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Address

FK-UPH Building 2nd floor
Boulevard Jendral Sudirman
Lippo Karawaci, Tangerang
phone (021) 54210130-54210131
e-mail:
medicinus.fk@uph.edu

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Factors Associated with Low Back Pain in Pre-Clinical Students in The Faculty of Medicine at Pelita Harapan University: Original Research

Edeline Samudra[1], Jane Florida Kalumpiu[1,2]

[1] Faculty of Medicine, University of Pelita Harapan, Jendral Sudirman Boulevard, Lippo Karawaci, Tangerang, Indonesia 15811
[2] Department of Parasitology, Siloam Hospital Lippo Village, Lippo Karawaci, Tangerang, Indonesia 15811

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Correspondance: Jane Florida Kalumpiu
Faculty of Medicine. Pelita Harapan University
E-mail: jane.kalumpiu@uph.edu
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Abstract

Background: Low back pain is one of the most common health problems globally, including in Indonesia, and can result in limitations on a person's activities. While low back pain is typically associated with adults and the elderly, its prevalence is also notably high among students, particularly medical students. Despite the various factors contributing to low back pain, there is limited data on its prevalence and associated factors in Indonesia.

Methods: A cross-sectional study was conducted at the Faculty of Medicine, Pelita Harapan University, utilizing consecutive sampling. Data were collected using the Nordic Musculoskeletal Questionnaire, Pittsburgh Sleep Quality Index (PSQI), International Physical Activity Questionnaire (IPAQ), and Perceived Stress Scale (PSS).

Results: Out of 179 students, 144 (80%) experienced low back pain, while 35 (20%) did not. Among students with low back pain, 1.4% had psychological history, 7.3% had history of spinal problems, 0.7% had family history, 15.3% were obese, 75% had poor sleep quality, 8.3% had high-risk physical activity, 6.9% had a high-risk position, and 7.6% had a high-risk stress level. While other factors showed no significant association with low back pain, sleep quality demonstrated a significant association with a p-value of 0.022 (OR 2.52, CI 1.18-5.43).

Conclusion: There is a significant association between sleep quality and low back pain in pre-clinical medical students at UPH, while other factors did not exhibit significant correlations.

Introduction

Low back pain is a sensation of pain that occurs in the lower back and can be defined as a consequence of manual handling, which is a problem resulting from one's efforts to maintain the speed and load they are lifting. Prolonged manual handling can lead to low back pain. This pain can originate from muscles, the lower part of the spine, nerves, or other surrounding structures. Therefore, based on the type of pain, it can be categorized as local pain, pain referring to the back, pain originating from the spine, radicular pain, and pain accompanied by muscle spasms. Furthermore, based on the onset of discomfort or discomfort, it can be categorized as acute (<4 weeks), subacute (4-12 weeks), and chronic (>12 weeks).

While low back pain itself is not fatal, it can diminish productivity and quality of life, becoming an economic burden for individuals and families.[1] According to the International Classification of Disease (11th version, 2021), low back pain is common,

affecting nearly everyone above 20 years old.[2] It was the leading cause of disability in 1990 and 2017, according to the Global Burden of Disease 2017.[3]

In Indonesia, low back pain remains a common issue. Studies indicate prevalence, such as 68.1% in Banda Aceh and around 40% in Central Java.[4,5] Among students, prevalence is high, reaching 81.1% at Universitas Kristen Indonesia in 2018, 94.3% at FK Universitas Yarsi in 2019, and 50.54% at FK Universitas Pelita Harapan (UPH) in 2022.[6–8]

Low back pain can be caused by various underlying conditions, including congenital factors, degenerative diseases, spinal infections, trauma, neoplasms, and other diseases such as metabolic disorders, visceral diseases, and chronic pain syndromes. Additionally, various factors can contribute to low back pain, such as age, gender, psychological disorders and stress, medical history, physical activity, position, lifestyle factors (smoking, obesity, sleep disturbances), and family and social history.[1,9–12] Broadly speaking, low back pain can impact daily life, work ability, and sexual function, but there's a lack of research on low back pain in adolescents.[13,14]

Material And Methods

Study Design and Variables

This study utilized an unmatched categorical comparative analytic study design with a cross-sectional method and was conducted at the Faculty of Medicine, UPH, from January 2023 to May 2023. The independent variable in this study is psychological history, history of spinal problems, family history, body mass index (BMI), sleep quality, physical activities, position, and stress. Meanwhile the dependent variable is low back pain, and the confounding variable is the duration of lectures.

Study Subjects

The subjects of this study are UPH Medical Faculty students from the 2020, 2021, and 2022 cohorts who were willing to participate as respondents and met the inclusion criteria of the study. These criteria include pre-clinical UPH Medical Faculty students who have experienced low back pain or discomfort in the lower back within the last month and students who were willing to participate in the study and had filled out the consent form. A total of 209 students were obtained with consecutive sampling techniques, of which 179 students were included in the final analysis.

Materials and Study Procedures

The materials used in this study include the Nordic Musculoskeletal Questionnaire to assess the prevalence of low back pain, the Pittsburgh Sleep Quality Index (PSQI) questionnaire to assess sleep quality, the International Physical Activity Questionnaire (IPAQ) to assess physical activity, and the Perceived Stress Scale (PSS) questionnaire to measure stress levels.

The study began by selecting study samples using consecutive sampling. Then, the selected subjects were asked to read and fill out the consent form. After agreeing to complete the questionnaires, the study participants were given questionnaires related to low back pain, sleep quality, physical activity, stress, and other factors that could influence the prevalence of low back pain. Data collection continued until the predetermined sample size was reached.

Study Ethics

This study was approved by Ethical Clearance from the Ethics Committee of the Faculty of Medicine, UPH, with approval number 029/K-LKJ/ETIK/I/2023.

Data Management and Statistical Analysis

The collected data were checked for completeness and clarity of responses. Then, the data were categorized based on their respective categories in Microsoft Excel. Subsequently, the classified data were input and analysed using SPSS

Statistics software. Chi-square Test and Fisher's Exact Test were employed based on expected cell counts.

Result

Table 1. Factors associated with low back pain in pre-clinical UPH Medical Faculty students

Risk Factors	%	OR (95% CI)	P-value
Psychological History	1.40%	1.246 (1.16-1.34)	1
History of Spinal Problems	7.30%	1.134 (0.3-4.3)	0.739
Family History	0.70%	1.245 (1.16-1.34)	1
BMI	15.30%	0.721 (0.28-1.86)	0.671
Sleep Quality	75%	2.526 (1.18-5.43)	**0.022**
High Risk Physical Activities	8.30%	0.79 (0.73-0.86)	0.127
High Risk Position	6.90%	1.537 (0.31-20.51)	0.694
Stress	7.60%	1.365 (0.29-6.46)	1

Discussion

Psychological history and its association with low back pain

In our study, a history of psychological issues did not show a significant association with LBP. This result aligns with the findings of Arma (2019) but contradicts the study by Mei (2019), which found a significant association between chronic LBP and unhealthy mental status (such as depression, anxiety, coercion, paranoia, and interpersonal sensitivity).[15,16] Takekawa (2015) discovered that chronic pain from LBP is associated with psychological stress or depression, kinesiophobia, and a passive coping style. This is because limitations in physical movement can lead to psychological distress, which can, in turn, worsen the pain.[17,18] However, in our study, the majority of participants experienced acute LBP, explaining why there were fewer instances of psychological issues, which are more common in chronic LBP.

History of spinal problems and its association with low back pain

The history of spinal problems did not show a significant association with LBP. This result is consistent with the findings of Ahmed (2022), who reported that the majority had no history of back injury, and most did not seek medical care due to the busy schedules of medical students.[19] In our study, most participants with LBP did not consult physicians or visit hospitals, making it challenging to obtain a diagnosis for spinal problems. This is supported by the studies of Negash (2022) and Pratami (2020), indicating that individuals with LBP often do not receive medical treatment or interventions.[7,20] Grabovac's study (2019) also found that as long as patients with LBP maintain work and sexual capacity, indicating satisfaction in the health domain, medical treatment is not necessary.[13] However, this contradicts the findings of Latina (2020), Mulfianda (2021), and Ganesan (2017), who reported that LBP is one of the most common reasons for hospital visits.[4,9,21]

Family history and its association with low back pain

No significant association was found between family history and LBP. This result aligns with the studies by Heikkala (2022) and Arma (2019) but contradicts the findings of Kientchockwiwat (2022), who reported that chronic LBP has a genetic factor that can predict future occurrences.[15,22,23] Given that the majority of participants with LBP in this study experienced acute symptoms, the results did not show a significant association between family history and LBP. Arma (2019) explained that genetic factors leading to LBP are certain spinal disorders

such as scoliosis, disc prolapse, ankylosing spondylitis, and spondylolisthesis. For non-specific LBP, there is no genetic association.[15] Kamson (2020) found that certain genes are related to the development of LBP and pain sensitivity, but environmental factors also play a role, indicating that not everyone with a family history will necessarily experience LBP.[24]

BMI and its association with low back pain

BMI did not show a significant association with LBP. This result is consistent with the study by Alturkistani (2020), which reported that only 14.3% of obese students reported LBP, and the majority of LBP participants had a normal BMI.[25] However, this contradicts the findings of Arma (2019), who reported that a BMI at risk (≥23.0) could lead to LBP because excessive weight can decrease abdominal muscle tone, making it easier for the center of gravity to shift forward, leading to fatigue in the paravertebral muscles.[15] This result also contradicts Boszczowski's study (2021), which found that underweight individuals could overwhelm the lumbar spine and ligaments due to a lack of lean body mass.[26] Kientchockwiwat's study (2022) reported an association between LBP and atrophy of the paraspinal and multifidus muscles, which commonly occurs in underweight individuals. This is because there is a connection between vitamin D insufficiency or deficiency and LBP, possibly mediated by IL-6. Vitamin D deficiency is more common in underweight people, explaining the association between being underweight and LBP.[23] However, in this study, there were not many participants who were underweight, so a significant association was not observed at the Faculty of Medicine Pelita Harapan University.

Sleep quality and its association with low back pain

Sleep quality showed a significant association with LBP, where poor sleep quality could increase the prevalence of LBP. This result is consistent with the studies by Gehart (2017) and Vinstrup (2020) but contradicts Looveren's study (2021), which found no strong association, only a high risk in the future.[27–29] Sleep itself is an essential process in maintaining homeostasis in various systems within the human body, particularly regarding human physical health.[28] Poor sleep quality can be a risk factor for both physical and physiological problems. The mechanisms can be divided into direct and indirect mechanisms.

Indirect mechanisms are based on sleep disturbances that can initially affect the immune system, where the immune system will be activated and enter a pro-inflammatory state mediated by glia. As a result, hyperalgesia occurs, interpreted as an increase in sensitivity and responsiveness to stimulation around damaged tissues.[29,30]

On the other hand, direct mechanisms are based on physiological processes and circadian rhythms during the sleep cycle, where human sensitivity increases at night, specifically from midnight to 3 am. This begins with the increased work of the sleep drive, a system that signals that the body needs sleep. The sleep drive then reduces the inhibition of pain and actually increases sensitivity to pain, especially chronic pain. Ultimately, poor sleep quality increases the body's response to pain stimuli, generally referred to as nociceptive stimuli, causing hypersensitivity to pain stimuli on that day.

This increased sensitivity to pain can also impact the pain healing process, where recovery is hindered and, in turn, worsens the perceived pain by the patient. Therefore, based on several previous studies, it can be concluded that one of the supportive therapy targets in pain management is to pay attention to good sleep quality.[29]

Physical activity and its association with low back pain

Physical activity did not show a significant association with LBP. This result is consistent with Kientchockwiwat's study (2022), which also investigated medical students.[23] There are many factors in medical students that can contribute to vulnerability to LBP, such as stress and high use of computers and laptops.[19] On the other hand, because medical students spend a lot of time studying, physical activity generally decreases, so other factors play a more crucial role in LBP among medical students.

Position and its association with low back pain

Position did not show a significant association with LBP. This result aligns with the studies by Boszczowski (2021) and Kientchockwiwat (2022) but contradicts Medicina's study (2021), which found greater discomfort after prolonged sitting compared to the control group.[23,26,31] Kientchockwiwat (2022) explained that there are various results due to differences in target populations, protocols, and environments. Bad postural habits indeed play a crucial role as a risk factor in the development of LBP, but not everyone has the same position, so answers can vary.[23] What generally leads to LBP is forward-leaning and slumped sitting, where discomfort in the lumbar region significantly increases with increasing stress on passive tissues due to decreasing lumbar lordosis, and passive tissues take the load of the upper body.[31] Therefore, to assess the relationship between position and LBP, specific interventions and settings regarding position and duration are necessary, then compared with a control group.

Stress and its association with low back pain

Stress did not show a significant association with LBP. This result is consistent with the studies by Alturkistani (2020) and Arma (2019) but contradicts Choi's study (2021).[15,25,32] Arma (2019) and Pillay (2016) explained that LBP is not caused by stress but that individuals with LBP or limited physical movement due to pain can cause psychological stress. This, in turn, worsens the pain because psychological vulnerabilities can alter the brain's perception, intensifying the pain. Someone with psychological stress has abnormalities in hormone regulation in the brain (dopamine), so when someone experiences stress or anxiety, everything becomes negative, and they cannot focus on anything, and the pain experienced becomes all-consuming.[15,18]

Conclusion

The results of this study show that there is a significant association between sleep quality and low back pain in pre-clinical medical students at UPH, with a p-value of 0.022. Other variables did not show significant correlations, but psychological history, history of spinal problems, family history, sleep quality, position, and stress were identified as risk factors for low back pain with an odds ratio >1.

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References

1. Fitriani TA, Salamah QN, Nisa H. Keluhan Low Back Pain Selama Pembelajaran Jarak Jauh pada Mahasiswa UIN Syarif Hidayatullah Jakarta Tahun 2020. Media Penelit dan Pengemb Kesehat. 2021;31(2):133–42. https://doi.org/10.22435/MPK.V31I2.4180

2. Harrison JE, Weber S, Jakob R, Chute CG. ICD-11: an international classification of diseases for the twenty-first century. BMC Med Inform Decis Mak. 2021 Nov 1;21.

3. Institute for Health Metrics and Evaluation (IHME). Findings from the Global Burden of Disease Study 2017. Seattle, WA: IHME; 2018.

4. Mulfianda R, Desreza N, Maulidya R. Faktor-faktor yang Berhubungan dengan Kejadian Nyeri Punggung Bawah (NPB) pada Karyawan di Kantor PLN Wilayah Aceh. J Healthc Technol Med. 2021;7(1):253–62. https://doi.org/10.33143/jhtm.v7i1.1415

5. Minghelli B. Low back pain in childhood and adolescence phase: consequences, prevalence and risk factors - a revision. J Spine. 2017; 6(1). http://dx.doi.org/10.4172/2165-7939.1000351

6. Anggiat L, Hon WHC, Baait S. The Incidence of Low Back Pain Among University Students. J Pro-Life. 2018; 5(3):677–87.

7. Pratami AR, Zulhamidah Y, Widayanti E. Hubungan Antara Sikap Duduk dengan Kejadian Low Back Pain pada Mahasiswa Fakultas Kedokteran Universitas YARSI Tahun Pertama dan Tahun Kedua. Maj Kesehat Pharmamedika. 2020;11(2):105–15. http://dx.doi.org/10.33476/mkp.v11i2.1324

8. Thiono J. Hubungan antara Prevalensi Low Back Pain dengan Body Mass Index pada Mahasiswa Pre-Klinik Fakultas Kedokteran Unviersitas Pelita Harapan. Tangerang: Universitas Pelita Harapan; 2022.

9. Ganesan S, Acharya AS, Chauhan R, Acharya S. Prevalence and risk factors for low back pain in 1,355 young adults: A cross-sectional study. Asian Spine J. 2017;11(4):610–7. https://doi.org/10.4184/asj.2017.11.4.610

10. Institute of Neurological Disorders N. Low Back Pain fact sheet. Natl Institutes Heal. 2020.

11. Bento TPF, Genebra CV dos S, Maciel NM, Cornelio GP, Simeão SFAP, Vitta A de. Low back pain and some associated factors: is there any difference between genders? Brazilian J Phys Ther. 2020;24(1):79. https://doi.org/10.1016%2Fj.bjpt.2019.01.012

12. Zaina F, Balagué F, Battié M, Karppinen J, Negrini S. Low back pain rehabilitation in 2020: new frontiers and old limits of our understanding. Eur J Phys Rehabil Med. 2020;56(2):212–9. https://doi.org/10.23736/s1973-9087.20.06257-7

13. Grabovac I, Dorner TE. Association between low back pain and various everyday performances: Activities of daily living, ability to work and sexual function. Wien Klin Wochenschr. 2019;131(21):541. https://doi.org/10.1007%2Fs00508-019-01542-7

14. Ferrari S, Vanti C, Frigau L, Guccione AA, Mola F, Ruggeri M, et al. Sexual disability in patients with chronic non-specific low back pain—amulticenter retrospective analysis. J Phys Ther Sci. 2019;31(4):360-365. https://doi.org/10.1589/jpts.31.360

15. Arma M, Septadina IS, Legiran. Factors Affecting Low Back Pain (LBP) among Public Transportation Drivers. Maj Kedokt Sriwij. 2019;51(4):206–15.

16. Mei Q, Li C, Yin Y, Wang Q, Wang Q, Deng G. The relationship between the psychological stress of adolescents in school and the prevalence of chronic low back pain: A cross-sectional study in China. Child Adolesc Psychiatry Ment Health. 2019;13(1):1–10. https://doi.org/10.1186/s13034-019-0283-2

17. Takekawa KS, Gonçalves JS, Moriguchi CS, Coury HJCG, De Sato TO. Can a self-administered questionnaire identify workers with chronic or recurring low back pain? Ind Health. 2015;53(4):340–345. https://doi.org/10.2486/indhealth.2014-0241

18. Pillay S. The psychology of low back pain - Harvard Health [Internet]. Harvard Health Publishing. 2016. Available from: https://www.health.harvard.edu/blog/psychology-low-back-pain-201604259537

19. Ahmed SSEKA, Bahar RKM, Ahmed LAM, Abbas AAE, Ahmed ESAE, Seedahmed RJA, et al. Prevalence and Associated Factors of Back Pain among Medical Students in Sudan. Health (Irvine Calif). 2022;14(9):931–938. https://doi.org/10.4236/health.2022.149066

20. Negash NA, Tadele A, Ferede AJ. Prevalence and Associated Factors of Low Back Pain Among Healthcare Professionals at University of Gondar Comprehensive and Specialized Hospital, Northwest Ethiopia: Cross-Sectional Study. 2022; 2022(15):1543-1552. https://doi.org/10.2147/jpr.s351987

21. Latina R, Petruzzo A, Vignally P, Cattaruzza MS, Buratti CV, Mitello L, et al. The prevalence of musculoskeletal disorders and low back pain among Italian nurses: An observationalstudy. Acta Biomed. 2020;91(12-S):1–10. https://doi.org/10.23750/abm.v91i12-s.10306

22. Heikkala E, Karppinen J, Mikkola I, Hagnäs M, Oura P. Association Between Family History of Surgically Treated Low Back Pain and Adolescent Low Back Pain. Spine (Phila Pa 1976). 2022;47(9):649–655. https://doi.org/10.1097/brs.0000000000004345

23. Kientchockwiwat K, ... Low Back Pain Prevalence and Associated Factors among Medical Students. Vajira Med J … [Internet]. 2022. Available from: https://he02.tci-thaijo.org/index.php/VMED/article/view/259078%0Ahttps://he02.tci-thaijo.org/index.php/VMED/article/download/259078/177333

24. Kamson S. Is Family History a Predictor of Low Back Pain? - Fix My Pain [Internet]. Spine Institue Northwest. 2020. Available from: https://www.fixmypain.ca/family-history-predictor-low-back-pain/

25. Alturkistani L, Hendi O, Bajaber A, Alhamoud M, Althobaiti S, Alharthi T, et al. Prevalence of Lower Back Pain and its Relation to Stress Among Medical Students in Taif University, Saudi Arabia. Int J Prev Med. 2020;11(1). https://doi.org/10.4103/ijpvm.ijpvm_264_19

26. Boszczowski N, Pinto RCR, de Araújo Junior FA. Low back pain in medical students: Prevalence and related factors. Coluna/ Columna. 2021;20(3):197–200. https://doi.org/10.1590/S1808-185120212003244850

27. James I. Gerhart, John W. Burns, Kristina M. Pos, David A. Smith LSP. Relationships Between Sleep Quality and Pain-Related Factors for People with Chronic Low Back Pain: Tests of Reciprocal and Time of Day Effects. Physiol Behav. 2017;176(3):139–148. https://doi.org/10.1007/s12160-016-9860-2

28. Vinstrup J, Jakobsen MD, Andersen LL. Poor sleep is a risk factor for low-back pain among healthcare workers: Prospective cohort study. Int J Environ Res Public Health. 2020;17(3): 996. https://doi.org/10.3390/ijerph17030996

29. Van Looveren E, Bilterys T, Munneke W, Cagnie B, Ickmans K, Mairesse O, et al. The association between sleep and chronic spinal pain: A systematic review from the last decade. J Clin Med. 2021;10(17): 3836. https://doi.org/10.3390/jcm10173836

30. Grandner MA, Kripke DF, Yoon IY, Youngstedt SD. Criterion validity of the Pittsburgh Sleep Quality Index: Investigation in a non-clinical sample. Sleep Biol Rhythms. 2006; 4(2):129. https://doi.org/10.1111/j.1479-8425.2006.00207.x

31. Jung KS, Jung JH, In TS, Cho HY. Effects of Prolonged Sitting with Slumped Posture on Trunk Muscular Fatigue in Adolescents with and without Chronic Lower Back Pain. Medicina (B Aires). 2021;57(1):1–8. https://doi.org/10.3390/medicina57010003

32. Choi S, Nah S, Jang HD, Moon JE, Han S. Association between chronic low back pain and degree of stress: a nationwide cross-sectional study. Sci Rep. 2021;11(1):1–7. https://doi.org/10.1038/s41598-021-94001-1

Deciphering Developmental Epileptic Encephalopathies (DEE): Unravelling the Key Signs

Evlyne Erlyana Suryawijaya[1], Shania Lokito[2]

[1] Department of Neurology, Faculty of Medicine, University of Pelita Harapan, Jendral Sudirman Boulevard, Lippo Karawaci, Tangerang, Indonesia 15811
[2] Faculty of Medicine, University of Pelita Harapan, Jendral Sudirman Boulevard, Lippo Karawaci, Tangerang, Indonesia 15811

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Correspondance: Shania Lokito
E-mail : shanialokito@gmail.com
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Abstract

Background: Epilepsy, a chronic neurological disorder affecting over 50 million people worldwide, is marked by recurrent seizures and loss of consciousness. It is categorized based on EEG features, etiologies, and comorbidities. Developmental Encephalopathy (DE) involves developmental delays and early-onset seizures without causing developmental regression. In contrast, Epileptic Encephalopathy (EE) features severe epilepsy syndromes where frequent seizures result in developmental delays or regression.

