} This review integrates cutting-edge global insights with Indonesia-specific considerations, aiming to guide clinicians in optimizing outcomes amid evolving evidence.

Pathophysiology of Preeclampsia

The pathogenesis of PE is multifaceted, primarily rooted in abnormal placentation, which leads to placental ischemia and the release of anti-angiogenic factors such as soluble fms-like tyrosine kinase-1 (sFlt-1) and soluble endoglin that disrupt maternal endothelial function.^{6,7} Recent studies highlight the role of genetic polymorphisms and epigenetic modifications in influencing susceptibility to PE, with maternal immune maladaptation playing a key role in early trophoblast invasion failure.^{8,9} In 2025, advancements in biomarker research, such as the sFlt-1/PIGF ratio, have enabled better differentiation between PE subtypes, including early-onset (before 34 weeks) and late-onset forms.^{10,11} These insights underscore the shift from a purely hypertensive view to a vascular and inflammatory paradigm, informing targeted therapies.

Epidemiology and Risk Factors

Globally, the incidence of PE ranges from 2–8%, with stable trends in high-income countries but increasing rates in LMICs due to improved reporting and urbanization.^{1,12} A 2025 analysis reveals a higher prevalence in upper-middle-income regions, linked to metabolic syndromes.¹³ Key risk factors include nulliparity, advanced maternal age (>35 years), obesity, chronic hypertension, and diabetes.¹⁴ In Indonesia, epidemiological data from 2024–2025 indicate that PE affects 3–5% of pregnancies, with anemia (26%), obesity (10%), and chronic hypertension (8%) as prominent contributors, often compounded by rural-urban disparities and delayed care-seeking.¹⁵ Sub-Saharan parallels suggest similar epidemiological patterns in Southeast Asia, emphasizing the need for context-specific surveillance.¹⁶

Diagnosis and Screening

The diagnosis of PE is based on blood pressure $\geq 140/90$ mmHg after 20 weeks of gestation, accompanied by proteinuria or signs of organ involvement, according to updated 2025 guidelines from World Health Organization (WHO) and The International Society for the Study of Hypertension in Pregnancy (ISSHP).⁶ Innovative screening integrates first-trimester algorithms combining maternal history, mean arterial pressure, uterine artery Doppler, and biomarkers such as placental growth factor (PIGF), achieving detection rates of up to 90% for preterm PE. In Indonesia, a 2025 study validates combined screening in local cohorts, demonstrating a 30% reduction in missed cases with traditional methods.¹⁵ Machine learning models further enhance predictive accuracy, particularly in diverse populations.⁸

Management Strategies

Management prioritizes maternal stabilization with antihypertensives such as labetalol or nifedipine, along with magnesium sulfate to prevent eclampsia.¹ For severe PE, delivery remains definitive treatment, with timing guided by gestational age—expectant management up to 37 weeks for mild cases according to 2024 syntheses.² Telemedicine and self-monitoring innovations have improved adherence in remote areas.³ In Indonesian teaching hospitals such as Rumah Sakit Cipto Mangunkusumo (RSCM) or Rumah Sakit Pendidikan Universitas Indonesia, initial management of preeclampsia generally

exhibits high compliance with national protocols for hypertensive disorders of pregnancy. However, persistent challenges include timely risk identification, drug availability, and the need of specialized training in managing severe cases.⁴ Long-term follow-up is essential to address cardiovascular risks, as PE doubles the risk of future hypertension.⁵

Prevention Approaches

Low-dose aspirin (150 mg), initiated before 16 weeks of gestation, reduces the risk of preterm PE by 62% in high-risk women, as supported by evidence from international guidelines and meta-analyses.^{6,7} Calcium supplementation and lifestyle interventions target modifiable risk factors.^{2,13} In Asia, including Indonesia, first-trimester screen-and-prevent programs have demonstrated feasibility, with 80% acceptability and reduced incidence of PE.¹⁰ Community health workers play a vital role in enhancing uptake in underserved regions, aligning with WHO initiatives to improve equitable access to care.^{3,6}

Implications for Practice in Indonesia

Indonesia's high maternal mortality ratio (305 per 100,000 live births) underscores the urgency of addressing PE, with significant regional variations—including higher rates in rural areas due to delayed referral systems.^{12,14} Integrating global tools, such as biomarker-based screening, into Puskesmas could reduce healthcare costs by 20% through early intervention.⁸ Policy recommendations include strengthening midwife training on updated clinical guidelines and leveraging digital health for monitoring, potentially halving PE-related mortality by 2030.^{15,16}

Conclusion

Advancements in PE research from 2024 to 2025 offer transformative potential, ranging from predictive modeling to personalized prevention strategies. In Indonesia, adapting these insights to local contexts, by addressing barriers such as healthcare access and patient education, could substantially mitigate the impact of PE. Future efforts should prioritize conducting multicenter clinical trials and strengthening health system to ensure equitable and sustainable maternal care.

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SCIENTIFIC JOURNAL OF PHARMACEUTICAL DEVELOPMENT AND MEDICAL APPLICATION

ISSN 1979-391X



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