Methods: This review explores the clinical definitions, epidemiology, and diagnostic criteria for DE, EE, and DEEs. It covers their etiologies, clinical features, diagnostic methods, and treatment strategies, including genetic, structural, metabolic, and immune-related factors.

Results: DE features developmental impairment with epilepsy, while EE involves severe epilepsy causing cognitive and behavioral dysfunction. DEEs are marked by early-onset severe epilepsy and EEG abnormalities that worsen developmental impairments. Essential diagnostic tools include EEG, neuroimaging, and genetic testing. Effective management requires personalized interventions to control seizures and address cognitive deficits.

Conclusion: DEEs are a complex epilepsy subset with major developmental and cognitive challenges. Early diagnosis and targeted treatments are crucial for improving outcomes. Ongoing research into DEEs' genetic and pathophysiological mechanisms is key to enhancing understanding and management.

Introduction

Epilepsy is a chronic disease of the brain that has affected more than 50 million people worldwide. Recurrent seizures, episodes of involuntary movements, and loss of consciousness are the characteristics of patients suffering from epilepsy. Epilepsy can be grouped and typed into different categories based on its EEG features, etiologies, and comorbidities.[1]

The International League Against Epilepsy (ILAE) task force in 2014 propose the clinical definition of epilepsy defined by any of the following conditions.[2]

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

The incidence of epilepsy varies between countries. The estimated incidence that could be found in developing countries is 187/100,000. Recent study has also revealed the maximum incidence occurs in the first year of age is 102/100,000 cases per year. In children from the age of 11 to 17 years old, the incidence is 21-24/100,000 cases per year.[3]

Developmental Encephalopathy (DE) is a heterogenous group of epilepsy subtype with the characteristics of developmental impairment with early onset. DE has been related with other neurological symptoms such as autonomy dysfunction, behavioral disorder, and motor impairment. The prominent feature that can be observed in patients suffering from DE is the delay in development, whereas epileptic activity does not appear to be associated with the developmental delay, regression, or stagnation.[4]

Meanwhile Epileptic Encephalopathy (EE) is another subtype of heterogenous group involving syndromes of severe epilepsy syndrome. EE is characterized with several types of seizure, frequent epileptiform activity on EEG, with developmental delay or regression. On EE, there is no history of developmental delay on pre-existing condition that could be found. But on the other hand, developmental delays that can be observed on EE happened because of disruption on brain physiological process regarding to frequent epilepsy activity.[5]

However, in some cases of severe epilepsy in early onset of life, it is usually difficult to know whether the underlying cause of epileptic encephalopathy would be the only reason causing developmental delay even in the absence of epilepsy. So that the term Developmental and Epileptic Encephalopathies (DEEs) was designated to define a heterogenous group of disorder characterized by early-onset, often severe epileptic seizures, and EEG abnormalities on a background of developmental impairment that tends to be worsen as a sequalae of epilepsy.[6]

DEE condition refers to when cognitive functions are influenced by seizures and interictal epileptiform activity with neurobiological process behind the epilepsy. DEEs manifests during early infantile or childhood period, although adults can be affected too. Genetic variants are recognized to be the etiologies on most patients with DEEs. A cohort study of DEEs that was conducted before (with total patients of 197) showed that almost one third had pathogenic variants in known genes. A greater number of genetics variants are associated with an increased risk of expressing DEEs. Other etiologies and risk factors associated with DEE include.[7]

- Structural: e.g tuberous sclerosis complex (TSC), hypothalamic hamartomas, hemimegalencephaly.[7]
- Metabolic: e.g pyridoxine or biotinidase deficiency, GLUT-1 deficiency.[7]
- Immune disorders: e.g. Rasmussen syndrome.[7]

Patients with DEE, especially in children onset need aggressive treatment.[6]

Developmental Encephalopathy

Developmental Encephalopathy (DE) is a term that has separate entity to DEE. The term "developmental encephalopathy" should be used in a condition of a person with developmental delay or intellectual disability, due to a non-progressive brain state who also has co-existing epilepsy. The degree of disability may become more prominent with brain maturation. The risk of epilepsy in this population is higher than the general population but not to the extent that epilepsy itself causes epileptic encephalopathy.[8]

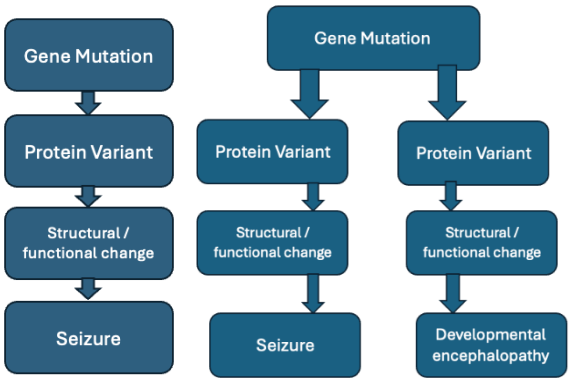

Figure 1. Pathological pathways of Developmental encephalopathy [9]

Epileptic Encephalopathy

Epileptic encephalopathy (EE) is a term that refers when epilepsy and/or epileptiform activity affects cognitive and behavioral functions. These conditions can be observed in patients whose preceding level of function was normal or near normal. The unremitting epileptic activity contributes to progressive cerebral dysfunction. The disease course usually is progressive or have waxing-waning course. The underlying etiology varies. Electroencephalographic features and clinical symptoms mirror the specific age-related epileptogenic reaction of immature brain.[9]

Some recognized syndromes for epileptic encephalopathies are Ohtahara syndrome, early myoclonic encephalopathy, West syndrome, Dravet syndrome, Lennox-gastaut syndrome, Epileptic encephalopathy with continuous spike-and-wave during sleep (CSWS), and Landau-Kleffner syndrome (LKS). [10]

Early infantile epileptic encephalopathies are a group of disorders comprised of Ohtahara syndrome or early infantile epileptic encephalopathy (EIEE), early myoclonic encephalopathy (EME), and malignant migrating partial seizures in infancy. Ohtahara syndrome is an epilepsy with onset from intrauterine period to 3 months of life. Tonic spasms can be observed and define seizure type that are very frequent and occur in both sleep and wakeful states. Interictal EEG shows burst suppression pattern with no sleep-wake differentiation. Burst can last for 2-6 seconds alternating with periods of suppression lasting for 3-5 seconds. The etiology is heterogenous. Most of the cases are attributable to static structural brain lesions such as focal cortical dysplasia, hemimegaloencephaly, and Aicardi syndrome. [10]

West's syndrome is characterized by epileptic spasms or "salaam attacks", hypsarrhythmia on EEG with developmental delay or regression. Onset is between 3 and 12 months of age. Cluster of sudden, brief, diffuse or fragmented, and tonic contractions of limb muscles are characteristic from epileptic spasm that can be observed from patient with West's syndrome. Symptoms can be accompanied by cry, laughter, or autonomic changes. [10]

Dravet syndrome is described as severe myoclonic epilepsy of infancy (SMEI) with the onset of 5 - 8 months of age. Symptoms would vary from prolonged febrile unilateral-clonic convulsions with alternating patterns in a previously normal child. Seizure is characterized by emergence of multiple seizure types such as myoclonic, atypical absences, and complex focal seizures which frequently progress to status epilepticus and associated with severe psychomotor deterioration. The progression of the symptoms will stop at around 10-12 years of age with decrease in seizure frequency and continue in neurologic sequalae. [10]

Table 1. Differentiation in patients with DEE [9]

	Developmental Encephalopathy (DE)	DEE with dual impact on cognition from developmental	DEE predominantly related to epileptic encephalopathy
Etiology	Condition due to underlying static etiology e.g. hypoxic brain insult	Condition due to underlying etiology e.g. TSC, Dravet syndrome, most commonly with gene mutation	Condition due to the impact of the epilepsy e.g. EE-CSWS
Clinical	May have systemic or focal neurological features, neurocutaneous markers. May be normal.	May have systemic or focal neurological features, neurocutaneous markers. May be normal	May be normal or hypotonic, depending on seizure control
Age at onset	*In utero* or shortly after birth	Any age, most have onset in infancy or early childhood	Any age but most in childhood
Past medical history	Often abnormal	Either abnormal or normal	Usually normal
Cognition	Abnormal	Abnormal - but may be normal and regress, or deteriorate from a low baseline	Regression, improves with seizure control
EEG	Abnormal in established cases	Abnormal in established cases	Abnormal. Can return to normal if seizures are controlled. Mostly slow with frequent epileptiform discharges
Outcome	Neurocognition and neurobehavior remain impaired even with seizure control	Neurocognition and neurobehavior remain impaired even with seizure control although some improvement may occur	Neurocognition and neurobehavior may significantly improve with control of seizures and resolution of interictal epileptiform activity.

Lennox-Gastaut syndrome (LGS) is one of the severe forms of epileptic encephalopathy with the onset of 1-8 years of age (mainly between 2-5 years of age). LGS is characterized by polymorphic seizures including tonic, atypical absence, atonic, and myoclonic seizures. "Drop attacks" can be observed in nearly 50% of children and frequently cause injuries to patients. Nonconvulsive status epilepticus happened in two-thirds of the patients, while twenty percent experienced epileptic spasms. The cognitive stagnation and deterioration are common and fluctuates with the frequency of seizures. [10]

Routine Investigations

Diagnostic investigation has become a very important factor in determining DEEs from other conditions. With collecting clinical history for risk factors, clinical markers, and seizure semiology, other diagnostic investigations have very been helpful in identifying electroclinical syndrome. Electroencephalograms (EEGs) are a diagnostic tool that can be very helpful in distinguishing different syndromes of DEEs. Specific syndromes such as Ohtahara syndrome can be found in EEG as suppression burst, hypsarrhythmia in West syndrome, and continuous slow spike-and-wave typically in 1,5-2,5 Hz during sleep in CSWS. Spike-wave discharge at frequency of <2,5 Hz can be found in Lennox-Gastaut syndrome. [11]

Neuroimaging can be useful in determining structural abnormalities such as malformations of cortical development and hypoxic injuries. The gold standard recommended for investigation of infants and children with epilepsy would be Brain MRI.

Metabolic workup and immune testing can be other investigations. Genetic examination with next generation sequencing (NGS) is suggested. [11]

Intervention of Care

In patients with DE, interventions should include seizures control. However, seizures control does not change the baseline of functioning in patients but can lead to an improvement in quality of life. Decline in seizure control can happen and during these phases, more aggressive seizure management should be considered. Status epilepticus would be an extreme version and should be considered for onset in the setting of an intercurrent respiratory infection. Chronic polypharmacy or high level of ASMs should be avoided since they are more likely to be harmful to a person with DE. [12]

In EE cases, patients develop specific epilepsy-driven encephalopathy. This condition requires aggressive antiseizure interventions as this can lead to significant improvement in cognition and behavior. Suppression of epileptiform abnormalities on the EEG might lead to improvement in cognitive function although usually it won't necessarily return to normal function. [13]

Patients with developmental and epileptic encephalopathies (DEE) require balanced management considering both their cognitive development and seizure control. Treatment aims for improved epilepsy control without over-medication, as uncontrolled seizures can worsen their condition. Despite the challenges, interventions are crucial for safety and quality of life. Targeted treatments, like new medications or gene therapy, show promise in this context. [12,13]

Conclusion

Developmental and Epileptic Encephalopathies (DEEs) are a subset of epilepsy disorders with early onset and significant developmental impairment, often requiring aggressive treatment. Genetic factors play a key role, alongside various structural, metabolic, and immune-related causes. Early intervention and targeted treatments are crucial for managing DEEs and improving patient outcomes. Further research is needed to better understand the underlying mechanisms and genetic pathways of DEEs.

References

1. Epilepsy. World Health Organization; 2024. Available from: https://www.who.int/news-room/fact-sheets/detail/epilepsy

2. Minardi C, Minacapelli R, Valastro P, Vasile F, Pitino S, Pavone P, Astuto M, Murabito P. Epilepsy in Children: From Diagnosis to Treatment with Focus on Emergency. J Clin Med. 2019;8(1):39. https://doi.org/10.3390%2Fjcm8010039

3. Giussani G., Cricelli C., Mazzoleni F., Cricelli I., Pasqua A., Pecchioli S., Lapi F., Beghi E. Prevalence and incidence of epilepsy in Italy based on a nationwide database. *Neuroepidemiology.* 2014;43(3-4):228–232. https://doi.org/10.1159/000368801

4. Cutri-French C, Armstrong D, Saby J, Gorman C, Lane J, Fu C, et al. Comparison of core features in four developmental encephalopathies in the Rett Natural History Study. Annals of Neurology. 2020;88(2):396–406. https://doi.org/10.1002/ana.25797

5. Guerrini R, Conti V, Mantegazza M, Balestrini S, Galanopoulou AS, Benfenati F. Developmental and epileptic encephalopathies: From genetic heterogeneity to phenotypic continuum. Physiological Reviews. 2023;103(1):433–513. https://doi.org/10.1152/physrev.00063.2021

6. Raga S, Specchio N, Rheims S, Wilmshurst JM. Developmental and epileptic encephalopathies: Recognition and approaches to care. Epileptic Disorders. 2021;23(1):40–52. https://doi.org/10.1684/epd.2021.1244

7. Hamdan FF, Myers CT, et al. High Rate of Recurrent De Novo Mutations in Developmental and Epileptic Encephalopathies. Am J Hum Genet. 2017; 101(5):664-685. https://doi.org/10.1016/j.ajhg.2017.09.008

8. Scheffer IE, Liao J. Deciphering the concepts behind “epileptic encephalopathy” and “developmental and epileptic encephalopathy.” European Journal of Paediatric Neurology. 2020;24:11–4. https://doi.org/10.1016/j.ejpn.2019.12.023

9. Specchio N, Curatolo P. Developmental and epileptic encephalopathies: What we do and do not know. Brain. 2021;144(1):32–43. https://doi.org/10.1093/brain/awaa371

10. Jain P, Sharma S, Tripathi M. Diagnosis and management of epileptic encephalopathies in children. Epilepsy Research and Treatment. 2013; 2023(1):1–9. http://dx.doi.org/10.1155/2013/501981

11. Gaillard WD, Chiron C, Helen Cross J, Simon Harvey A, Kuzniecky R, Hertz-Pannier L, et al. Guidelines for imaging infants and children with recent-onset epilepsy. Epilepsia. 2009;50(9):2147–53. https://doi.org/10.1111/j.1528-1167.2009.02075.x

12. Kalser J, Cross JH. The epileptic encephalopathy jungle – from dr west to the concepts of aetiology-related and developmental encephalopathies. Current Opinion in Neurology. 2018;31(2):216–22. https://doi.org/10.1097/wco.0000000000000535

13. Korff CM, Brunklaus A, Zuberi SM. Epileptic activity is a surrogate for an underlying etiology and stopping the activity has a limited impact on developmental outcome. *Epilepsia* 2015; 56(10):1477-1481. https://doi.org/10.1111/epi.13105

Characteristics of High-Risk Behaviours Related to Alcohol and Illicit Drug Use and their Associated Factors among Adolescents in Middle and High School

Melanie Widjaja[1], Abdul Latief[1], Rini Sekartini[1]

[1] Department of Pediatrics, Faculty of Medicine, University of Pelita Harapan, Jendral Sudirman Boulevard, Lippo Karawaci, Tangerang, Indonesia 15811

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Correspondance: Melanie Widjaja
Department of Pediatrics, Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia, Jl. Salemba VI, 10430, Indonesia
Phone: +62 813
E-mail: melaniewidjaja@gmail.com
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Abstract

Background: Use of narcotics, psychotropic and addictive substances (NPA) in adolescents has become one of the major social problems we are facing in society and gives a negative impact. This study was done to determine the characteristics and factors that influence high-risk behaviour of NPA use in adolescents in middle and high school, also introducing CRAFFT questionnaire as an early screening tool for alcohol an illicit drugs use.

Methods: Quantitative study (validated questionnaire) was conducted among 514 subjects aged 12-18 years old. CRAFFT questionnaire was used to detect a high-risk behavior of alcohol and illicit drugs use and self-reported questionnaire used to determine the risk factors of NPA.

Result: Most participants (19,6%) were involved in high-risk behaviour of alcohol and illicit drugs, with the majority was males (12,4%). This study showed smoking behaviour (23,8%), drinking alcohol (15,8%) and illicit drugs use (13,6%). The type of drugs being used were cannabis (52,7%), tramadol (15,2%), dextromethorphan (10,7%) and methamphetamine (6,3%). CRAFFT questionnaire has a good internal consistency with Cronbach's α 0,73. Education level, authoritarian parenting style, unharmonious parents, peer pressure or threat, and extracurricular activities were factors that influenced high-risk behavior of alcohol and illicit drug use

Conclusions: Early detection, comprehensive treatment, and intervention of risk factors of NPA use are needed. CRAFFT can be use as one of the screening tools for detection of alcohol and illicit drugs use in adolescents.

Introduction

The use of Narcotics, Psychotropic and Addictive (NPA) substances in adolescents has become one of the major social problems we face in society. According to *Badan Narkotik Nasional* (BNN) survey in 2011, the use of NPA among High School and junior high school students is estimated to be around 7,3% with prevalence of 7,1% in males and 1,9% in females. The prevalence of NPA use is higher among high school students compared to lower grade students.[1] World Health Organization reported among youth aged 13-15 years, at least one out of five students are smokers. In a survey conducted by the Indonesian Ministry of Health in 2007, 2.6% of adolescents aged 13-15 years consumed alcohol and 11,8% smoked or used other tobacco products.[2]

Narcotics, psychotropic, and addictive substances use has a negative impact and is often associated with disruption of social function such as behavioural changes, lower academic achievement, school dropout, and violence.[3] Other than the social problem, NPA also negatively affect health ranging from mild to life-threatening medical condition, such as nausea, vomiting, muscle spasm, hallucinations, hearing loss, liver and kidney injury, anxiety, to death caused by overdose.

Adolescents are the future of the nation and hold a crucial role in the development of a country. Indonesia as a developing country has 28% percentage of adolescents from total population.[4] Based on the survey, adolescent NPA users in Indonesia are progressively increasing, which will negatively impact the future and increase the burden of the country. Prevention of drug use is very important and will be much more efficient and cost-effective compared to the intervention. Problems arising from the use of NPA in adolescents stand for 60-70% of social problem. More than two-thirds of deaths and illnesses during adulthood are associated with high-risk behaviours in adolescent, such as drinking alcohol, smoking, drug use, and unprotected sexual intercourse.

Early detection of NPA use is very important and can be done using screening tools. A process of gathering information to evaluate whether further comprehensive action is required. There are lots of existing screening tools.

CRAFFT screening tool is used in this study because it is simple, easy to use, has already been validated (92.3% sensitivity and 82.1% specificity), has a good reliability (Cronbach's α = 0.79), and recommended by American Academy of Paediatrics. Based on the awareness of negative effects of NPA use, we conduct this study, hopefully it can bring valuable implication in preventing risky behavior and eventually can be used as health promotion for the health of teenagers.

Methods

We performed a cross-sectional study and subjects were recruited with random sampling method. The target population was 12-18 years old Junior and Senior High School students in Central Jakarta from April to June 2014. Initially, the CRAFFTS and Risk Factor Questionnaire were tested for validation by giving the questionnaire to thirty adolescents aged 12-18 years old who are not included in the selected school. The questionnaire's validity and reliability were analyzed using Pearson correlation and Cronbach's α test. The questionnaire is considered valid if it has p-value <0.05 and reliable if the Cronbach's α test values ≥ 0.7. After the questionnaire validity had been proven, data was collected at 2 Junior High schools and 2 senior high schools that were selected randomly. The explanation about this study was given to the subject. Then, the parental consent and student assent forms were obtained prior to the study. The questionnaire will be filled independently by the subjects and took 10-15 minutes. Inclusion criteria were students aged 12-18 years, willing to participate in the study, had parental consent to join the study, and able to fill the questionnaire completely. The exclusion criteria were physical and/or psychological disorders that does not allow the student to join the study and refusal to be included.

The collected data were processed and analyzed using SPSS version 22. All dependent and independent variables were analyzed descriptively. Continuous data will be presented as mean value (X) and standard deviation (SD) if the data distribution was normal or presented as median value and min-max range if the data

distribution was abnormal. The categorical was presented as number (n) and percentage (%). The association between dependent and independent variable will be presented in the crosstable. The association between the categorical independent variable and the dependent variable will be analyzed by chi-square test, Fisher-exact test or Kolmogorov-Smirnov test. The association between two dichotomous variables will be presented as odds ratio (OR) with 95% confidence interval (CI). Then, the analysis will be followed by multivariate logistic regression analysis.

Result

The collected subjects were 514 adolescents, consisted of 43,3% males and 56,5% females with a median age of 15 years (range 12-18 years). Most of the subjects (95,7%) stay with their parent(s) and have middle-class financial status (**Table.1**)**.** Most of the subjects (55.3%) also had family members consuming drugs. The most common drug used by family members is cigarettes (54.6%) (**Table 2**).

Table 1. Research Subjects Characteristics.

Characteristics	Categories	N (%)
Age		Median 15 years old (range 12-18 years old)*
Gender	Male	223 (43,4)
	Female	291 (56.6)
Education background	Junior High school	248 (48.2)
	Senior High School	266 (51.8)
Residence	With parents	492 (95,7)
	Not with parents	22 (4.3)
Father's occupation	Entrepreneur	215 (41.8)
	Employees	213 (41.4)
	Civil servants	70 (13.6)
	Unemployed	16 (3.1)
Mother's occupation	Entrepreneur	68 (13,2)
	Employees	56 (10.9)
	Civil servants	18 (3.5)
	Housewife	372 (72.4)
Father's education	High	166 (32.3)
	Medium	270 (52.5)
	Low	78 (15,2)
Mother's education	High	117 (22,8)
	Medium	271 (52,7)
	Low	126 (24.5)
Peer group	Yes	351 (68.3)
	No	163 (31,7)
Family financial status.	Low (< Rp. 972.210,-)	60 (11.7)
	Lower-middle (Rp.973.179-1.837.176,-)	218 (42,4)
	Upper-middle (Rp.3.838.116 - 11.849.690,-)	214 (41.6)
	High(>Rp.1.850.629,-)	22 (4.3)

*The median central tendency value was measured because the data is abnormally distributed

Table 2. The risk factor of NPA use among adolescents.

Characteristics	Category	N (%)
Extracurricular activities	Yes	371 (72,2)
	Never	143 (27,8)
Academic grading	≥75	348 (67,7)
	<75	166 (32,3)
Parents marital status	Married	436 (84,8)
	Divorced/ separated	35 (6,8)
	Widow/ widower	43 (8,4)
Authoritarian parenting	Yes	143 (27,8)
	No	371 (72,2)
Parents harmonious relationship	Yes	433 (84,2)
	No	81 (15,8)
Family member of NPA users	Yes	284 (55,3)
	No	230 (44,7)
Religious activity	Yes	374 (72,8)
	No	140 (27,2)
School distance to nightclub	Yes	39 (7,6)
	No	475 (92,4)
Student NPA user	Yes	316 (61,5)
	No	198 (38,5)
Drugs easily available	Yes	337 (65,5)
	No	177 (34,4)
Peer pressure	Yes	69 (13,4)
	No	445 (86,6)
Desire for peer acceptance	Yes	36 (7)
	No	478 (93)

Assessment of the subjects was done using CRAFFT questionnaire with cut-off value of ≥ 2 considered as high-risk behaviour. The results showed 19.6% of subjects had high-risk behaviour. Most of the subjects involved in high-risk behaviour were male (12.4%) (**Table 3**)

Table 3. High-Risk Behaviour in Adolescent

CRAFFT Score	Gender	N=101(%)
<2	Male	159 (31%)
	Female	254 (49,4%)
≥ 2	Male	64 (12,4%)
	Female	37 (7,2%)

The results showed that most of the adolescent who were involved in high-risk behaviours of NPA, and alcohol use were male (63.4%) and at Senior high school (71.3%) (**Table 4**). The smoker subjects were 23.8% and can be divided into daily

smoker (8.6%) and occasional smoker (15.2%). Age of first smoking based on the developmental phase of adolescence appeared mostly from early adolescence 10-13 years old (18.9%). The results showed that 21.6% of adolescent had consumed alcoholic beverages and can be further divided into daily drinker (0.4%), occasional drinker (15.4%), and former drinker (5.8%). Based on the age of first trying to drink alcohol, mostly started from middle age (14-16 years) (**Table 5**).

Table 4. Distribution of high-risk behaviour in adolescents based on the used substance

No	High-Risk Behaviour	N (%)
1	Smoking	
	-Daily Smoker	44 (8,6)
	-Occasional smoker	78 (15,2)
	-Ex-smoker	58 (11,3)
	-Non-smoker	334 (65)
2	Alcohol drinking	
	-Daily drinker	2 (0,4)
	-Occasional drinker	79 (15,4)
	-Ex-drinker	30 (5,8)
	-Non-drinker	403 (78,4)
3	Narcotics, psychotropic and addictive substances	70 (13,6)
	-User	444 (86,4)
	-Non-user	
4	Involved in at least 1 high-risk behaviour	210 (40,8%)

Table 5. Distribution of high-risk behaviour in adolescents based on the age of first NPA substance use

No	Type of High-Risk Behaviour	Age	N (%)
1	Smoking Behaviour	Early adolescence (10-13 years old)	97 (18,9)
		Mid-adolescence (14-16 years old)	78 (15,2)
		Late adolescence (≥17 years old)	5 (1)
2	Alcohol drinking behaviour	Early adolescence (10-13 years old)	42 (8,2)
		Mid-adolescence (14-16 years old)	65 (12,6)
		Late adolescence (≥17 years old)	4 (0,8)
3	Narcotics, psychotropic and addictive substances using behaviour	Early adolescence (10-13 years old)	15 (2,9)
		Mid-adolescence (14-16 years old)	47 (9,1)
		Late adolescence (≥17 years old)	8 (1,6)

Results of the study in adolescent showed that 13.6% of adolescents had used NPA (**Table 4**). The most commonly used substances in this study were marijuana (52.7%), tramadol (15.2%), dextromethorphan (10.7%), and shabu-shabu (6.3%) (**Table 6**)

Table 6. The percentage of Narcotics, psychotropic and addictive substances that were used by adolescent

Drugs Type	N (%)
Marijuana	59 (52,7%)
Cocaine	1 (0,9%)
Shabu-Shabu (methamphetamine)	7 (6,3%)
Ecstasy	2 (1,8%)
BK Pill- “Koplo” pill	4 (3,6%)
Amphetamine	1 (0,9%)
Glue-sniffing	4 (3,6%)
Alprazolam	3 (2,7%)
Dextromethorphan	13 (10,7%)
Tramadol	17 (52,2%)
Mushroom	1(0,9%)

Factors significantly associated ($p<0,05$) with the high-risk behaviour of NPA use were age, gender, educational background, academic grading, extracurricular activities, parenting technique, parents’ harmony, family member NPA user, religious activity, school location, student NPA user, NPA availability, peer pressure, and desire for peer acceptance. Parents marital status did not have a significant association (p-value = 0.079) to the high-risk behaviour of NPA use in adolescents. **(Table 7).**

Table 7. Association between high-risk of NPA use and risk factors

Risk Factors	CRAFFT		OR (95% CI)	P
	High Risk	Low Risk		
Age				
Mid-Late Adolescence (14-18 years)	98	366	4.20 (1.28-13.77)	0.011
Early Adolescence (10-13 years)*	3	47		
Gender				
Male	64	159	2.76 (1.76-4.34)	0.000
Female*	37	254		

Educational Level				
High School	72	194	2.80 (1.75-4.50)	0.000
Junior High School*	29	219		
Extracurricular Activities				
No	40	103	0.51 (0.32-0.80)	0.003
Yes*	61	310		
Academic Achievement				
Poor (<75)	41	125	1.58 (1.01-2.47)	0.047
Good (>75)*	60	288		
Parental Marital Status				
Married*	80	356	1.64 (0.94-2.86)	0.079/ NS
Divorced/Widowed	21	57		
Authoritarian Parenting Style				
Yes	86	57	35.8 (19.35-66.27)	0.000
No*	15	356		
Harmonious Parents				
No	43	38	7.32 (4.37-12.27)	0.000
Yes*	58	375		
Family Member Using Illicit Drugs				
Yes	77	207	3.19 (1.94-5.25)	0.000
No*	24	24		
Religious Activities				
Yes*	48	326	4.14 (2.62-6.53)	0.000
No	53	87		
School Location				
Yes	13	26	2.20 (1.09-4.46)	0.025
No*	88	387		
Student Drug Use				
Yes	74	242	1.94 (1.20-3.14)	0.007
No*	27	171		
Ease of Access to Illicit Drugs				
Yes	85	252	0.30 (0.17-0.52)	0.000
No*	16	161		
Peer Pressure or Threat				
Yes	35	34	5.91 (3.47-10.14)	0.000
No*	66	379		
Desire for Social Acceptance				
Yes	26	10	13.97 (6.47-30.12)	0.000
No*	75	403		

The multivariate and logistic regression analysis showed the factors that contribute to high-risk behaviour of NPA use in adolescents, sorted from strongest to lowest association, were educational background, authoritarian parenting, broken-home, peer pressure and extracurricular activity (**Table 8**).

Table 8. Multivariate analysis of the factors associated to high-risk behaviour of NPA use in adolescent.

	B	S.E.	Wald	df	Sig.	Exp (B)	95% C.I for EXP (B)	
							Lower	Upper
Adolescent Educational Level	2.257	.399	32.014	1	.000	9.557	4.373	20.889
Extracurricular Activities	.714	.361	3.909	1	.048	2.043	1.006	4.147
Authoritarian Parenting Style	3.305	.388	72.697	1	.000	27.249	12.747	58.251
Disharmonious Parents	1.387	.402	11.886	1	.001	4.003	1.819	8.807
Family Member Using Illicit Drugs	.646	.355	3.314	1	.069	1.908	.952	3.824
Peer Pressure or Threat	1.183	.430	7.577	1	.006	3.254	1.406	7.576
Desire for Social Acceptance	1.086	.563	3.719	1	.054	2.963	.982	8.935
Constant	5.639	.541	108.599	1	.000	.004		

- The included variable in step 1: age, gender, educational background, extracurricular activities, academic grading, parents' marital status, authoritarian parenting, parents' relationship, family member of NPA user, religious activities, school location, students NPA user, accessibility to NPA, peer pressure or threat, desire for peers' acceptance.

Discussion

One of the main goals of this study was to find a way to screen high-risk behaviour of NPA and alcohol use using simple questionnaire. In our study, we found that 19,6% of the subjects had positive CRAFFT questionnaire (≥2), which indicated high-risk behaviour for NPA and alcohol consumption. Previous study by Levy et al. also showed similar results which was 16,1%.[6]

CRAFFT questionnaire is a screening instrument for high-risk behaviour of drugs and alcohol use. This questionnaire is recommended by AAP to be used in under <21 years old population. This questionnaire

has been used and adopted in many other countries, and thus has also been translated into many languages. The study about questionnaire's reliability, sensitivity and specificity had been done. CRAFFT questionnaire's reliability using Cronbach's α score 0,68-0,86, with 49-100% sensitivity and 61,8%-96,6% specificity. [7-12] This study Cronbach's α reliability score was 0,73. Therefore, CRAFFT questionnaire is a good screening instrument which has good reliability as early screening measures. It is recommended to be used in every patient visit, especially for adolescents.

Smoker adolescents (daily and occasional smoker) were 23,8%. Our result was higher than studies from other countries, such as, Thailand (8,8%), Malaysia (11,5%), Myanmar (2%), Cambodia (2,4%), Filipina (11%), India (11,2%) and People's Republic of China (8,9%).[16–22] Lower result of 11,1% was also found in Indonesia health survey in 2007.[2] We also found out that there was lower prevalence of smoking habit in other developing countries other than Indonesia such as Kenya (13,9%), Uganda (4,3%), Zimbabwe (5,8%), Argentina (21%), Peru (17,3%), and Uruguay (10,5%).[23–28] As well as smoking habit in developed countries such as United States of America (4,9%) and England (13%).[29-31]

Our research revealed 18,9% of adolescents using cigarettes for the first time at age 10-13 years old. This result was similar to a study in India with mean age 12,4 years old.[22] Cigarettes are considered as a gateway drug to high-risk behaviour and another illicit substance usage.[32] This statement synchronized with our study which found that the age of first-time smoking cigarettes was early adolescent (10-13 years old). It will open the door to other illicit substances use at the older age. The study in the United States of America found that teenagers who smoke at the age of under 13 years old had a higher risk of marijuana usage (OR 3,3; CI 95% 2,3-4,6).[33]

High smoking prevalence in our study (23,8%) was presumed to be due to the lack of government effort to implement the law limiting cigarettes access to the minors. Indonesian government regulation number 105, year 2012 about the Protection of tobacco addictive substance to Health, regulated in article 25, stated that "every person is prohibited to sell any tobacco products to minors under 18 years old..."[34] Nevertheless, our study surprisingly found out that minors under 18 years old could buy cigarettes freely and easily in shops or stalls. Lack of strong implementation of government regulation makes progressively increasing smoking behaviour in adolescent and causing health problem in the future and further burden to the country.

At least 26,1 % of adolescent had tried drinking alcoholic beverage. Prevalence of adolescent drinker (daily drinker and occasional drinker) in this study was 15,8% and most of them tried drinking alcohol at age 14-16 years old. This result was similar to other countries such as Philippines (18,7%), Thailand (15,6%), Kenya (14,6%), Zimbabwe (15,4%), and Peru (27,1%).[16,20,23,25,27] Higher prevalence of alcohol drinker was found in Argentina (51,8%), Uruguay (45%), and United States of America (30,8%), whereas lower prevalence was found in Malaysia (8,6%), Myanmar (0,8%), Cambodia (7,3%), People's Republic of China (13%), and Maldives (4,9%).[17–19,21,26,28,31,35,36]

Indonesia has a higher prevalence compared to other countries in South-East Asia. This condition is caused by the lack of government regulations to restrict alcohol beverage distribution. Indonesia Ministry of trade regulation number 43/M-DAG/PER/9/2009 about Alcohol beverage procurement, distribution, sales, supervision, and control in article 17 subsection 4, stated that "alcoholic beverage buyer must show ID card older than 21 years old."[37] However, adolescent under the age of 18 years old was able to purchase alcoholic drinks easily without restrictions and the need of showing ID cards. This is presumed to be due to the lack of strong implementation of alcohol restriction law.

The study showed 13,6% of adolescent had used at least one type of illicit drugs or other addictive substances. Most of them

tried it for the first time at the age of 14-16 years old (9,1%). This result was higher if compared with BNN survey in 2011 around 7,3% and study in Thailand which was 6%.[1,38]

The most common illicit drugs used by adolescent were marijuana (52,7%), tramadol (15.2%), dextromethorphan (10.7%), and shabu-shabu (methamphetamine) (6,3%). These findings were similar to BNN survey, Marijuana as the most commonly used drugs.[1]

The use of marijuana will increase sexual desire and have an effect on cognitive function, including memory loss.[39,40] Studies in the United States report that teenagers who use marijuana have a higher risk of sexual behavior.[39] The use of marijuana in adolescents is largely initiated by smoking behaviour and consumption of alcoholic beverages.[33] Studies in Thailand found that the use of marijuana and alcohol was the gateway to methamphetamine use.[41] A large number of cannabis use in the study was due to the ease of obtaining marijuana and more affordable price than other types of illicit substances.

Tramadol is an analgesic drug that works selectively as an opioid agonist at μ receptor. It has the same structure as morphine and codeine. The study in Iran finds that 4.8% of adolescent routinely abusing tramadol.[42] The use of tramadol is also associated with marijuana use (OR: 5; 95% CI: 1.5-21.9), ecstasy (OR: 8.9, 95% CI: 2.7 -29.4), methamphetamine (OR: 0,5, 95% CI: 0.03-7.0), opioid (OR: 2.3, 95%CI: 0.7-7.4), and drinking alcoholic beverages (OR: 2.2, 95% CI: 0.74-7.4).[42] Tramadol addiction was also reported in 64% of people who bought it freely in Iran.[43]

Dextromethorphan (DXM) is a methorphan analogue that acts on sigma-type opioid receptors. This drug is commonly used as an antitussive, but lately abused, especially by adolescent. Dextromethorphan has a hallucinogenic effect and in high doses (5-10 times of therapeutic dose) can cause confusion, euphoria, disorientation, and drowsiness. Studies in the United States showed that there were 74.5% cases of DXM abuse among adolescents ages 9-17 years old, with the highest frequency at age 15-16 years.[44] Each country has its own policy of drug classification of DXM. The Singaporean state classified it as prescription drug, while Canada classified it as over-the-counter drug. Since June 2014, The Government of Indonesia has classified DXM as a prescription drug and withdraws all drugs containing DXM from the market.[45]

Shabu-shabu is classified as the methamphetamine group. The effects including improved mood, increasing alertness, concentration, and energy in people who feel tired. Studies by Embry and colleagues found that adolescent girls who use methamphetamine also use marijuana.[46] Methamphetamine use in adolescents was associated with increased risk of sexual and anti-social behavior.[46,47] Based on the results of this study, more governmental attention was required in preventing illicit drug and other addictive substances abuse, especially in adolescents.

The result of our study indicated that gender was not a risk factor for high-risk behaviour of drug use in adolescents. This was similar with studies in the United States who also didn't report gender as a risk factor for drug involvement in adolescents.[48] In contrast, study in Thailand found that the male had a higher risk of using illicit substances (OR: 3.7, 95% CI: 1,89-10,98; p value= 0.022)[38] and smoking behaviour (OR 2.44, 95% CI: 1.66-2.58).[14] The previous study in Makassar, South-Sulawesi reported similar result of 30,7% of population had high-risk behaviour of drug use, with higher male user percentage.[13] Studies from other countries such as Thailand and Pakistan also stated that 40% and 34% adolescent population had involved in at least one high-risk behavior.[14,15]

Education level was a risk factor for high-risk behaviour of drug use. Middle-aged teenagers (14-18 years old) were more involved in high-risk drugs and alcohol use behaviour than early-adolescent (10-13 years old). Senior high school students had a greater risk than the lower level (OR: 9.56;

95% 95% CI: 4.37-20.89; p-value = 0,000). Similarly, a study in Makassar also reported that adolescents with higher education had higher risk of high-risk behaviour than those in lower educational stages (OR = 0,514; 95% CI= 0,276-0,959).[13] Alcoholic drinking behaviour progressively increases with education levels, 7th grade (2.5%), 10th grade (10%), 12th grade (10.2%).[14]

Older age was also a predictor of the increased drugs use, however in this study, there was no association between ages with the risk of drug use. This may be due to unevenly distributed subject age and small sample size.

Authoritarian parenting is defined as rigid parenting, dictators and expect absolute obedience from a child without any questioning. People with this parenting style often use punishment and are not willing to explain the reasoning behind their rules. Authoritarian parenting is a risk factors for increased high-risk behaviours in adolescents.[50] This is consistent with the results of our study (OR 27,25; 95% CI 12,75-58,25; p value= 0,000). The result was thought to be due to poor parental relationships leading to increased risk of drug use. Studies in Pakistan showed that 75% of drug users had a bad relationship with parents, 49% did not have close relationship with parents, 63% were unable to communicate with parents, and 43% had a parental dispute.[15]

Parents have an important role in shaping healthy behaviour. They have roles as guardians, teachers, and supervisors of children. Lack of parental knowledge and skills, as well as community support, can be an obstacle in performing this role effectively.[14]

Inharmonious parents have a crucial role in increasing the high-risk behaviour of drug use, due to the lack of attention and affection of parents, and putting the adolescent in a stressful state with the frequent quarrel between parents.[14] There is a close relationship between drug abuse with family problems, such as parental conflicts, lack of parental support and supervision, and separation from parents early in life (before age 7).[51] Results of the study found that parent-inharmonious relationship (OR 4.00; 95% CI 1.82-8,81 p value= 0.001) was significantly associated with high-risk behaviour of drug and alcohol use in adolescents.

Adolescence is a transitional phase from childhood to young adulthood marked by physical and psychological changes, as well as attempts to establish self-identity and gain self-reliance.[52] Peer group influence is one of the most important factors of this period, where adolescents uphold high values of friendship and relationships with peers compared with family. Peer group influence has a large role on adolescents engaged in drug use and juvenile delinquency.[41] Positive effects can be achieved if at this time given a good education, and held training programs for adolescents, such as counsellors and educators for peer groups.

The influence and pressure of the peer group posed a risk to smoking behaviour (OR 2.90, 95% CI 1.93-4.35) and drinking alcoholic beverages (OR 1.72; 95% CI 1.36-2.17).[14] Adolescents have a tendency to use drugs if they have similar peer groups.[53,54] Wongtongkam et al. found a close relationship between adolescents with peers using prohibited substances such as alcohol drinking and drug use, particularly marijuana and methamphetamine.[41] Having drug user friends was associated with drug abuse in adolescents, especially marijuana (OR 6.94; 95% CI 4.12-11,71) . The results showed the same thing about peer group pressure on drug and alcohol use behaviour (OR 3.26; 95% CI 1.41-7.58; p-value = 0.006). [41]

Extracurricular activities such as participation in school organizations, arts, bands, and academic clubs have a role in reducing the risk of adolescent involvement in drug use.[55] In contrast, adolescents engaged in sports extracurricular activities have a higher risk of engaging in alcoholic drinking behavior.[55, 56] Studies in Pakistan showed opposite results, with 74% of teenagers who had never taken drugs, were actively involved in sports activities.[15] They also found that adolescents who did not

attend extracurricular activities were at higher risk of involvement in drug and alcohol use behaviour (OR 2.04; CI 95% 1.01-4.15; p-value = 0.048). In our study, we did not assess the type of extracurricular activities that exist. The amount of free time without supervision in adolescents provided more opportunities for adolescents to try illegal drugs than if they have activities.[38]

This study was conducted using a quantitative method to assess high-risk behaviour of drug use in adolescents. Questionnaires were submitted in writing and completed independently by the research subjects.

There were some limitations to this study. First, the results of this study could not be considered to represent all teenagers in Central Jakarta due to the wide scope and variation in various aspects of population. The study was limited to school students and did not involve adolescents outside of the regular general school system, and only performed in four different locations. This study was designed as a preliminary study to look at the characteristics and risk factors of high-risk drug use in adolescents who meet the criteria of inclusion in a consecutive way to meet the required number of samples. Nevertheless, the results of this study can still be used to provide an overview of high-risk behaviour of drug use in school-age adolescents with similar characteristics.

Second, the data used in the analysis in this study was based on information obtained by independently filled questionnaire. The researcher must rely on the assumption that the information provided was accurate and correct. Some of the questions asked were sensitive questions and the responses received might not be accurate. Third, there are limitations on the variables of extracurricular activities by using dichotomous assessment so that no specific data about the type and form of extracurricular activities are found.

Conclusion

The study concludes that the CRAFFT questionnaire is a reliable and effective tool for screening adolescents at risk of alcohol and illicit drug use. The research highlights that mid to late adolescence, particularly males, are most vulnerable to high-risk behaviors. Key contributing factors include individual characteristics, familial dynamics, and peer influence. These findings underscore the importance of targeted interventions to address these risk factors and reduce the incidence of substance use among adolescents.

Recommendation

Early adolescence (10-13 years) is a critical period to initiate school-based education on the dangers of drug use. Effective prevention strategies include providing educational materials, developing drug-free school programs, conducting random urine tests, promoting extracurricular activities under teacher supervision, and training teachers about the risks associated with drugs and alcohol. Parental involvement is crucial, as parents should be role models and receive training to improve their awareness of substance abuse risks. Health care professionals, including general practitioners and pediatricians, are encouraged to use the CRAFFT questionnaire for early detection of drug use risks in adolescents. Additionally, the government should enforce stricter regulations and penalties for the sale of cigarettes, alcohol, and other addictive substances. Further research with larger populations is necessary to understand drug use in Indonesian adolescents and to identify protective extracurricular activities.

Conflict of Interest: Nothing to declare.

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References

1. Badan Narkotik Nasional Republik Indonesia. Hasil penelitian BNN tahun 2011. Jakarta: Pusat Penelitian Data dan Informasi Badan Narkotika Nasional; 2011.

2. Prasodjo RS. Indonesia global school-based student health survey. Jakarta: World Health Organization; 2007 h.14‑5.

3. Chen K, Sheth AJ, Elliot DK, Yeager A. Prevalence and correlates of past year substance use, abuse, and dependents in a suburban community sample of high school students. Addict Behav. 2004;29(2):413‑423. https://doi.org/10.1016/j.addbeh.2003.08.013

4. Badan Pusat Statistik and Macro International. Indonesia young adult health reproductive survey 2007. Maryland: BPS and Macro International; 2008. h.53‑84.

5. World Health Organization. European strategy for child and adolescent health and development. Geneva: World Health Organization; 2005.

6. Levy S, Sherritt L, Gabrielli J, Shrier LA, Knight JR. Screening adolescents for substance use related high risk sexual behaviors. J Adolesc Heal. 2009;45(5):1‑9. https://doi.org/10.1016%2Fj.jadohealth.2009.03.028

7. Knight JR, Shrier LA, Bravender TD, Farrell M, Vander Bilt J, Shaffer HJ. A new brief screen for adolescent substance abuse. Arch Pediatr Adolesc Med. 1999;153(6):591‑596. https://doi.org/10.1001/archpedi.153.6.591

8. Knight JR, Sherritt L, Shrier L , Harris SK, Chang G. Validity of the CRAFFT substance abuse screening test among adolescent clinic patients. Arch Pediatr Adolesc Med. 2002;156(6):607‑614. https://doi.org/10.1001/archpedi.156.6.607

9. Jull A. The CRAFFT test was accurate for screening for substance abuse among adolescent clinic patients. Evid Based Nurs. 2003;6(1):23. https://doi.org/10.1136/ebn.6.1.23

10. Knight JR, Sherritt L, Harris SK, Gates EC, Chang G. Validity of brief alcohol screening tests among adolescents: a comparison of the AUDIT, POSIT, CAGE, and CRAFFT. Alcohol Clin Exp Res. 2003;27(1):67‑73. https://doi.org/10.1097/01.alc.0000046598.59317.3a

11. Knight J, Harris S, Sherritt L, Van Hook S, Lawrence N, Brooks T, dkk. Adolescents' preference for substance abuse screening in primary care practice. Subst Abus. 2007;28(4):107‑117. https://doi.org/10.1300/j465v28n04_03

12. Subramaniam M, Cheok C, Verma S, Wong J, Chong SA. Validity of a brief screening instrument- CRAFFT in a multiethnic Asian population. Addict Behav. 2010;35(12):1102‑1104. https://doi.org/10.1016/j.addbeh.2010.08.004

13. Hidayningsih PS, Tjandrarini DH, Mubasyiroh R, Supanni. Faktor-faktor yang berhubungan dengan perilaku berisiko remaja di kota Makasar tahun 2009. Bul Penelit Kesehat. 2011;39(2):88-98. https://dx.doi.org/10.22435/bpk.v39i2%20Jun.72.88-98

14. Ruangkanchanasetr S, Plitponkarnpim A, Hetrakul P, Kongsakon R. Youth risk behavior survey: Bangkok, Thailand. J Adolesc Health. 2005;36(3):227-35. https://doi.org/10.1016/j.jadohealth.2004.01.013

15. Siddiqui S, Niaz U, Hassan S, Husain H, Ahmed S, Akhter R. A survey of physchosocial correlates of drug abuse in young adults aged 16-21 in Karachi: identyfing "high risk" population target intervention strategies. Pak J Med Sci. 2005; 21(3):271-277. https://pjms.com.pk/issues/julsep05/pdf/drug_abuse.pdf

16. Kramomtong P. Thailand global school-based student health survey. Nonthaburi: World Health Organization; 2008. h.1-2.

17. Ahmad NA. Malaysia global school-based student health survey. Kuala Lumpur: World Health Organization; 2012. h. 32-5.

18. Tun A. Myanmar global global school-based student health survey. Yangon: World Health Organization; 2007. h. 1-2.

19. Tepirou C. Cambodia global school-based student health survey. Phnom Penh: World Health Organization; 2013. h. 17-9.

20. Segarra AB. Philippines global school-based student health survey. Manila: World Health Organization; 2011. h. 3-4.

21. Tian B. China (Beijing) global school-based student health survey. Beijing: World Health Organization; 2003. h. 1-2.

22. Agarwal M, Nischal A, Agrawal A, Verma J. Substance abuse in children and adolescents in India. J Indian Assoc Child Adolesc Ment Heal. 2013;9(3):62-79. http://dx.doi.org/10.1177/0973134220130302

23. Ogwell A. Kenya global school-based student health survey. Nairobi; 2003. h. 14-5.

24. Twa J. Uganda global school-based student health survey. Kampala: World Health Organization; 2003. h. 1-2.

25. Sithole EG. Zimbabwe global school-based student health survey. Harare: World Health Organization; 2003. h. 1-32.

26. Linetzky B. Argentina global school-based student health survey. Buenos Aires: World Health Organization; 2007. h. 1-2.

27. Baca ME. Peru global school-based student health survey. Lima: World Health Organization; 2010. h. 4–5.

28. Grumbaum S. Uruguay global school-based student health survey. Montevideo: World Health Organization; 2012. h. 3–4.

29. Hibell B, Guttormsson U, Ahlström S, Balakireva O, Bjarnason, Thoroddur Kokkevi A, dkk. The 2011 ESPAD report: substance use among students in 36 European countries. Stockholm: The Swedish Council for Information on Alcohol and Other Drugs (CAN); 2011. ISBN 978-91-7278-233-4

30. The NHS Information Centre Lifestyles Statistics. Statistics on drug misuse : England 2011. London: The Health and Social Care Information Centre; 2011. h. 5–6.

31. Centers for Disease Control and Prevention. Trends in the prevalence of tobacco , alcohol, and illegal drug use on school property national YRBS : 1991–2011. Atlanta; 2011.

32. Epps RP, Manley MW, Glynn TJ. Tobacco use among adolescents : strategies for prevention. Pediatr Clin North Am. 1995;42:389–402. https://doi.org/10.1016/S0031-3955(16)38953-2

33. Merril JC, Kleber HD, Shwartz M, Liu H, Lewis SR. Cigarettes, alcohol, marijuana, other risk behaviors, and American youth. Drug Alcohol Depend. 1999;56(3):205–212. https://doi.org/10.1016/s0376-8716(99)00034-4

34. Republik Indonesia. Peraturan Pemerintah Republik Indonesia No. 109 Tahun 2012 tentang Pengamanan Bahan yang Mengandung Zat Adiktif berupa Produk Tembakau Bagi Kesehatan. Jakarta: Biro Peraturan Perundang-undangan Sekretariat Kabinet Republik Indonesia; 2012.

35. Centers for Disease Control and Prevention. Trends in the prevalence of tobacco, alcohol, and illegal drug use on school property national YRBS : 1991-2011. Atlanta; 2011.

36. Luna JM. Maldives global school-based student health survey. Male: World Health Organization; 2009. h. 33–4.

37. Republik Indonesia. Peraturan Menteri Perdagangan Republik Indonesia No. 43/M-DAG/PER/9/2009 Tahun 2009 tentang Pengadaan, Peredaran, Penjualan, Pengawasan, dan Pengendalian Minuman Beralkohol. Jakarta: Kementrian Perdagangan Republik Indonesia; 2009.

38. Pengpid S, Peltzer K. Prevalence and psychosocial correlates of illicit drug use among school-going adolescents in Thailand. J Soc Sci. 2013;34(3):269–275. http://dx.doi.org/10.1080/09718923.2013.11893138

39. Bryan AD, Schmiege SJ, Magnan RE. Marijuana use and risky sexual behavior among high-risk adolescents: trajectories, risk factors, and event-level relationships. Dev Psychol. 2012;48(5):1429‑1442. https://doi.org/10.1037/a0027547

40. Gorzalka BB, Hill MN, Chang SC. Male‑female differences in the effects of cannabinoids on sexual behavior and gonadal hormone function. Horm Behav. 2010;58(1):91‑99. https://doi.org/10.1016/j.yhbeh.2009.08.009

41. Wongtongkam N, Ward PR, Day A, Winefield AH. The influence of protective and risk factors in individual, peer and school domains on Thai adolescents' alcohol and illicit drug use: a survey. Addict Behav. 2014;39(1):1447‑51. https://doi.org/10.1016/j.addbeh.2014.05.026

42. Nazarzadeh M, Bidel Z, Carson K V. The association between tramadol hydrochloride misuse and other substances use in an adolescent population: phase I of a prospective survey. Addict Behav 2014;39(1):333‑7. https://doi.org/10.1016/j.addbeh.2013.09.013

43. Zabihi E, Hoseinzaadeh A, Emami M, Mardani M, Mahmoud B, Akbar MA. Potential for tramadol abuse by patients visiting pharmacies in northern Iran. Subst Abuse. 2011;5:11‑5. http://dx.doi.org/10.4137/SART.S6174

44. Bryner JK, Wang UK, Hui JW, Bedodo M, Macdougall C, Anderson IB. Dextromethorphan abuse in adolescence. Arch Pediatr Adolesc Med. 2008;160(12):1217‑1222. https://doi.org/10.1001/archpedi.160.12.1217

45. Badan Pengawas Obat dan Makanan Republik Indonesia (Badan POM RI). Keputusan Kepala Badan Pengawas Obat dan Makanan Republik Indonesia No HK.04.1.35.07.13.3855 tahun 2013 tentang Perubahan Atas Keputusan Kepala Badan Pengawas Obat yang Mengandung Dekstrometorfan Sediaan Tunggal. Jakarta: Badan Pengawas Obat dan Makanan Republik Indonesia; 2013.

46. Embry D, Hankins M, Biglan A, Boles S. Behavioral and social correlates of methamphetamine use in a population-based sample of early and later adolescents. Addict Behav. 2009;34(4):343‑351. https://doi.org/10.1016/j.addbeh.2008.11.019

47. Springer AE, Peters RJ, Shegog R, White DL, Kelder SH. Methamphetamine use and sexual risk behaviors in U.S. high school students: findings from a national risk behavior survey. Prev Sci. 2007;8(2):103‑113. https://doi.org/10.1007/s11121-007-0065-6

48. The National Center on Addiction and Substance Abuse at Columbia University. Adolescent substance use: america's #1 public health problem. New York: CASA Columbia; 2011.

49. Ljubotina D, Galić J, Jukić V. Prevalence and risk factors of substance use among urban adolescents: questionnaire study. Croat Med J. 2004;45:88‑98. ISBN 0353-9504

50. Swadi H. Individual risk factors for adolescent substance use. Drug Alcohol Depend. 19991;55:209-24. https://doi.org/10.1016/s0376-8716(99)00017-4

51. Zimić JI, Jukić V. Familial risk factors favoring drug addiction onset. J Psychoactive Drugs. 2012;44:173‑85. https://doi.org/10.1080/02791072.2012.685408

52. Kakleas K, Kandyla B, Karayianni C, Karavanaki K. Psychosocial problems in adolescents with type 1 diabetes mellitus. Diabetes Metab. 2009;35(5):339‑350. https://doi.org/10.1016/j.diabet.2009.05.002

53. Malatestinić D, Mićović V, Kendel G, Baricev-Novaković Z. Assessment of psychological and social factors in adolescents risk behavior: questionnaire study. Croat Med J. 2005;46:81‑7. ISBN 0353-9504

54. Sookung P, Kim HS, Kim H, Sung K. Exploration of the prevalence and correlates of substance use among sheltered adolsecents in South Korea. Adolescence. 2007; 42:603‑16. ISBN 0001-8449 PMID: 18047242

55. Eccles JS, Barber BL. Student council, volunteering, basketball, or marching band: what kind of extracurricular involvement matters? J Adolesc Res. 1999; 14:10‑43. https://doi.org/10.1177/0743558499141003

56. Fredricks JA., Eccles JS. Participation in extracurricular activities in the middle school years: are there developmental benefits for African American and European American youth? J Youth Adolesc. 2008;37:1029‑43. http://dx.doi.org/10.1007/s10964-008-9309-4

Relationship Between Breast Milk Feeding and COVID-19 Incidence in Children Aged 0-2 Years at Siloam Hospital Kelapa Dua During The Pandemic

Jovanicha P. Setiawan[1], Dwi S. Rivami[1]

[1] *Faculty of Medicine, University of Pelita Harapan, Jendral Sudirman Boulevard, Lippo Karawaci, Tangerang, Indonesia 15811*

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Correspondance: Jovanicha Putri Setiawan.
E-mail: jovanichasetiawan@gmail.com
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Abstract

Background: The COVID-19 pandemic has claimed more than 6 million lives worldwide, and children are not spared from its danger. Breast milk is known to protect babies from various kinds of infections. Until now there are few data regarding the relationship between breastfeeding and the incidence of COVID-19 in children aged 0-2 years in Indonesia. This study aims to further examine the relationship between breastfeeding and the incidence of COVID-19 in children aged 0-2 years. Siloam Hospitals Kelapa Dua (SHKD) was chosen as a location because it was one of the referral hospitals for treating COVID-19 for pediatric patients in Tangerang that can be accessed by the researcher.

Methods: This study was conducted using a cross-sectional study method on a sample of children aged 0-2 years from the medical record database of Siloam Hospitals Kelapa Dua for the period 2020 to 2022.

Result: Upon calculation, it was found that the p-value is 0,154 (p>0,05). From 61 sample, 37,7% of the samples were breastfed and 44,3% was COVID-19 positive.

Conclusions: No significant relationship was found between breastfeeding and COVID-19 infection among children aged 0-2 years old in SHKD.

Introduction

Breast milk is considered the best natural food for newborns as it satisfies the energy and nutritional needs of children up to 6 months of age.[1] It contains protective factors that shield children from infections like diarrhea, ear inflammation, cough, and cold.[2] The World Health Organization (WHO) recommends exclusive breastfeeding for the first six months, followed by continued breastfeeding alongside complementary foods until the child reaches two years of age.[3]

The Coronavirus Disease 2019 (COVID-19) pandemic has caused about 158,000 deaths in Indonesia as of October 2022. Children are not exempt from COVID-19 infection and are at risk of complications like mild to severe pneumonia.[4] COVID-19 in children typically presents with mild symptoms such as cough, fatigue, nasal congestion, and fever, along with digestive symptoms like nausea, vomiting, and diarrhea. However, severe complications like Acute Respiratory Distress Syndrome (ARSD) and septic shock can still occur.[5]

This study aims to explore the relationship between breastfeeding and the incidence of COVID-19 in children aged 0-2 years. Given the previous studies by Pérez et al. (2021) and Nurhidayah et al. (2021) have shown conflicting results, this study aims to further investigate the relationship between breastfeeding and COVID-19, [4,6] This age group is chosen because they are still recommended by WHO to receive breast milk. SHKD Hospital in Tangerang was chosen as the sample collection site since it is one of the hospitals that treats COVID-19, including pediatric patients from many regions of Indonesia as well.

Material And Methods

This research was carried out at Siloam Hospitals Kelapa Dua from January to March 2023, adopted a non-paired categorical comparative analytic study with a cross-sectional design, focusing on secondary data from medical records between March 2020 and December 2022. The study targeted infants and children aged 0-2 years receiving breast milk, specifically from Siloam Hospitals Kelapa Dua, chosen through purposive sampling based on inclusion and exclusion criteria. The initial sample size calculated was 45, which was increased by 10% to 50 to account for variability.

The inclusion criteria were children in the specified age group treated at SHKD with documented COVID-19 status confirmed by PCR or antigen swab tests, and having information about breastfeeding in their records. Exclusion criteria encompassed factors like low birth weight, a history of premature birth, and incomplete immunization history. The data were transferred to Microsoft Excel (2021) and processed using SPSS software for analysis.

Ethical approval for the study was obtained from the Ethics Committee of the Faculty of Medicine at Universitas Pelita Harapan. The necessary permissions for using the medical records were granted by the hospital, ensuring compliance with ethical standards in the research process.

Result

The highest percentage of children receiving breast milk were those aged 0 years, accounting for 60.9%. In terms of gender, the majority of breastfed children were female, with 65.2% of all female samples consuming breast milk. Geographically, the majority of the samples originated from the Banten province, comprising 47.8%.

Table 1. The Profile of Breastfeeding in Children Aged 0-2 Years at SHKD

Variabel		Breastfed (+)	Breastfed (-)	Total
Age	0	14	24	38
	1	7	8	15
	2	2	6	8
Sex	Male	8	23	31
	Female	15	15	30
Provence	Banten	11	16	27
	Jakarta	2	4	6
	West Java	2	4	6
	Central Java	1	0	1
	North Sumatra	1	0	1
	No Data	6	14	20
Total		23	38	61

The data also indicated that the majority of COVID-19 positive cases were among children aged 0 years, representing 55.6%. Concerning gender, the majority of COVID-19 positive cases were male, accounting for 59.3%, with most samples coming from Banten, making up 40.7%.

Table 2. The Profile of COVID-19 in Children Aged 0-2 Years at SHKD

Variabel		COVID-19 (+)	COVID-19 (-)	Total
Age	0	15	23	38
	1	9	6	15
	2	3	5	8
Sex	Male	16	15	31
	Female	11	19	30
Provence	Banten	11	16	27
	Jakarta	3	3	6
	West Java	3	3	6
	Central Java	0	1	1
	North Sumatra	0	1	1
	No Data	10	10	20
Total		27	34	61

In this study, the chi-square test was utilized to analyze the relationship between breastfeeding and the occurrence of COVID-19 in children aged 0-2 years at Siloam Hospitals Kelapa Dua. From the analysis, the p-value obtained was 0.154 (>0.05), indicating no significant relationship between breastfeeding and the occurrence of COVID-19 at Siloam Hospitals Kelapa Dua.

Table 3. The Relationship Between Breastfeeding and the Incidence of COVID-19

	COVID-19 (+)	COVID-19 (-)	Total	P Value	OR
Not Breast-fed	20	18	38	0,154	0,394 (0,132-1,174)
Breast-fed	7	16	23		
Total	27	34	61		

Discussion

The study on breastfeeding in Indonesia reveals that breastfeeding rates for children aged 0-2 years are significantly below WHO recommendations, with 62.29% of the sample at Siloam Hospitals Kelapa Dua not breastfed at the time of their medical records. This aligns with Suja et al. (2022)'s findings of inadequate breastfeeding practices in Indonesia, even in urban areas, due to factors like uneven breastfeeding education, maternal employment, and education levels.[10]

Regarding gender, male children are less likely to be breastfed compared to females, a trend also noted by Shafer et al. (2017), though the reasons behind this remain unclear.[11] Geographically, breastfeeding rates are lower across all regions in Indonesia, consistent with findings by Suja et al. (2022), pointing towards similar influencing factors.[10]

In terms of COVID-19 incidence, infants aged 0 years are most affected, likely due to their inexperienced immune systems. Boys were found to be more susceptible to COVID-19, aligning with Purwati et al. (2022)'s research, suggesting biological factors in female children offer more resistance to viral infections.[12]

The study also observed a higher prevalence of COVID-19 in non-breastfed children aged 0-2 years. Previous studies have shown conflicting results on this relationship. While Pérez et al. (2021) in Spain found that breast milk containing antibodies against SARS-CoV-2 can benefit children, another study by Nurhidayah et al. (2021) in Central Java raised concerns about the vertical transmission of COVID-19 from mother to child through breastfeeding.[4,6] This study however found a result more aligned with Pérez et al. (2021)'s study, where there is a possibility of protectivity between breastfeeding and COVID-19 incidence, instead of the possibility of increasing the incidence as Nurhidayah et al's theory might suggest. Pérez et al (2021), Pace et al (2021), and Dong et al (2020) suggests maternal immune cells are transferred to the child through breast milk, offering protection against various infectious diseases, including acute respiratory infections. [6–8]

However, this study is found contrasting with Verd et al. (2021)'s findings that indicated a significant correlation between breastfeeding and reduced COVID-19 incidence, in this study the difference is not found to be significant.[13] Although, differences in sample size and data collection methods might explain this difference of outcome.

The study's strengths lie in its exclusion of confounding factors and its pioneering nature in the Indonesian context, but it faces limitations due to varied and incomplete medical record data.

Conclusion

Based on the research conducted regarding the relationship between breastfeeding and the incidence of COVID-19 in children aged 0-2 at Siloam Hospitals Kelapa Dua, it was found that the rate of breastfeeding among children aged 0-2 years at Siloam Hospitals Kelapa Dua is 37.7%. Notably, a large proportion of these breastfed children are infants aged 0 years (60.9%) and the majority are female (65.2%). Regarding the incidence of COVID-19, it was observed that the virus more commonly infected children at the age of 0 years (55.6%), with a higher incidence in male children (59.3%) compared to females. The majority of these pediatric COVID-19 cases were from the Banten region, accounting for 40.7%. Interestingly, the study concluded that there is no significant correlation between breastfeeding and the occurrence of COVID-19 in children within this age group at Siloam Hospitals Kelapa Dua.

This study holds significant relevance, particularly in understanding public health dynamics during the COVID-19 pandemic. It offers crucial insights into breastfeeding rates and practices among infants and toddlers, enhancing our understanding of maternal and child health in this demographic. Importantly, the research reveals that there is no significant link between breastfeeding and the incidence of COVID-19 in children aged 0-2, providing vital information for healthcare decisions. This finding is instrumental in guiding healthcare policies and parental choices, reassuring that breastfeeding, with its well-documented health benefits, does not elevate the risk of COVID-19 in young children, thus aiding in developing comprehensive pediatric care strategies during the pandemic.

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References

1. Bhesh Bhandari, Nidhi Bansal, Zhang M, Schuck P. Handbook of Food Powders: Processes and Properties. Woodhead Publishing Limited; 2013. 437–464. http://dx.doi.org/10.1533/9780857098672.3.437
2. Palmeira P, Carneiro-Sampaio M. Immunology of breast milk. Rev Assoc Med Bras (1992). 2016; 62(6):584–93. https://doi.org/10.1590/1806-9282.62.06.584

3. Infeksi Emerging Kementerian Kesehatan RI. Available from: https://infeksiemerging.kemkes.go.id/dashboard/covid-19

4. Nurhidayah I, Tamara M, Setyorini D, Keperawatan F, Padjadjaran U. Karakteristik Covid-19 Pada Anak. Jurnal Ilmu Keperawatan. 2021; 4(1). http://dx.doi.org/10.26594/jika.4.1.2021.7-18

5. Qiu H, Wu J, Hong L, Luo Y, Song Q, Chen D. Clinical and epidemiological features of 36 children with coronavirus disease 2019 (COVID-19) in Zhejiang, China: an observational cohort study. Lancet Infect Dis. 2020; 20(6):689–96. https://doi.org/10.1016/S1473-3099(20)30198-5

6. Pérez-bermejo M, Peris-ochando B, Murillo-llorente MT. Covid-19: Relationship and impact on breastfeeding—a systematic review. Nutrients. 2021; 13(9). https://doi.org/10.3390/nu13092972

7. Pace RM, Williams JE, Järvinen KM, Belfort MB, Pace CDW, Lackey KA, et al. Characterization of SARS-CoV-2 RNA, Antibodies, and Neutralizing Capacity in Milk Produced by Women with COVID-19. mBio. 2021; 12(1):1–11. https://doi.org/10.1128/mbio.03192-20

8. Dong Y, Chi X, Hai H, Sun L, Zhang M, Xie WF, et al. Antibodies in the breast milk of a maternal woman with COVID-19. Emerg Microbes Infect. 2020; 9(1):1467–9. https://doi.org/10.1080%2F22221751.2020.1780952

9. Vassilopoulou E, Feketea G, Koumbi L, Mesiari C, Berghea EC, Konstantinou GN. Breastfeeding and COVID-19: From Nutrition to Immunity. Front Immunol. 2021; 12. https://doi.org/10.3389%2Ffimmu.2021.661806

10. Suja MDD, Budiarti I. Gambaran Pemberian Air Susu Ibu (ASI) Eksklusif pada Wanita 15-49 Tahun di Perkotaan Indonesia. BIOGRAPH-I: Journal of Biostatistics and Demographic Dynamic. 2022; 2(1):48. https://doi.org/10.19184/biograph-i.v2i1.30977

11. Shafer EF, Hawkins SS. The Impact of Sex of Child on Breastfeeding in the United States. Matern Child Health J. 2017; 21(11):2114–2121. https://doi.org/10.1007/s10995-017-2326-8

12. Purwati NH, Noprida D, Agustia W, Imroatun T, Sarini S, Sahariah S, et al. Impact of Age and Gender on the Incidence of COVID-19 in Children at Pasar Rebo Hospital, Jakarta. KnE Life Sciences. 2022: 460-466. https://dx.doi.org/10.18502/kls.v7i2.10341

13. Verd S, Ramakers J, Vinuela I, Martin-Delgado MI, Prohens A, Díez R. Does breastfeeding protect children from COVID-19? An observational study from pediatric services in Majorca, Spain. Int Breastfeed J. 2021; 16(1):83-88. https://doi.org/10.1186/s13006-021-00430-z

Anemia and Erythropoietin Use Among Hemodialysis Chronic Kidney Disease Patients at Rumah Sakit Umum Siloam

Margaret Merlyn Tjiang[1], Elliscia Caroline[2], Jeremia Immanuel Siregar[1]

[1] Department of Internal Medicine, Faculty of Medicine, University of Pelita Harapan, Jendral Sudirman Boulevard, Lippo Karawaci, Tangerang, Indonesia 15811
[2] Faculty of Medicine, University of Pelita Harapan, Jendral Sudirman Boulevard, Lippo Karawaci, Tangerang, Indonesia 15811

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Correspondance : Margaret Merlyn Tjiang
E-mail : margaret.tjiang@uph.edu
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Abstract

Background: Chronic kidney disease (CKD) affects an estimated 8-16% of the population and is increasing in prevalence. Anemia, a common and significant complication of CKD, is primarily caused by reduced erythropoietin production, which is essential for red blood cell production. Erythropoietin, a kidney-produced hormone, stimulates bone marrow to produce red blood cells. This study examines trends in the use of erythropoiesis-stimulating agents (ESAs) and the management of anemia in dialysis CKD patients before and after the implementation of ESA reimbursemen.

Methods: This cohort study was conducted at Rumah Sakit Umum Siloam, Tangerang, Indonesia, from February to July 2017. Patients who received blood transfusions or iron supplements during the study were excluded. Data collected included age, gender, dry weight, history of diabetes mellitus, hypertension, hemodialysis adequacy, and nutritional status. Statistical analysis with a 95% confidence interval (CI) was used to assess the association between hemoglobin levels (Hb) and erythropoietin use.

Results: Sixty patients completed the study. The proportion of anemic patients (Hb <10 g/dL) increased from 22 (36.7%) to 28 (46.7%) after erythropoietin administration. A mean dose of 6000 IU/week (CI: 4679 to 7321 IU/week) was effective in achieving target hemoglobin levels, while a dose of 4131 IU/week (CI: 3479 to 4782 IU/week) was sufficient to maintain them. Additionally, a dosage of 103.31 IU/kg/week increased hemoglobin by 1 g/dL in anemic patients.

Conclusions: Erythropoietin use should be optimized given the increasing prevalence of anemia. A dosage of 103.31 IU/kg/week is recommended to achieve target hemoglobin levels, while 4131 IU/week is suggested for maintaining hemoglobin within the target range.

Introduction

Chronic kidney disease (CKD) defined as a persistent abnormality of kidney structure or function (glomerular filtration rate <60ml/min/1.73m2 or albuminuria ≥30mg per 24 hours) for more than 3 months. In the worldwide, CKD is estimated to be 8-16% and continues to grow.[1] Increase CKD remains the leading cause of morbidity and mortality especially in the elderly population. Presence of CKD increase risk of cerebrovascular disease (CVD), dyslipidemia, mineral bone disorders and anemia.[2,3]

Anemia is the most common and clinically significant complication in patients with CKD.[4] Patients in early stages of chronic kidney disease may develop

anemia and tends to worsen as progresses. Anemia is developed when the kidney loses its ability to produce the erythropoietin essential to the production of hemoglobin.[5,6] Anemia in CKD can be driven by multifactor, reduced erythropoietin production to support erythropoiesis is the primary causes. There is also the result of nutritional deficiency (iron, folic acid, and vitamin B12), diabetes mellitus, hematological disorder, advanced CKD stages, and history of hemodialysis.[7] Estimated iron losses in hemodialysis CKD patients is 1-3 gram per year, due to chronic bleeding from uremia-associated platelet dysfunction, frequent phlebotomy, and blood trappin in dialysis apparatus.[8] Anemia in CKD patients has an adverse clinical outcomes include: angina, cardiorenal anemia syndrome, cognitive impairment, left ventricle hypertrophy, higher healthcare, reduced quality of life, increased hospital admission rate, worsening CKD, accelerated progression of heart disease, and increase mortality.[9]

Erythropoietin (EPO) is a hormone produced by the kidneys that responsible to stimulate bone marrow in red blood cell production. Decreased erythropoietin in CKD linked with downregulation of hypoxia inducible factor (HIF), transcription factor for erythropoietin expression.[5] Then bone marrow does not provide enough blood cells for the body and anemia occurred.[3] The Third National Health and Nutrition Examination Survey in the USA has reported 46% men with advanced CKD had a hemoglobin (Hb) less than 12 g/dL and 21% of women had less than 11 g/dL. Intravenous injection or subcutaneous of EPO is strongly a recommended treatments because the remarkable ability to correct anemia and reduce the need to blood transfusion.[6]

Erythropoietin stimulating agents and adjuvant iron therapy are the main therapy for anemia associated with CKD. However, ESA is expensive and not limited to patients on renal replacement therapy but extended to non-dialysis patients. Recent studies have reported 20%-30% of patients received ESAs before dialysis. About 20% of dialytic patients had a Hb concentration less than 11 g/dL, whereas more than 70% of CKD patients had a Hb concentration less than 11 g/dL at the initiation of the dialysis. ESA prescription shows a significantly higher Hb concentration in patient with non-dialytic and dialytic chronic kidney disease.[4,11]

In recent decades, the treatment of anemia in patients with end-stage renal disease has aroused considerable attention, and there have been many clinical trials on the appropriate target Hb concentrations. These clinical studies raised serious concerns about intensive treatment of anemia using ESAs in patients with CKD.[12] However, little is known about the trends in the treatment of anemia with ESAs in patients with CKD that require dialysis in Indonesia. In this study, we tried to elucidate the trend of the use of ESA and anemia in dialysis CKD patients before and after the reimbursement of ESAs. This study hypothesis was ESAs usage as a maintenance in hemodialysis CKD patients especially end stage renal disease (ESRD) shown a significant increase of Hb concentration

Material And Methods

Study population

This was a cohort study at Rumah Sakit Umum Siloam, Tangerang, Indonesia. Consecutive sampling from the hemodialysis center. The study was conducted 6 months from February until July 2017. We included adult (age ≥18 yr),

dialytic CKD patients proven by laboratory and ultrasound examination that have a routine hemodialysis for at least 6 months with an estimated glomerular filtration rate less than 30mL/min/1.73m2. Patients were excluded if the Hb concentration <8g/dL at any point of enrollment, because according to hospital protocol the patients will be given blood transfusion. Patients with Hb <8g/dL at any point of the study will be excluded, because according to hospital protocol the patients will be given blood transfusion or iron supplements. Patients with other causes of anemia including active malignancy, chronic inflammatory disorder, systemic infections and active bleeding were excluded. The initial dose of ESA was administered according to manufacturer's recommendation and subsequent dosage titrated according to Hb levels so as not to exceed 12 g/dL. The following information from each patient was collected: age, gender, history of hypertension, history of diabetes mellitus, dry weight, nutritional status, and haemodialysis adequacy. Control studies was using patient CKD on hemodialysis with mild anemia with Hb concentration >10 g/dL.

Study design

We investigated baseline demographic and clinical data such as age, gender, presence of diabetes mellitus (DM), hypertension and nutritional status at the time of enrollment. Laboratory data such as Hb values were obtained at the commencement of the study, and 6 months during the follow-up period. For ESAs, we defined the doses and number of days of each prescription. Hb concentration of the patients is being evaluated and EPO administration based on Hb and dry weight of the patients.

Outcomes

This study primary outcomes were patient Hb target attainment and laboratory values. The study outcomes were Hb <10 g/dL and >12 g/dL in follow up and the Hb range 10–12 g/dL was considered the reference category. The secondary outcomes were EPO dosage for in patients anemia to reach target of the HB and the dosage for maintenance. cohort included patients from the first cohort who had transitioned to dialysis.

Statistical analysis

Using multivariable Poisson regression models with modified variances to estimate both unadjusted and adjusted prevalence ratios, along with their corresponding 95% confidence intervals (CIs). In the multivariable models, adjustments were made for age, sex, diabetes, hypertension, cerebrovascular disease, hemoglobin levels, and ESA dosage. Patient characteristics were described using means and standard deviations for numeric variables, and frequencies and percentages for categorical variables, analyzed over 6-month periods. Multivariable Pearson correlation coefficients were applied for numeric variables, while the Chi-square test was used for categorical variables. Statistical results were reported with 95% confidence intervals (CIs) and p-values, with statistical significance defined at the 0.05 level. All descriptive and multivariate analyses were conducted using SAS software, version 9.1 (SAS Institute Inc., Cary, NC, USA).

Ethics committee

The study protocol was approved by the institutional review board (IRB) of Rumah Sakit Umum Siloam (approval number: 2017-004-01). The IRB waived the requirement for documentation of written informed consent from patients to follow up as this study was conducted by cohord. All patients provided informed consent

Result

Tabel 1 Showed that the total of 60 CKD stage V patients, with the mean age was 51.4 ± 13.3 years old. Of the 60 patients of CKD, 42 were males which are 70% and 18 were females. About half of the patients had hypertension (55%) and few had diabetes mellitus (13.3%). The mean dry weight 56.30 ± 10.59 kg and majority had good nutritional status (90%). Most patients had adequate haemodialysis (81.7%).

Table 1. Demographic of The Sample

Variables	Total (=60)	%
Age (years ± SD)	81.4 ±13.3	
Gender		
Males	42	70
Females	18	30
Other associated disease		
Hypertension	33	55
Diabetes	8	13.3
Others	19	31.7
Dry weight (kg±SD)	56.30 ± 10.59	
Nutritional status		
Good	54	90
Bad	6	10
Hemodialysis		
Adequate	49	81.7
Inadequate	11	18.3
Hemoglobin (g/dL; mean ±SD)	10.37 ± 1.12 g/dL	

The mean epo administered was 6150 ± 2279 IU/week or 113.26 ± 46.47 IU/kg/week. At the start of the study, the mean Hb was 10.37 ± 1.12 g/dL and 36.7% of the patients were anemic (Hb <10 g/dL). Throughout the study, the mean Hb was decreased slightly to 10.22 ± 0.89 g/dL and fewer patients (53.3%) were within target value (Hb ≥10 g/dL).

Table 2. The Distribution of Patients Based on Hb

Base Hb	Hb on epo	N	%
<10 g/dL	<10 g/dL	16	26.67
	≥10 g/dL	6	10.00
≥10 g/dL	<10 g/dL	12	20.00
	≥10 g/dL	26	43.33

There is evidence of negative linear association between Hb and administration of epo (r=-0.94, p<0.001).

In anemic patients, an increase in 1000 IU/week of epo decreased Hb on average by 0.36 g/dL (95% CI 0.30 to 0.43, p<0.001). Increase in 100 IU/kg/week of epo decreased Hb on average by 1.40 g/dL (95% CI 0.85 to 2.0, p<0.001). Regardless, data suggested that 103.31 IU/kg/week of epo made up for each unit of Hb deficit.

In non-anemic patients, increase in 1000 IU/week of epo decreased Hb on average by 0.41 g/dL (95% CI 0.35 to 0.46, p<0.001). Increase in 100 IU/kg/week of epo decreased Hb on average by 1.55 g/dL (95% CI 1.20 to 1.90, p<0.001). The mean epo administered for each Hb group was shown in Table 3.

Age, gender, hypertension, diabetes mellitus, dry weight, nutritional status, and haemodialysis adequacy were not correlated with Hb.

Table 3. The Mean Epo Administered in Each Hb Group

Base Hb	Hb on Epo	N	Epo (IU/week)			P value	Epo per weight (IU/kg/week)			P value
			Mean	95% CI			Mean	95% CI		
<10 g/dL	<10 g/dL	16	8700	8467	8933	p<0.001	153.31	142.17	164.45	p<0.001
	≥10 g/dL	6	6000	4679	7321		106.12	81.31	130.93	
≥10 g/dL	<10 g/dL	12	7200	6686	7714		146.01	123.37	168.66	
	≥10 g/dL	26	4131	3479	4782		75.14	61.75	88.54	

Discussion

Some studies have evaluated Hb predictors in cross-sectional designs. Early studies in Korean by Kim et al (2016) have addressed the value of treating anaemia during the transition to dialysis. The reimbursement of ESAs is associated with the increment of the prescription rate of ESAs and Hb concentration in non-dialytic CKD population.[13]

According to National Health and Nutrition Examination Survey (NHANES), a higher prevalence of anemia on CKD observed in US nursing home residents aged>64 with CKD stages 3-5. By the age 40, kidney filtration began to fall approximately 1% per year. It would lead to anemia by decreasing the production of hemoglobin. The previous study showed that there were many cases of anemia on CKD among the 50 – 59 age group where the prevalence of a rGFR of <60 ml/min/1.73 m2 was higher in the elderly compared to the young one.[14]

On the Okinawa General Health Maintenance Association (OGHMA) data, the prevalence of anemia increased as CKD progressed below an eGFR of 60 ml/min per 1.73 m^2 in both genders. The association of lower kidney function with anemia was found to be more prevalent from approximately 50 ml/min per 1.73 m^2. A previous study presented that among individuals with CKD, at all levels of GFR, anemia portended a poor prognosis and was associated with increased mortality compared to those individuals with preserved hemoglobin. The progression of anemia as the CKD stages increased can be the leading cause of death.[15]

Study that carried out by National Institute of Health (NIH), the increased CVD associated with ESRD estimated the anemia of CKD increases morbidity and mortality from cardiovascular complications (angina, left ventricular hypertrophy (LVH) and worsening heart failure), which may lead to further deterioration of renal function and the establishment of a vicious cycle termed the “cardiorenal anemia syndrome”. The presence of LVH is associated with decreased survival of patients on dialysis.[16]

In our analysis of patients an estimated 55% patients with CKD had a hypertension and 13.3% had diabetes mellitus. The mean of dry weight from patient weighted after dialysis were 56.30 ± 10.59 kg. At the start of the study 36.7% patient were anemic with Hb concentration <10g/dL and the mean of total 60 patients were 10.37 ± 1.12 g/dL.

We studied the use of Erythropoietin use as treatment of anemia in CKD patients on dialysis We found that the use of erythropoietin contributed to significantly higher Hb concentration in CKD patients on dialysis. The mean Hb concentration after being given erythropoietin, dosage of 103.31 IU/kg/week can be used in anemic patients to achieve. Erythropoietin use in patients with Hb≥ 10g/dL for maintenance has been given 4131 IU/week.

These findings are in contrast with increase Hb concentration trends in dialysis patients. Frankenfield et al, management of anemia in hemodialysis patients with end stage renal disease show the effective anemia management with the p value <0.001.[17] In this studies age, gender, hypertension, diabetes mellitus, dry weight, nutritional status, and haemodialysis adequacy were not correlated with Hb concentration. In anemic patients using EPO 1000 IU/week decrease Hb by 0.36 g/dL, increase in 100 IU/kg/week decreased Hb by 1.4g/dL. Control studies in non anemic patients

shows decrease Hb on average by 0.41g/dL and increased 100 IU/kg/week decreased Hb by 1.55 g/dL. The difference of the targeted EPO dosage to increase Hb to achieve target range were 103.31 IU/kg/week. EPO dosage to maintain Hb within target value were 4131 IU/week.

Our study has several limitations. Considering a single center-based study and the main population is rural, the result cannot be extrapolated generally to all of the population. Our study enrolled a small number of patients compared to other studies. Underlying diseases were nor included in the analysis. We suggest for the next studies to center based on more population and using more number of patients. Comorbids of the patients can be analysis to excluded other risk factor that can causes anemic.

Conclusion

Anemia is the most common complication of CKD because of reduce EPO and less production of red blood cell. Erythropoietin use could be improved considering increase prevalence of anemic patients.This study hypothesis was ESAs usage as a maintenance in hemodialysis CKD patients especially end stage renal disease (ESRD) shown an decrease of Hb concentration when EPO dosage increased in anemic patients and control studies. A dosage of 103.31 IU/kg/week might be used in anemic patients to achieve target range. A dosage of 4131 IU/week might be used to maintain Hb within target value in patients with Hb>10g/dL.

References

1. Chen TK, Knicely DH, Grams ME. Chronic Kidney Disease Diagnosis and Management: A Review. JAMA. 2019; 322(13):1294-1304. https://doi.org/10.1001/jama.2019.14745
2. Peralta CA, Vittinghoff E, Bansal N, et al. Trajectories of kidney function decline in young black and white adults with preserved GFR: results from the Coronary Artery Risk Development in Young Adults (CARDIA) study. *Am J Kidney Dis*. 2013;62(2):261–266. https://doi.org/10.1053/j.ajkd.2013.01.012
3. Rubahshini G, Surudarma W, Wihandani DM, Sutadarma WG. Prevalence of Anemia on Chronic Kidney Disease and Its Influenced Factors in Sanglah General Hospital 2015-2017, Bali. *Intisari Sains Medis*, 2020: 11(1): 248. https://doi.org/10.15562/ism.v11i1.247
4. Vecchio LD, Locatelli F. *Anemia in chronic kidney disease patients: treatment recommendations and emerging therapies. Expert Review of Hematology*. 2014 7(4), 495–506. https://doi.org/10.1586/17474086.2014.941349
5. Kim SM, Kim KM, Kwon SK, Kim HY. *Erythropoiesis-stimulating Agents and Anemia in Patients with Non-dialytic Chronic Kidney Disease. Journal of Korean Medical Science.* 2016. 31(1), 55–60. https://doi.org/10.3346%2Fjkms.2016.31.1.55
6. Palaka E, Grandy S, Haalen HV, McEwan P, Darlington O. The Impact of CKD Anaemia on Patients: Incidence, Risk Factors, and Clinical Outcomes—A Systematic Literature Review. *International Journal of Nephrology*. 2020; 2020(7692376): 21. https://doi.org/10.1155/2020/7692376

7. Shiferaw WS, Akalu TY, Aynalem YA. Risk Factors for Anemia in Patients with Chronic Renal Failure: A Systematic Review and Meta-Analysis. Ethiop J Health Sci. 2020 Sep;30(5):829-842. https://doi.org/10.4314%2Fejhs.v30i5.23

8. Babitt JL, Lin HY. Mechanisms of anemia in CKD. J Am Soc Nephrol. 2012 Oct;23(10):1631-4. https://doi.org/10.1681%2FASN.2011111078

9. Adera H, Hailu W, Adane A, Tadesse A. Prevalence Of Anemia And Its Associated Factors Among Chronic Kidney Disease Patients At University Of Gondar Hospital, Northwest Ethiopia: A Hospital-Based Cross Sectional Study. *Int J Nephrol Renovasc Dis*. 2019;12:219-228. https://doi.org/10.2147/IJNRD.S216010

10. Stauffer ME, Fan T. Prevalence of anemia in chronic kidney disease in the United States. PLoS One. 2014 Jan 2;9(1):e84943. https://doi.org/10.1371/journal.pone.0084943

11. Portolés J, Martín L, Broseta JJ, Cases A. Anemia in Chronic Kidney Disease: From Pathophysiology and Current Treatments, to Future Agents. Front Med (Lausanne). 2021 Mar 26;8:642296. https://doi.org/10.3389%2Ffmed.2021.642296

12. Valderrabano F, Horl WH, Macdougall IC, Rossert J, Rutkowski B, Wauters JP. PRE-dialysis survey on anaemia management. Nephrol Dial Transplant 2003; 18(1): 89-100. https://doi.org/10.1093/ndt/18.1.89

13. Kim, S. M., Kim, K. M., Kwon, S. K., & Kim, H.-Y. *Erythropoiesis-stimulating Agents and Anemia in Patients with Non-dialytic Chronic Kidney Disease. Journal of Korean Medical Science, 2016; 31(1), 55.* https://doi.org/10.3346%2Fjkms.2016.31.1.55

14. Swaraj. S Sunil. G, Poornima. V. Prevalence of anemia and cardiovascular diseases in chronic kidney disease patients: a single tertiary care centre study. . International Journal of Advances in Medicine. 2016; 4(1):247-251. https://doi.org/10.18203/2349-3933.ijam20170120

15. Chang P, Chien L, Lin Y, Wu M, Chiu W, Chiou H. Risk factors of gender for renal progression in patients with early chronic kidney disease. Medicine. 2016; 95(30):e4203. https://doi.org/10.1097/md.0000000000004203

16. Virani S, Khosla A, Levin A. Chronic kidney disease, heart failure, and anemia. Canadian Journal of Cardiology. 2008;24:22B-24B. https://doi.org/10.1016%2Fs0828-282x(08)71026-2

17. Frankenfield, D. L., & Johnson, C. A. *Current management of anemia in adult hemodialysis patients with end-stage renal disease. American Journal of Health-System Pharmacy. 2002;* 59(5), 429–435. https://doi.org/10.1093/ajhp/59.5.429

Prevalence and Risk Factors of Occupational Contact Dermatitis in Healthcare Workers

Muljani Enggalhardjo[1], Alan Dwi Setiawan[2], Putra Niko Laksamana Oceano Christianto[2]

[1] Department of Dermato-Venereology, Faculty of Medicine, University of Pelita Harapan, Jendral Sudirman Boulevard, Lippo Karawaci, Tangerang, Indonesia 15811
[2] Faculty of Medicine, University of Pelita Harapan, Jendral Sudirman Boulevard, Lippo Karawaci, Tangerang, Indonesia 15811

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Correspondance: Muljani Enggalhardjo
E-mail: muljani.enggalhardjo@lecturer.uph.edu
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Abstract

Background: Occupational contact dermatitis (OCD) is prevalent among healthcare workers, especially during the COVID-19 pandemic. Symptoms include dryness, itchiness, and redness, with hands being the most affected. Risk factors include frequent hand washing, increased glove use, allergies, and lack of health and safety training. This review emphasizes the need for targeted prevention strategies and awareness programs.

Methods: We conducted a systematic review using PubMed, focusing on studies involving healthcare workers and OCD. Keywords included "occupational contact dermatitis," "contact dermatitis," "healthcare workers," and "risk factors for OCD." Data were collected using a structured, interviewer-administered questionnaire, including the Nordic Occupational Skin Questionnaire (NOSQ-2002).

Result: The review included 2,706 healthcare workers. Hand dermatitis was the most common, affecting 22% of participants. Key risk factors were a personal history of allergies, frequent hand washing, high glove usage, and insufficient health and safety training.

Conclusions: This review identifies significant risk factors for OCD among healthcare workers, highlighting the need for interventions focused on reducing hand washing frequency, managing glove use, and improving health and safety training.

Introduction

Ninety percent of workplace-related skin illnesses are caused by occupational contact dermatitis (OCD). It has two types: allergic contact dermatitis and irritant contact dermatitis, the latter accounting for 80% of cases. Both types of usually present as eczematous lesions on exposed areas, especially the hands.[1] Occupational contact dermatitis (OCD) can be triggered by allergens or irritants that contact the skin, often originating from the workplace. Hand sanitizers, frequent hand washing, and personal protective equipment (PPE) such as masks, goggles, face shields, hazmat suits, closed shoes, and shoe covers are used to protect healthcare workers from infections. However, PPE use has also been identified as a source of various skin health issues for these workers.[2] Several factors affecting OCD in healthcare workers include physical, chemical, and biological exposures in the workplace. These risks can exacerbate contact dermatitis. Contributing factors include frequent hand washing, prolonged glove use, exposure to chemicals like methacrylate agents and cleaning agents, and microbial exposure such as methicillin-resistant Staphylococcus aureus.

Healthcare workers with a history of psoriasis or eczema are more likely to experience OCD. Women who handle household chores have a higher incidence of OCD. Since healthcare workers are predominantly women, this increases the risk of OCD in the medical workforce.[2] A study in Saudi Arabia estimated the prevalence and investigated the risk factors of occupational contact dermatitis among healthcare workers during the COVID-19 pandemic. The prevalence was found to be 46.4%, with risk factors including female gender, a history of eye allergies, and being in the young age group.[3]

Alluhayyan et al. reported that the most common skin symptom was dryness (92.9%). The majority (76%) of healthcare workers wore latex gloves, which adversely affected the skin. Additionally, females and younger healthcare workers (mean age 26.4 years) were more prone to developing contact dermatitis.[3] In Ethiopia, a study investigated the prevalence (31.5%) and risk factors (hand washing frequency, number of gloves used per day, personal history of allergies, and lack of health and safety training) of occupational contact dermatitis among healthcare workers in Gondar town.[4] Mekonnen et al. reported that hand dermatitis was the most common type, affecting 22% of participants. Risk factors included a personal history of allergies, frequent hand washing, using multiple pairs of gloves per day, and lack of health and safety training.[4]

Contact dermatitis is an inflammation of the skin characterized by spongiosis or intercellular edema of the epidermis, resulting from irritants or external allergens interacting with the skin. It can manifest as: a) allergic contact dermatitis or b) irritant contact dermatitis, depending on the substances involved.

Allergic contact dermatitis is a type IV hypersensitivity reaction, which is cell-mediated or delayed. It occurs when a person becomes sensitized to an allergen and subsequently reacts upon exposure, regardless of the amount. Reactions can range from minor to severe and may develop within days or take months or years. Irritant contact dermatitis results from repeated exposure to mild irritants (e.g., detergents) over a long period or from exposure to strong irritants (e.g., acids, alkalis) that cause immediate skin damage. Only the skin in direct contact with the irritant is affected.[5,6]

PRISMA Chart

Five studies met the screening and inclusion criteria, involving 2,706 healthcare workers with occupational contact dermatitis. After evaluating these studies using the Newcastle-Ottawa Scale (NOS), they were found to be compatible and relevant. All studies demonstrated a significant association between healthcare workers and occupational contact dermatitis.

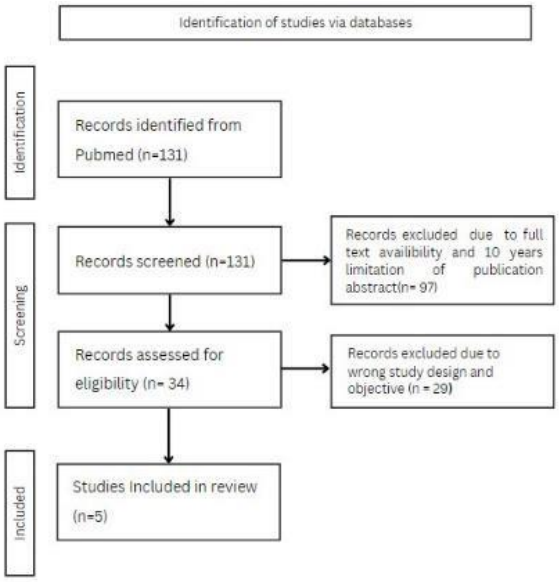

Figure 1. PRISMA Chart

Material And Methods

This systematic review included cross-sectional and retrospective cohort studies on contact dermatitis among healthcare workers and its risk factors, involving a total of 2,706 participants. Studies were included if they reported contact dermatitis in healthcare workers; those involving individuals with no direct patient contact were excluded. Data were sourced from the US National Library of Medicine's PubMed database on July 9, 2024, using keywords such as "contact dermatitis," "healthcare worker," and "risk factor and prevalence." The literature search covered publications from the past 10 years, with no restrictions on language or publication status.

A total of 131 journals were identified from the PubMed database using a combination of keywords and screened. Of these, 5 were selected for review based on their relevance within a 10-year period and were included as reference journals. The quality of these cohort and cross-sectional studies was assessed using the Newcastle-Ottawa Scale (NOS), focusing on study group selection, comparability, and outcomes. All included journals were rated as of fair quality. Data extraction from the database was performed independently by two reviewers, with any disagreements resolved through discussion with a third reviewer.

Result

The study involved cohort and cross-sectional analyses of 2,706 healthcare workers, evaluated using the Newcastle-Ottawa Scale, which indicated fair quality across the studies. The review included four cross-sectional studies and one retrospective cohort study. Three studies assessed the prevalence, risk factors, and clinical features of contact dermatitis in healthcare workers. One study focused on hand eczema and contact allergy related to occupational exposures, and one study investigated whether healthcare work was associated with contact allergy to thiuram mix, a rubber accelerator used in protective gloves.

Prevalence of Contact Dermatitis

Mekonnen et al. reported that occupational contact dermatitis was found in 31.5% of healthcare workers, with nurses experiencing the highest proportion (12.1%), followed by midwifery professionals (11.8%).[4] Alluhayyan et al. found that 46.3% of healthcare workers reported skin changes, with nurses having the highest prevalence of contact dermatitis. Erdem Y et al. detected hand eczema in 54 of 107 participants (50.5%).[3]

Hamnerius et al. reported that 193 (62%) healthcare workers had occupational hand eczema. Among these, 22 (11%) had occupational contact allergy, including 17 with allergies to rubber additives (14 related to surgical gloves, 3 to nitrile examination gloves), 1 to myristyl alcohol, and 4 to formaldehyde or formaldehyde releasers.[9]

Risk Factor of Contact Dermatitis

According to Mekonnen et al., healthcare workers who washed their hands 11 or more times per day were 1.80 times more likely to develop contact dermatitis compared to those who washed their hands 5 or fewer times daily. Additionally, those using 5 or more pairs of gloves per day had 3.22 times higher odds of developing contact dermatitis than those using only one pair daily. Workers who had not received training on workplace health and safety were 2.12 times more likely to develop contact dermatitis compared to those who had received such training.

Finally, individuals with a previous diagnosis of allergies were 2.37 times more likely to develop occupational contact dermatitis than those without a history of allergies.[4] Alluhayyan et al. found that participants aged 20-29 years were more likely to have contact dermatitis. Female healthcare workers had 2.36 times the odds of reporting contact dermatitis compared to males. Pharmacists and interns had 3.69 and 4.90 times higher odds of developing contact dermatitis than other occupations.

According to Erdem et al., healthcare workers with a history of hand eczema (HE) within the past year had an odds ratio (OR) of 18.5 (95% CI: 3.82–89.9), and those washing their hands more than 20 times per day had an OR of 3.28 (95% CI: 0.995–10.8), both independently associated with a higher risk of HE.[3] Hamnerius et al. found that sick leave was associated with allergic contact dermatitis (ACD) with an adjusted odds ratio (OR) of 5.1. Sick leave was also linked to contact allergy to glove-related allergens, with an adjusted OR of 5.6. Schwensen et al. reported that healthcare workers with occupational contact dermatitis, hand dermatitis, and those over 40 years old were more likely to have an allergy to thiuram mix.[9]

Symptoms of Contact Dermatitis

According to Mekonnen et al., the most commonly reported skin changes were redness (28.6%, n=38) and burning (17.3%, n=93). The hand was the most affected body site (22%, n=93), followed by the face (5%, n=9).[4] Alluhayyan et al. found that the most recorded symptoms were dryness (92.9%), itchiness (50%), and redness (46.4%). The hand was the most affected site (93.5%). The top three factors worsening skin changes in the workplace were hand cleansers/soaps (59.2%, n=109), antiseptics/disinfectants (47.8%, n=88), and protective gloves (2.2%, n=75).[3] Erdem et al. reported that the most common clinical type was irritant contact dermatitis (96.3%), the most frequent morphology was erythemato-squamous (75.9%), and the most affected area was the hand dorsum (85.2%).[10] Hamnerius reported that 71% of healthcare workers with hand eczema found it difficult to use alcoholic hand disinfectants, while the majority had no difficulty using disposable gloves.[9]

Discussion

In our review, we found that 31.5% to 62% of healthcare workers have occupational contact dermatitis, with nurses exhibiting the highest prevalence. This may be due to the high proportion of nurses among the participants and their extensive direct patient contact. A 2020 study noted that increased hand hygiene could lead to skin changes such as dryness. The pandemic has intensified the need for frequent hand hygiene, contributing to these adverse skin changes.[11]

In our systematic review, the identified risk factors for contact dermatitis include frequent hand washing, glove use (particularly those containing thiuram mix), a history of allergic dermatitis, being female, and being aged 20-29.

Frequent hand washing is crucial for preventing infections in healthcare settings but can damage the skin barrier and lead to irritant contact dermatitis due to prolonged exposure to water, soaps, and detergents, which strip away natural oils from the skin. This review consistently links frequent hand washing to a higher risk of contact dermatitis among healthcare workers. Strategies such as using moisturizers and implementing skin protection protocols are essential to mitigate this risk while maintaining effective hand hygiene practices.

Gloves are vital for protecting healthcare workers from infectious agents, chemicals, and other irritants. However, gloves made from latex or containing irritants like thiuram mix can cause allergic reactions or irritant contact dermatitis. Prolonged use of such gloves can exacerbate dermatitis due to sweating, mechanical friction, and occlusion of the skin. Mekonnen et al. noted that individuals sensitized to thiuram mix may experience delayed-type hypersensitivity reactions when exposed to gloves containing this chemical.

Healthcare workers with a history of allergic dermatitis are at increased risk of developing exacerbations upon exposure to allergens present in the healthcare environment. Allergic contact dermatitis results from an immune response to specific allergens, such as latex, certain chemicals used in healthcare products, or medications. [2,6,11]

Alluhayyan et al. stated that common allergens in healthcare settings include latex, formaldehyde (used in some disinfectants and medical products), and various preservatives and fragrances found in skincare products. Individuals with a known history of allergic dermatitis should undergo comprehensive skin assessments to identify potential triggers.[3] According to Mekonnen et al., female healthcare workers have a higher prevalence of contact dermatitis compared to their male counterparts. This gender disparity may be due to biological differences in skin structure, hormonal influences, and variations in skincare practices. Hormonal fluctuations during menstrual cycles, pregnancy, or menopause can affect skin sensitivity and reactivity, potentially exacerbating dermatitis. Additionally, women generally have thinner skin than men, making it more susceptible to irritants and allergens.[4] Alluhayyan et al. also identified healthcare workers aged 20-29 years as a high-risk group for contact dermatitis. This demographic often includes new professionals who may be less experienced with skin protection practices or more prone to taking risks with personal protective equipment. Younger healthcare workers might underestimate the importance of skin protection or feel less compelled to follow protocols due to perceived invulnerability or inexperience. Additionally, individuals in their 20s may have varying levels of skin sensitivity and resilience, influenced by genetic factors, skincare habits, and prior exposures to irritants or allergens. Their immune systems may still be maturing, making them more susceptible to developing allergic sensitization or exaggerated inflammatory responses from repeated exposure to allergens.[3]

In our systematic review, dryness, itchiness, and redness were the primary symptoms of occupational contact dermatitis. Mekonnen et al. found redness to be the most common symptom, while Alluhayyan et al. reported dryness as the most prevalent symptom. Despite this difference, the hand was the most common site of occupational contact dermatitis in both studies. A 2020 study indicated that increased hand hygiene could lead to skin changes such as dryness. The pandemic has heightened the need for frequent hand hygiene, thereby exacerbating these unwanted skin changes.[11] Alluhayyan et al. reported hand cleanser/soap, antiseptic/disinfectants, and protective gloves were factors that worsened contact dermatitis.[3] According to Fitzpatrick et al., irritants for occupational contact dermatitis include wet work, soaps and detergents, alcohol, ethylene oxide, and medications. Allergens identified include latex gloves, anesthetics, antibiotics, antiseptics, phenothiazines, formaldehyde,

glutaraldehyde, and chloroxylenol.[6] Extended contact with water or moist environments leads to significant changes in the skin's structure. It causes swelling of the outermost layer of skin (stratum corneum) and disrupts the organization of fats between skin cells. Consequently, the skin becomes more permeable and sensitive to irritants, whether physical or chemical.[12] Wearing protective gloves for long periods can lead to excessive sweating and moisture buildup, which exacerbates the skin's inflammatory response to irritants. Common household cleaning products like soaps, surfactants, detergents, and solvents are generally mild irritants that most people tolerate well. However, frequent exposure to these substances can result in chronic, cumulative irritant contact dermatitis. This happens because these products can strip away protective skin oils, damage skin proteins, alter the structure of keratin in the epidermis, and harm the outer layer of skin cells (keratinocytes).[13]

Conclusion

In conclusion, the prevalence of occupational contact dermatitis among healthcare workers ranges from 31.5% to 62%, with nurses showing a higher prevalence. Our review identified several risk factors: frequent hand washing, use of gloves containing thiuram mix, a history of allergic dermatitis, being female, and being aged 20-29. The primary symptoms reported were dryness, itchiness, and redness. To reduce the prevalence of occupational contact dermatitis, especially among women of reproductive age, it is crucial to address these risk factors. Future research should further investigate these risk factors, and comprehensive training for healthcare workers is essential to mitigate the prevalence of occupational contact dermatitis.

References

1. Hollins LC, Flamm A. Occupational Contact Dermatitis: Evaluation and Management Considerations. Dermatol Clin. 2020 Jul 1;38(3):329–38. https://doi.org/10.1016/j.det.2020.02.001
2. Yuindartanto A, Sawitri, Astindari, Sigit Prakoeswa CR, Damayanti, Anggraen S, et al. Occupational Contact Dermatitis Risk Factors on Healthcare Workers Isolation Ward During the COVID-19 Pandemic. Berkala Ilmu Kesehatan Kulit dan Kelamin. 2023 Mar 31;35(1):27–39. https://doi.org/10.20473/bikk.V35.1.2023.27-39
3. Alluhayyan OB, Alshahri BK, Farhat A, Alsugair S, Siddiqui JJ, Alghabawy K, et al. Occupational-Related Contact Dermatitis: Prevalence and Risk Factors Among Healthcare Workers in the Al'Qassim Region, Saudi Arabia During the COVID-19 Pandemic. Cureus.2020; 12(10):e10975. https://doi.org/10.7759/cureus.10975
4. Mekonnen TH, Yenealem DG, Tolosa BM. Self-report occupational-related contact dermatitis: Prevalence and risk factors among healthcare workers in Gondar town, Northwest Ethiopia, 2018 - A cross-sectional study. Environ Health Prev Med. 2019 Feb 14;24(1):11. https://doi.org/10.1186/s12199-019-0765-0
5. Djuanda A, Hamzah M, Aisah S. 2007. Skin disease -- Venereal disease (5th ed.). Jakarta: Balai Penerbit Fakultas Kedokteran Universitas Indonesia. Fitzpatrick's Dermatology.

6. Guertler A, Moellhoff N, Schenck TL, Hagen CS, Kendziora B, Giunta RE, et al. Onset of occupational hand eczema among healthcare workers during the SARS-CoV-2 pandemic: Comparing a single surgical site with a COVID-19 intensive care unit. Contact Dermatitis. 2020;83(2):108–14. https://doi.org/10.1111%2Fcod.13618

7. Schwensen JF, Menné T, Sommerlund M, Andersen KE, Mortz CG, Zachariae C, et al. Contact allergy in danish healthcare workers: A retrospective matched case-control study. ActaDerm Venereol. 2016;96(2):237–40. https://doi.org/10.2340/00015555-2202

8. Hamnerius N, Svedman C, Bergendorff O, Björk J, Bruze M, Engfeldt M, et al. Hand eczemaand occupational contact allergies in healthcare workers with a focus on rubber additives. Contact Dermatitis. 2018;79(3):149–56. https://doi.org/10.1111/cod.13042

9. Guertler A, Moellhoff N, Schenck TL, Hagen CS, Kendziora B, Giunta RE, et al. Onset of occupational hand eczema among healthcare workers during the SARS-CoV-2 pandemic: Comparing a single surgical site with a COVID-19 intensive care unit. Contact Dermatitis. 2020;83(2):108–14. https://doi.org/10.1111%2Fcod.13618

10. Beiu C, Mihai M, Popa L, Cima L, Popescu MN. Frequent Hand Washing for COVID-19 Prevention Can Cause Hand Dermatitis: Management Tips. Cureus. 2020; 12(4):E7506. https://doi.org/10.7759%2Fcureus.7506

11. Warner RR, Boissy YL, Lilly NA, Spears MJ, McKillop K, Marshall JL, et al. Water disrupts stratum corneum lipid lamellae: Damage is similar to surfactants. Journal of Investigative Dermatology. 1999;113(6):960–6. https://doi.org/10.1046/j.1523-1747.1999.00774.x

12. Khosrowpour Z, Ahmad Nasrollahi S, Ayatollahi A, Samadi A, Firooz A. Effects of four soaps on skin trans-epidermal water loss and erythema index. J Cosmet Dermatol. 2019;18(3):857–61. https://doi.org/10.1111/jocd.12758

Sudden Onset of Diabetic Ketoacidosis in a Patient with Discordant HbA1C: A Unique Case of Fulminant Type 1 Diabetes Mellitus (FT1DM) in a Middle-aged Man

I Gusti Ayu Nadine Hirania[1], Jeremia Immanuel Siregar[2], Yonesha Rahmania Prasetya[3]

[1,3] Faculty of Medicine, University of Pelita Harapan, Jendral Sudirman Boulevard, Lippo Karawaci, Tangerang, Indonesia 15811
[2] Internal Medicine Department, Faculty of Medicine, University of Pelita Harapan, Jendral Sudirman Boulevard, Lippo Karawaci, Tangerang, Indonesia 15811

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Correspondance : Jeremia Immanuel Siregar
E-mail : jeremia.siregar@uph.edu
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Abstract

Introduction: Diabetic Ketoacidosis (DKA) is an acute complication of diabetes mellitus (DM) which present as the first manifestation in fulminant type 1 diabetes mellitus (FT1DM) without significant elevation of HbA1C. We present a unique case of a 52-years-old male with DKA without previous history of DM and HbA1c of 6.6.

Case Illustration: A 52-years-old male was brought to hospital due to persistent vomiting. He experienced polyuria and unexplained weight loss but denied previous history of DM. He was diagnosed with DKA due to his blood glucose of 1107 mg/dL along with elevated blood ketone and metabolic acidosis. However, his HbA1c was a mere 6.6. His serum lipase was increased, consistent with pancreatic damage. He was then discharged with basal-bolus insulin.

Discussion: Although the symptoms of this patient was consistent with hyperglycemic crisis, the presentation of DKA is usually associated with elevated HbA1c, approximately 10.4 - 16.9%. This unusual HbA1c points to the diagnosis of FT1DM. It is caused by sudden beta-cell destruction triggered by viral infections, alongside genetic disposition, leading to sudden depletion of insulin occurred less than a week and presents with ketoacidosis. It is characterized by low HbA1c (< 8.7%) yet extremely high blood glucose (≥ 288 mg/dl) and elevated pancreatic enzymes (depicting pancreatic damage). A diagnosis of FT1DM can be ascertained in this patient as his presentations matches its characteristics.

Conclusion: FT1DM is a sub-type of T1DM which can suddenly occur in patients and associated with discordant HbA1c. It is important to recognize and treat it accordingly to avoid fatal outcomes.

Introduction

Diabetic Ketoacidosis (DKA) is an acute complication of diabetes which may occur in people with a known history of diabetes, or present as the first manifestation in people with Type 1 Diabetes, specifically in those with fulminant type 1 diabetes mellitus (FT1DM).[1,2] This sub-type of type 1 diabetes mellitus (T1DM) is characterized by rapid development of pancreatic b-cell destruction and dysfunction that can result in DKA within less than 7 days,

accompanied with an increase in pancreatic enzymes, low C-peptide levels, no pancreatic b-cell auto- antibodies, and near-normal HbA1c or glycosylated hemoglobin.[2] Until recently, HbA1c has been the gold-standard for assessment of glycemic control and complications of diabetes. However, it is important to know that the usage and reliability of HbA1c is dependent on multiple factors which may result in a falsely elevated or lowered result.[1,3]

Here, we discuss a unique case of a 52-years-old male presenting with DKA which occurred in a week, with no previous history of diabetes symptoms, and a HbA1c of less than 7%.

Case Illustration

A 52-years-old Indonesian male was brought to the emergency department due to nausea and vomiting which started four days prior to admission. The symptoms had started in the evening with an increase in thirst and mouth dryness, alongside an increase in micturition frequency and amount. He claimed that within 15 minutes after drinking water, he had to go back to the toilet to urinate. Due to intense thirst, he drank approximately more than 2 litres of water. The patient's vomit was described to be watery and without blood. The patient denied any projectile vomiting and any experience of intense headache. The day before, patient was also brought to the emergency department due to nausea and vomiting with similar characteristics. The patient claimed to have been described medicine which he drank once after being discharged. He claimed to have gone home feeling better than he had on his first admission.

The patient had a history of sore throat which was first documented by the patient on the day before admission with a VAS of 4/10. The pain was quite debilitating, as the patient had difficulties in eating and drinking due to it. The patient denied any coughing or phlegm. He also admitted to experiencing colicky pain on his upper left abdomen for 3 months ago. The pain was described as a feeling of tightness and fullness with nothing to exacerbate nor relieve it. The patient denied any radiation towards his back, jaw, or left arm.

The patient also denied ever experiencing these symptoms prior to onset. He had denied any tingling in his extremities, blurry vision, increase in hunger, or any complaints regarding towards micturition and defecation. He had also denied any history of diabetes mellitus, hypertension, heart disease, and others. The patient admitted to a history of surgery for a mass in his right armpit in 2019, which was then followed by a regimen of medicine for 9 months which he completed. He confessed of not remembering the name of the medicine but remembered that he experienced abdominal discomfort and tingling in his hands while completing that regimen. He also admitted to smoking 2 years ago but had stopped since then.

On presentation, the patient looked moderately sick, but conscious. His blood pressure was 93/60, with a heart rate of 73 bpm, respiratory rate of 17 breaths per minute, and temperature of 37^{o}C. On physical examination, the patient had an oral lesion near his left glossopharyngeal arc (*arcus glossopharyngeus sinistra*), dry oral mucosa, with normal skin turgor. The patient also had a single noticeable mass around his left supraclavicular area, approximately 4x5 cm in size, with a soft consistency and a smooth surface with no nodules. On abdominal examination, the

patient had tenderness around his epigastric and left hypochondriac area, and a single lump which was felt on deep palpation, approximately 3.5x5 cm in size, which felt hard but smooth with no nodules.

The patient received initial fluid resuscitation and was started on intravenous rapid-acting insulin infusion during the treatment in the emergency departemnt. The patient was also started on antibiotics, natrium bicarbonate, and kalium. He was then admitted to the hospital ward.

Due to the state of presentation, various laboratory examinations were done. One of them was random blood glucose (RBG). When admitted to the emergency department, his initial RBG was found to be 629. The overall hematology tests were normal. Blood chemistry tests showing results as follows, eGFR were decreased, blood ketone was positive, ureum were slightly increased, liver function test was slightly increased, HbA1c were 6.6% on the first day of admission and 6.9% on the last day. Urinalysis test was done, and the results are yellowish colored, cloudy, protein and nitrit were negative, occult blood positive (+2), ketone (+2) and glucose (+2).

On the second day of admission, the patient's ECG showed sinus tachycardia with tall T which was in accordance with the patient's serum K+. Meanwhile, there were no abnormalities shown in the patient's chest x-ray. Due to his LUQ tenderness, whole abdomen USG was done. It resulted in findings such as cholelithiasis with *adenomyomatosis* and fatty liver. Other intra-abdominal organs showed no abnormalities.

Throughout his stay, the patient's random blood glucose kept track of diligently. During the 5 days of hospital stay, random blood glucose was checked every 6 hours starting from 00.00AM until 10.00 PM showing fluctuations of the random blood glucose level in the patient's laboratorium results throughout his admission in the hospital. The lowest RBG level was on the last day of hospital stay, 74mg/dL and the highest level was on the first day of hospital admission, 486mg/dL.

Discussion

Glycosylated haemoglobin or HbA1c has been a validated diagnostic tool and a marker for glycaemic control in those with diabetes. It is based on the formation between haemoglobin and glucose. Haemoglobin is a metalloprotein in the erythrocytes which transports oxygen. It consists of two alpha-globin chains (HbA1 and HbA2) and two non-alpha globin chains (beta, gamma, delta). Normally, an adult haemoglobin consists of two alpha chains and two beta chains. However, in the condition of high glucose concentration, a process of chemical condensation of haemoglobin and glucose occurs slowly in accordance with the average erythrocyte's lifespan (120 days), resulting in a minor component called A1c. The formation of A1c is proportional to the concentration of glucose throughout an erythrocyte's lifespan. Therefore, chronic hyperglycaemia is associated with an increase in A1c formation.

In this case, a HbA1c amount of 6.6 and 6.9 was found. According to ADA (American Diabetes Association), a value of 5.7-6.4% is pre-diabetic, while a value above 6.5% signifies a person to suffer from diabetes.[4] This indicates that the patient in the case above to be diabetic. However, studies found that type 2 diabetes mellitus patients with DKA are usually associated with markedly elevated HbA1c, approximately a level of 10.4-

16.9%.[1] While the HbA1c found in this patient qualifies as diabetic and points to a possible diagnosis of type 2 diabetes mellitus, it is not elevated enough and does not match the usual presentation. This is because type 2 diabetes mellitus is a chronic insidious process, which results in chronic hyperglycaemia, represented by an extremely elevated HbA1c. The unusually low HbA1c which is in discordance with the patient's blood glucose levels insinuates another diagnosis, which is type 1 diabetes mellitus.[1,2]

In type 1 diabetes mellitus with DKA as its complication, low HbA1c is explained by the sudden onset of *insulinopenia*. This may be caused by abrupt destruction of complete beta-cell destruction in the pancreas. This results to a low HbA1c value which does not reflect the blood glucose level, as HbA1c values reflects glycaemic control in the time span of an erythrocyte (120 days).[1,3] A condition of sudden hyperglycaemia due to beta-cell destruction which leads to sudden depletion of insulin can be found in one the sub-types of diabetes mellitus – fulminant type 1 diabetes mellitus or FT1DM.[2]

FT1DM is a result of rapidly occurring pancreatic beta-cell destruction, usually in less than a week. Patients usually present with hyperglycaemic symptoms such as polydipsia, polyuria, and sudden weight loss in the same time frame. Studies has also found that the development of DKA in less than a week is one of its characteristics. Increased serum pancreatic enzyme levels and unusually low HbA1c levels with extremely elevated blood glucose levels can also be found in those suffering from FT1DM. Its aetiology is still unknown, but multiple factors have been suspected to be the cause of it, such as genetic factors e.g. human leukocyte antigens (HLA) and environmental factors like viral infections.[2]

Conclusion

FT1DM is a sub-type of T1DM which can suddenly occur in patients and associated with discordant HbA1c which caused by rapid pancreatic beta-cell destruction. The presence of DKA in T1DM with low HbA1c is explained by the sudden onset of insulinopenia. It is important to recognize and treat it accordingly to avoid fatal outcomes.

References

1. O Chukwuma E, Longo-Mbenza B, Blanco-Blanco E. Glycosylated haemoglobin is markedly elevated in new and known diabetes patients with hyperglycaemic ketoacidosis. Afr Health Sci. 2014; 14(3): 526–532. https://doi.org/10.4314%2Fahs.v14i3.5

2. Keskin M, Savaş-Erdeve Ş, Çetinkaya S, Aycan Z. Low hemoglobin A1c levels in a patient with diabetic ketoacidosis: Fulminant type 1 diabetes mellitus. Turk J Pediatr. 2018; 60(2):201-205. https://doi.org/10.24953/turkjped.2018.02.015

3. Li G, Han L, Wang Y, Zhao Y, Li Y, Fu J, Li M, Gao S, Willi SM. Evaluation of ADA HbA1c criteria in the diagnosis of pre-diabetes and diabetes in a population of Chinese adolescents and young adults at high risk for diabetes: a cross-sectional study. BMJ Open. 2018; 8(8):1-9. https://doi.org/10.1136/bmjopen-2017-020665

4. Hosokawa Y, Hanafusa T, Imagawa A. Pathogenesis of fulminant type 1 diabetes: Genes, viruses and the immune mechanism, and usefulness of patient-derived induced pluripotent stem cells for future research. J Diabetes Investig. 2019; 10(5):1158-1164. https://doi.org/10.1111/jdi.13091
5. You W, Yang J, Liu Y, Wang W, Zhu L, Wang W, Yang J, Chen F. Fulminant type 1 diabetes mellitus: Two case reports. Medicine (Baltimore). 2019; 98(5):e14319. https://doi.org/10.1097/md.0000000000014319
6. Yang D, Zhou Y, Luo S, Zheng X, Ling P, Qiu L, Xu W, Liang H, Yao B, Weng J, Yan J. Clinical Characteristics of Fulminant Type 1 Diabetes Compared with Typical Type 1 Diabetes: One-Year Follow-Up Study from the Guangdong T1DM Translational Medicine Study. J Diabetes Res. 2020; 2020(2020): 8726268. https://doi.org/10.1155%2F2020%2F8726268

Uncommon Presentation of Perianal Condyloma Acuminata in a Young Male: A Case Report

Natalia Maria Christina[1], Patricia Diana Prasetyo [2], Albert Cendikiawan[3], Jeremiah Hilkiah Wijaya[1]

[1] Department of Surgery, Faculty of Medicine, Jendral Sudirman Boulevard, Lippo Karawaci, Tangerang, Indonesia 15811
[2] Department of Pathology, Faculty of Medicine, Jendral Sudirman Boulevard, Lippo Karawaci, Tangerang, Indonesia 15811
[3] Department of Radiology, Mayapada Hospital, Tangerang, Banten, Indonesia

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Correspondance : Natalia Maria Christina
E-mail : **natalia.christina@uph.edu**
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Abstract

Background: Perianal warts, also known as anogenital warts or condyloma acuminata, represent a significant health concern in the young male population. Here, we present a unique case of a large perianal wart in a 26-year-old male patient.

Case Description: The patient came to the surgical clinic with complaints of an anal lump for 7 months ago. The lump first appeared in February 2019 as big as a green bean, it increased in size, bled easily and painful to be touched. The patient has a history of anal intercourse 1 month before the lump appeared. The lump size was about 8 x 5 cm and resembled “cauliflower”. Diagnosis of suspected anal papilloma was made. In July 2019, an incisional biopsy was performed, and the result showed papilloma squamosa with condyloma acuminata as a differential diagnosis. In September 2019, perianal soft tissue tumor excision with advancement flap was performed and the result showed condyloma acuminata.

Discussions: The case highlights the importance of careful evaluation and diagnosis in such clinical scenarios, as the initial diagnosis of anal papilloma was later refined to condyloma acuminata based on the biopsy and surgical findings. Early detection and appropriate management are crucial in cases like this to ensure the best possible patient outcomes.

Introduction

Perianal warts, also known as anogenital warts or condyloma acuminata, represent a significant health concern in the young male population. These warts are caused by the human papillomavirus (HPV) infection and primarily affect the skin and mucous membranes in the anal and genital areas. The prevalence of perianal warts has been steadily rising in recent years, leading to increased attention from the medical and scientific community.[1]

HPV is one of the most common sexually transmitted infections (STIs) globally, with numerous strains responsible for various manifestations of the disease.[1,2] Perianal warts are typically caused by high-risk HPV strains, such as HPV-6 and HPV-11. Transmission occurs through direct skin-to-skin contact during sexual activity, making sexually active young males particularly susceptible to infection.[3] While perianal warts may not be life-threatening, they can significantly impact the quality of life and mental well-being of affected individuals.[1] The physical symptoms, which

include the presence of painless, cauliflower-like growths in the anal and genital regions, can cause discomfort and embarrassment. Moreover, the social stigma associated with HPV and its link to sexual activity can lead to psychological distress and negatively affect intimate relationships. Current treatment options include topical therapies, cryotherapy, electrosurgery, laser therapy, and immunomodulatory agents.[1,4]

Here, we present a unique case of a large perianal wart in a 26-year-old male patient. Perianal warts are more commonly seen in females, and the presentation of a large, cauliflower-like perianal wart in a young male is less common. Additionally, the patient had a history of anal intercourse, which is a risk factor for the development of condyloma acuminata. We constructed this case report according to the CARE guideline for case report and all informed consent was gained personally to the patient by all authors.

Case Description

In September 2019, a 26-year-old man came to our clinic with a lump initially appeared as a small corn kernel in February 2019 but progressively increased in size, became prone to bleeding, and caused discomfort upon touch (Figure 1). The patient, sexually active with both a female partner and a male partner for approximately one month before the lump appeared. Apart from the anal lump, the patient denied experiencing fever, weight loss, or lumps in other body parts. Upon physical examination, the multinodular lump exhibited a cauliflower-like appearance, measured approximately 8 x 5 x 2 cm that felt soft, tender, and immobile (Figure 2). Based on these findings, a suspected diagnosis of anal papilloma was made, and subsequent excisional biopsy of the entire lump area confirmed the presence of a large condyloma acuminata (Figure 3), thus guiding the clinicians in determining the suitable management approach and prognosis. Before conducting objective investigations, healthcare providers should inquire about the patient's sexual behavior, including the timing of first sexual intercourse, the number of sexual partners, and specific sexual practices, as this information may offer critical insights into the etiology of the perianal lump.

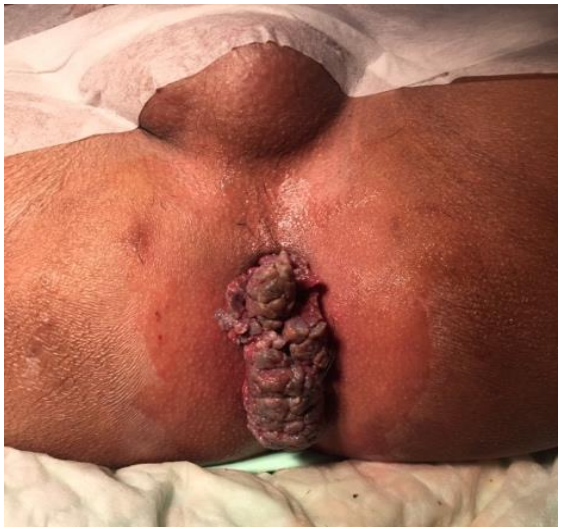

Figure 1. Pre-operative conditions of the perianal wart in a 26-year-old male patient

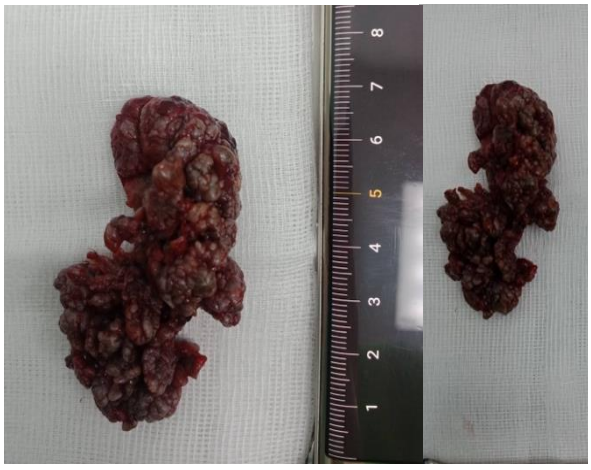

Figure 2. The actual size of a cauliflower like mass lesion after surgery

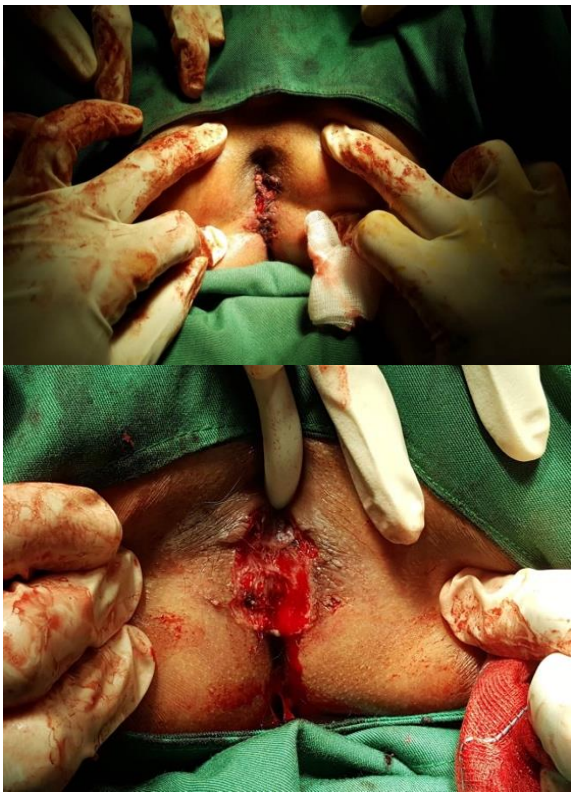

Figure 3. Intraoperative surgical excision of the mass

In the context of this study, a significant perianal lump displaying certain characteristics prompted consideration of potential differential diagnoses, including precancerous or cancerous growths such as verrucous carcinoma and squamous cell carcinoma. It was recognized that these conditions might infiltrate the mucous, skin, or deeper layers, necessitating more than excisional treatment alone, but also chemo-radiation therapy as an adjuvant approach. However, after conducting an incisional and excisional biopsy, the definitive diagnosis was established as condyloma acuminata. The recommended non-pharmacological therapy for the patient involved comprehensive education on condyloma acuminata, covering its causes, transmission, risk factors, and available treatment options. Additionally, the patient was advised to undergo testing for other sexually transmitted diseases in both themselves and their sexual partner, and to utilize protected sexual intercourse methods, such as condom usage. Ultimately, the patient underwent a perianal excision of the soft tissue tumor, followed by repair and advancement flap procedures. No specific pharmacological therapy was administered in this case. On a 4 week follow up duration, the patient did not suffer any symptoms of infection, bleeding, recurrent lesion growth. Digital rectal examination was unremarkable.

Discussion

The approach employed in this case exhibited several noteworthy strengths. Firstly, the clinician demonstrated a thorough assessment by acquiring a comprehensive sexual history, including the crucial evaluation of anal intercourse, which aids in assessing the risk factors for condyloma acuminata. Additionally, a meticulous physical examination was conducted, diligently observing the perianal wart's size, appearance, and tenderness, thereby facilitating a precise differential diagnosis. Furthermore, the utilization of an incisional biopsy played a pivotal role in establishing the definitive diagnosis of papilloma squamosa, while also considering condyloma acuminata as a potential alternative diagnosis, guiding subsequent management decisions.

Based on the limited number of available reports, this condition appears to be more prevalent among women, with only a few cases reported in males.[5–7] While many individuals have shown no symptoms, some have experienced itching and burning, and the condition has been persistent in all cases. The localization of this condition to the genitoperineal area is likely due to the area's moist and warm environment.[5]

The conclusions drawn in this case report are substantiated through a comprehensive analysis of the patient's clinical presentation, diagnostic assessment, and treatment response. The patient's atypical manifestation of a large perianal wart, more commonly observed in females, and the history of anal intercourse aligned with a diagnosis of condyloma acuminata. The definitive diagnosis of papilloma squamosa was confirmed through incisional biopsy, with condyloma acuminata considered as a potential differential diagnosis. The chosen course of action, an excision with advancement flap procedure, resulted in the successful eradication of the perianal wart, further supporting the diagnosis of condyloma acuminata and the efficacy of the selected treatment modality. Nonetheless, it is crucial to acknowledge the absence of long-term follow-up or recurrence data in the case report, which could have enhanced the validation of the conclusions.

Certain limitations were encountered during the course of this case. The inability to perform a digital rectal examination due to the obstruction caused by the sizeable perianal wart restricted the assessment of the lesion's extent. Furthermore, the case report lacks comprehensive information concerning the various treatment options considered and the rationale behind opting for the excision with advancement flap procedure. Moreover, the post-operative course of the patient, including potential complications and perianal wart recurrence, was not adequately detailed, limiting the overall understanding of the case's long-term outcomes.

Perianal warts predominantly arise from HPV infection, typically linked to anal intercourse. Therefore, a comprehensive sexual history must be elicited during patient evaluations. These warts can cause significant distress, necessitating a tactful approach characterized by empathetic communication and utmost confidentiality. Condyloma acuminata, a benign lesion, manifests as single or multiple cauliflower-like lumps of skin color, predominantly found in the anogenital region. However, certain cases may progress to malignant forms like verrucous carcinoma or squamous cell carcinoma, presenting with rapid growth, easy bleeding, deep tissue invasion, and systemic symptoms like weight loss and fever. For extensive perianal warts, a diagnostic and therapeutic approach involving surgical excision and biopsy is crucial to guide subsequent treatments, as medicinal interventions may yield unsatisfactory outcomes. Preventive measures against HPV infection encompass condom usage during sexual intercourse, cessation of smoking, and HPV vaccination, which can begin at the age of 12 for both sexes.

Conclusion

Here, we presented an uncommon case of perianal warts in a young male. The case highlights the importance of careful evaluation and diagnosis in such clinical scenarios, as the initial diagnosis of anal papilloma was later refined to condyloma acuminata based on the biopsy and surgical findings. Early detection and appropriate management are crucial in cases like this to ensure the best possible patient outcomes.

References

1. Werner, R. N., Westfechtel, L., Dressler, C., & Nast, A. (2017). Anogenital warts and other HPV-associated anogenital lesions in the HIV-positive patient: A systematic review and meta-analysis of the efficacy and safety of interventions assessed in controlled clinical trials. Sexually Transmitted Infections, 93(8), 543–550. https://doi.org/10.1136/sextrans-2016-053035

2. Ates, M., Akbulut, S., Tuncer, A., Sahin, E., Karabulut, E., & Sarici, K. B. (2022). Squamous Cell Carcinoma Arising from Perianal Buschke-Lowenstein Tumor (Giant Condyloma Acuminatum): Comprehensive Literature Review. Journal of Gastrointestinal Cancer, 53(4), 1083–1092. https://doi.org/10.1007/s12029-021-00713-y

3. Hunter Handsfield, Md, H. H. (1997). Clinical Presentation and Natural Course of Anogenital Warts. The American Journal of Medicine, 102(5), 16–20. https://doi.org/10.1016/S0002-9343(97)00179-4

4. Klotz, T., Munn, Z., Aromataris, E. C., & Greenwood, J. E. (2020). Imiquimod to prevent keloid recurrence postexcision: A systematic review and meta-analysis. Wound Repair and Regeneration: Official Publication of the Wound Healing Society [and] the European Tissue Repair Society, 28(1), 145–156. https://doi.org/10.1111/wrr.1276

5. Wong, T. Y., & Mihm, M. C. (1994). Acantholytic dermatosis localized to genitalia and crural areas of male patients: A report of three cases. Journal of Cutaneous Pathology, 21(1), 27–32. https://doi.org/10.1111/j.1600-0560.1994.tb00687.x

6. Krishnan, R. S., Ledbetter, L. S., Reed, J. A., & Hsu, S. (2001). Acantholytic dermatosis of the vulvocrural area. Cutis, 67(3), 217–219, 220. https://cdn.mdedge.com/files/s3fs-public/Document/September-2017/067030217.pdf

7. Wang, L., Yang, X., Hao, F., Mei, Y., & Ye, Q. (2009). Papular acantholytic dyskeratosis of the vulva. European Journal of Dermatology: EJD, 19(4), 402–403. https://doi.org/10.1684/ejd.2009.0697

Age, Onset, and Tumor Size Differences in Newly Diagnosed Breast Cancer Patients Before and During the SARS-Cov-2 Pandemic at Siloam Hospital Lippo Village (April 2019 – December 2020)

Freda Susana Halim

Department of Surgery, Faculty of Medicine, Jendral Sudirman Boulevard, Lippo Karawaci, Tangerang, Indonesia 15811

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Correspondance: Freda Susana Halim
E-mail: Freda.halim@uph.edu
Online First: June 2023

Abstract

Background: The current pandemic condition has caused delays in cancer treatment therefore surveillance should be increased.

Methods: By total sampling, this retrospective cross-sectional study enrolled 108 samples, who were newly diagnosed breast cancer patients at the outpatient department of Siloam Hospital Lippo Village (April 2019 - December 2020). Data obtained from medical records and interviews from December 2020 – February 2021.

Result: From the total of 108 samples which consisted of 54 samples before the pandemic (April 2019 – February 2020) and 54 samples during the pandemic (March 2020 – December 2020), accompanied by an increasing trend. The age during pandemic was younger than before pandemic (51,167 years old ± 11,255 vs 47,537 years old ± 9,824, p value=0,038), the tumor size during pandemic was bigger than before pandemic (3,403 cm ± 3,024 vs 4,262cm ± 4,212, p value=0,046) but the onset of patient during pandemic was not longer than before pandemic (281,69 days ± 401,387 vs 178,09 days ± 292,563, p value=0,036).

Conclusions: Newly diagnosed patients have younger age and larger tumor size during pandemic when we compare to before pandemic period, but no difference in onset term. Surveillance to society is needed to ensure older people with smaller tumor size to seek medical attention.

Introduction

Breast cancer is one of most common cancer in whole world women population, as well as in Indonesia according to Global Cancer Incidence, Mortality and Prevalence (GLOBOCAN) 2020 with high mortality.[1] The health care to this population therefore important, with each delay with contribute to significant morbidity and mortality.[2]

COVID-19 (Corona Virus Disease-19) is caused by SARS-COV-2 (Severe Acute Respiratory Syndrome-Coronavirus 2), an aerosol and airborne transmitted disease that rapidly spread from Wuhan, China to whole world within 3 months since its finding. WHO declared the pandemic condition since March 11th, 2020, and affecting whole healthcare services as well as the socioeconomic condition. Indonesian government itself has established the emergency health condition caused by the SARS-COV-2 since February 29th, 2020. Social mobilization prompt by local government

and fear of COVID-19 spread withing families making the patients especially elderly are afraid to go to public places including hospital. [3]

Reach and quality of care is essentially important for cancer patient, and it is disrupted in every healthcare service during COVID-19 pandemic. Many patients are often underserved, and breast cancer patients is no exception. A cross-sectional study by Kaufman, et al 2020 in United States of America find decreased cancer patient weekly volume up to 46.6% with newly diagnosis breast cancer patient decreased 51.8%. Decreased patient's average age, means the patient who are having the breast cancer treated are younger than before the pandemic period, also noted in this study. [4] Similar results also reported by Kiziltan, et al 2020 noting decreased newly breast cancer patients' volume who are being treated in pandemic period. [5] Study by Vanni et al 2020 also found increased of tumor diameter/size during pandemic period although this finding was not significant statistically.[6]

Breast cancer service in Indonesia is still not well developed and it's decreased in quality and reach is most likely disrupted during the SARS-COV-2 pandemic period. There is still no report from Indonesia to conclude such reduction, and comparative simple research to conclude such conclusion is needed. The purpose of this review is to find out the characteristics such as age, onset, and tumor size differences of newly diagnosed breast cancer patients before and during the SARS-COV-2 pandemic at Siloam Hospital Lippo Village.

Material And Methods

Patients

This retrospective cross-sectional study collects 108 newly diagnosed breast cancer patients who came to outpatient department clinic at Siloam Hospital Lippo Village. We use total sampling method, collecting data spanned from April 2019-December 2020. Fifty-four patients were newly diagnosed before pandemic times (April 2019-Feb 2020) and another 54 patients during pandemic times (March 2020-Dec 2020). All diagnoses were made using biopsy, done by certified general surgeon and oncologist surgeon, all were interpreted by certified pathologists. Age was defined as the age of patient when they are newly diagnosed with breast cancer, expressed in years. Tumor size was defined as the largest diameter found in operation or pathological data, expressed in centimeter (cm). Tumor onset was defined as the period between the patient knew about the lump/tumor to first time they went to Siloam Hospital Lippo Village for treatment, expressed in days.

All data investigations were conducted according to the principles expressed in the Declaration of Helsinki. The Institutional Review Board of the Pelita Harapan University and Siloam Hospital Lippo Village approved the study, and all participants provided informed consent via google form sent via whatsapp.

Data Collection.

Due to pandemic condition, investigator cannot meet the patient directly. All patients data (age, onset of tumor and tumor size) were recorded from secondary data in the medical record, with some of the missing data were interviewed using google form sent via whatsapp. All patients were asked for permission/informed consent before filling the google form. Interview was done from January-February 2021.

Statistical analysis.

Statistical analysis was performed using SPSS® (version 25) towards age, onset of tumor, and tumor size within the before pandemic and during pandemic group. We used T-test for normally distributed data, and it is considered significant if the p value meets < 0.05. With abnormal data distributed data, analysis will use Non-parametric Mann-Whitney, and it is considered significant if the p value meets <0.05.

Result

At total we find 237 patients (136 patients from before pandemic period and 101 patients during pandemic period). Most of exclusion reason are due to incomplete medical record, inactive phone number (cannot be contacted), or the patient does not reply to the text. All the data collection were explained from the Chart 1 and 2 below:

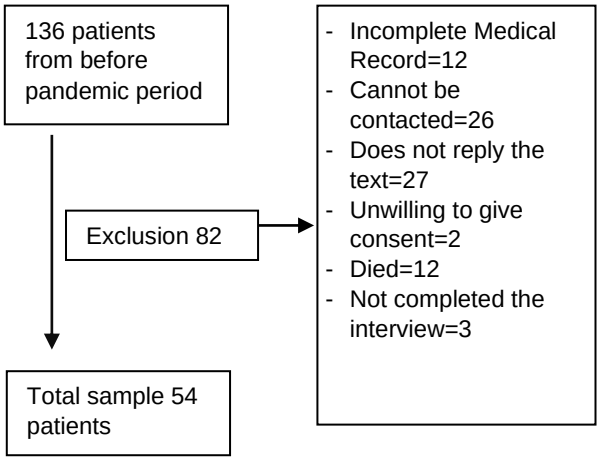


Chart 1. Patient Data Collection for Newly Diagnosed Breast Cancer Patients from Before SARS-COV-2 Pandemic Period

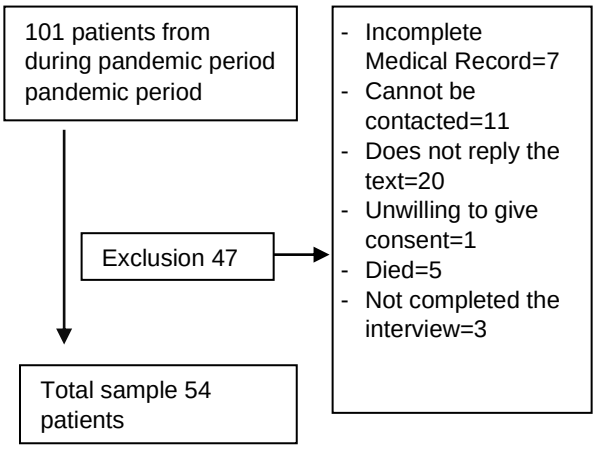
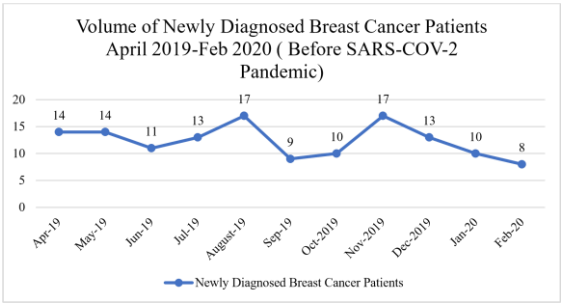
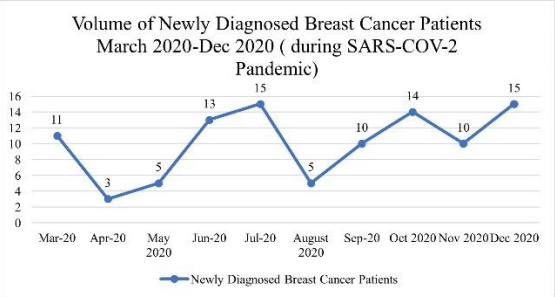


Chart 2. Patient Data Collection for Newly Diagnosed Breast Cancer Patients from During SARS-COV-2 Pandemic Period

The volume of newly diagnosed breast cancer patients during early pandemic was decreased during early pandemic months (March-May 2020). It bounced back to pre-pandemic period in June-July 2020. Although it was decreased again in August 2020 (probably due to large scale social restriction instructed by Indonesian government due to increasing of COVID-19 cases across the country, causing patients to restrain their mobilization).



Graph 1. Volume of Newly Diagnosed Breast Ca Patients Before SARS-COV-2 Pandemic



Graph 2. Volume of Newly Diagnosed Breast Ca Patients During SARS-COV-2 Pandemic

For age variable, the data is found in table 1:

Table 1. Age of Newly Diagnosed Breast Cancer Patients Before and During SARS-COV-2 Pandemic

Age (yrs) (n = 108)				
	Mean ±SD	**Median**	**Min-Max**	**P value**
Before pandemi (n=54)	51,167 ± 11,255	49	29 – 77	0,038
During pandemi (n=54)	47,537 ± 9,824	48,5	22 – 80	

In this variable, we found it is significant difference statistically for the age of newly diagnosed patient before and during pandemic, with mean and median are younger. Thus, from here we see that age are significantly younger in during SARS-COV-2 pandemic.

For onset of the tumor, the data is found in table 2

Table 2. Onset of Newly Diagnosed Breast Cancer Patients Before and During SARS-COV-2 Pandemic

Onset (days) (n = 108)				
	Mean ±SD	**Median**	**Min-Max**	**P value**
Before pandemi (n=54)	281,69 ± 401,387	125	1 – 1825	0,036
During pandemi (n=54)	178,09 ± 292,563	90	1 – 1825	

The onset of disease are shorter in during pandemic group, suggesting the patient are faster to get medical attention rather than to wait at home for the disease but it is statistically insignificant (p value 0.036)**.**

For tumor size, the data is found in table 3:

Table 3. Tumor size of Newly Diagnosed Breast Cancer Patients Before and During SARS-COV-2 Pandemic

Tumor size (cm) (n = 108)				
	Mean ±SD	**Median**	**Min-Max**	**P value**
Before pandemi (n=54)	3,403 ± 3,024	3	0,3 – 20	0,046
During pandemi (n=54)	4,262 ± 4,212	3,225	0,5 – 30	

The tumor size also bigger in during pandemic period, with significant statistical result, suggesting the patient with smaller size probably are not coming to hospital to get treatment.

Discussion

In the chart 1 and 2 data shows that increasing trend of patient volume after the 3rd months of SARS-COV-2 pandemic period is shown, although probably variability is still shown. Some months are showing decreased volume, but the increased trend is still expected, showing the patient belief towards Siloam Hospital Lippo Village security in terms of sterility. A similar result was found in study by Zhongqing Xu, et al 2021 in Shanghai, which shows decreased patient volume in January-June 2020 compared to January-June 2019.[7] the report also noted the society belief is strong to the health care services or hospital, then increased volume after the early pandemic is

expected, although still decreased compared to the normal period.[7]

In this study average age of newly diagnosed breast cancer patient in pre-pandemic period is 51.167 years old, meanwhile during pandemic period is 47.537 years old, with p value < 0.038. Kaufmann, et al 2020 in United States of America also found similar result, although Vanni et al 2020 in Italia found no difference in age of newly diagnosed breast cancer patient in both periods 4,6 Because if it was true, then the older age patient is underserved during this pandemic period for their breast health service. In other words, more vigilant surveillance regarding breast cancer awareness towards society are needed, if it is proven.[8]

Indonesian governments are working vigillantly to restrict social mobilization and this could be main reason why older patient are not coming to hospital due to social limitation for people with 45 years old age although it is not correctly proven in our study. [9,10] Therefore longer, more careful study, with society-based population is needed to prove such observation.

Onset of our patients are shorter in during pandemic period, which is exhilarating both for patients and clinicians, because shorter onset correlates to earlier stadium. [11] In this tsudy average onset for before pandemic patients are 282,462 days, compared to 178,056 days during pandemic period. This is contradictory with previous study by Kaufman, et al 2020 in US and Kiziltan,et al 2020 in Turkey which show that lateness are more profound during pandemic period. [4,5] This finding is not statistically significant, and it could be from recall bias due to long period from occurrence to interview. Also, the interview is not done directly by primary investigator to the patient due to social limitation in hospital and society.

In tumor size variable, average of tumor size before pandemic is 3,403 cm (min– max=0,3–20) and 4,262 cm (min–max=0,5–30) during pandemic period. In statistical analysis increase of the tumor size is found significantly meaningful (p 0.046). Other report by Vanni et al 2020 in Italy found that no significant increase of size in both groups.[6]

The tumor size itself reflect the lateness towards medical attention in cancer patient,which could also alter the prognosis later. The tumor size also impacts the stadium, which a main factor to be considered when we want to triage and prioritize which breast cancer patient to be treated first. [12,13]

This study has never been done before in Indonesia, especially in Tangerang. Some disadvantages are profound, and some cannot be undone. Recall bias is very likely due to long period from onset to interview. Indirect interview via whatsapp also could make bias, where we realize that direct interview with direct contact with patient is best to recall long time information. Due to inability of primary investigator to go to patients location and inability of patient to go to hospital frequently then it is cannot be avoided.

Some of the patients are having incomplete medical record and no phone number could be contacted in the medical record, some also cannot be contacted due to inactive phone number. Homogenecity of the sample due to just one study location also noted. Finally, confounding variable such as stadium and histological grade is not analyzed, due to inadequate sample amount.

Despite all of the deficiencies of our study, the investigator hopes this result could be reference study to be developed in more elaborate, longer period and more careful observation in society-based population. Such study hopefully could help to make breast cancer health care and services better in Indonesia in SARS-COV-2 Pandemic.

Conclusion

Newly diagnosed patients have younger age and larger tumor size during pandemic when we compare to before pandemic period, but no difference in onset term. Surveillance to society is needed to ensure older people with smaller tumor size to seek medical attention. This result is yet has to be proven in more elaborate, longer period and more careful observation in the next study.

References

1. WHO. GLOBOCAN 2020: New Global Cancer Data [Internet]. 2020. Available from: https://www.uicc.org/news/globocan-2020-new-global-cancer-data

2. Ng CH, Bhoo Pathy N, Taib NA, Teh YC, Mun KS, Amiruddin A, et al. Comparison of breast cancer in Indonesia and Malaysia - A clinico-pathological study between dharmais cancer centre Jakarta and university Malaya medical centre, Kuala Lumpur. Asian Pacific J Cancer Prev. 2011;12(11):2943–6. https://journal.waocp.org/article_25991_170657be316e64ec920745c8cc917a67.pdf

3. Kemenkes RI. Pedoman Pencegahan dan Pengendalian COVID-19. 2020.

4. Kaufman HW, Chen Z, Niles J, Fesko Y. Changes in the Number of US Patients with Newly Identified Cancer before and during the Coronavirus Disease 2019 (COVID-19) Pandemic. JAMA Netw Open. 2020; 3(8): e2017267. https://doi.org/10.1001%2Fjamanetworkopen.2020.17267

5. Kiziltan G, Tumer BKC, Guler OC, Ozaslan C. Effects of COVID-19 pandemic in a breast unit: Is it possible to avoid delays in surgical treatment? Int J Clin Pract. 2021; 75(12):1–5. https://doi.org/10.1111/ijcp.14995

6. Vanni G, Materazzo M, Pellicciaro M, Ingallinella S, Rho M, Santori F, et al. Breast cancer and COVID - 19: The effect of fear on patients' decision-making process. In Vivo (Brooklyn). 2020; 34:1651–1659. https://doi.org/10.21873/invivo.11957

7. Xu Z, Fan J, Ding J, Feng X, Tao S, Zhou J, et al. The Impact of COVID-19 on Primary Care General Practice Consultations in a Teaching Hospital in Shanghai, China. Front Med. 2021;8: 642496. https://doi.org/10.3389/fmed.2021.642496

8. Papautsky EL, Hamlish T. Patient-reported treatment delays in breast cancer care during the COVID-19 pandemic. Breast Cancer Res Treat. 2020; 184(1):249–54. https://doi.org/10.1007/s10549-020-05828-7

9. Undang Undang Nomor 6 tahun 2018 tentang Kekarantinaan Wilayah. Undang Undang Nomor 6 tahun 2018 tentang Kekarantinaan Wilayah. Natl Stand Agency Indonesia [Internet]. 2018;31–4. Available from: https://jdih.bsn.go.id/produk/detail/?id=730&jns=2

10. Malik D. Satgas COVID-19 Minta Orang Tua Usia 45 Tahun ke Atas Tak Keluar Rumah. 2020. Available from: https://www.viva.co.id/berita/nasional/1303383-satgas-covid-19-minta-orang-tua-usia-45tahun-ke-atas-tak-keluar-rumah

11. Kemenkes RI. Panduan Penatalaksanaan Kanker Payudara. 2018. p. 7–11. Available from: http://kanker.kemkes.go.id/guidelines/PPKPayudara.pdf

12. Breastcancer.org. Special Report: COVID-19's Impact on Breast Cancer Care. 2022. Available from: https://www.breastcancer.org/treatment/covid-19-and-breast-cancer-care

13. Curigliano G, Cardoso MJ, Poortmans P, Gentilini O, Pravettoni G, Mazzocco K, et al. Recommendations for triage, prioritization and treatment of breast cancer patients during the COVID-19 pandemic. Breast [Internet]. 2020; 52:8–16. https://doi.org/10.1016/j.breast.2020.04.006

Intracranial Solitary Fibrous Tumor in A 25-Year-Old Woman

Patricia Diana Prasetyo[1], Stephanie Marisca[1], Eka J. Wahjoepramono[2]

[1] Department of Anatomical Pathology, Faculty of Medicine, Jendral Sudirman Boulevard, Lippo Karawaci, Tangerang, Indonesia 15811
[2] Department of Neurosurgery, Faculty of Medicine, Jendral Sudirman Boulevard, Lippo Karawaci, Tangerang, Indonesia 15811

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Correspondance: Patricia Diana Prasetyo
E-mail : patricia.diana@uph.edu
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Abstract

Introduction: Intracranial solitary fibrous tumors (ISFTs) are extremely rare spindle cell tumors originating from dendritic mesenchymal cells expressing CD34 antigens that are usually benign, although malignant transformation had been reported. The knowledge of natural course and prognostic factors of ISFTs is still limited and the tumor is easily misdiagnosed.

Case Presentation: An intra-cranial extra-axial tumor tissue resection from a 25-year-old woman was evaluated in the Surgical Pathology Laboratory. Histologic findings (cellular spindle cell tumor with 'patternless' pattern, staghorn blood vessels and <5 mitoses per 10 hpf) and immunophenotype (positive for CD34, weakly and focally positive for STAT6) suggested a diagnosis of intracranial solitary fibrous tumor WHO Grade II.

Discussion: ISFTs have very low incidence in the CNS and are difficult to distinguish radiologically from meningiomas, thus post operative pathological examination and immunohistochemistry markers evaluations are the mainstay for diagnosis. ISFT is associated with NAB2-STAT6 gene fusion and may exhibits a wide spectrum of histological features. STAT6 immunohistochemistry is considered as one of the most sensitive diagnostic methods, while the evaluation of CD34 expression can be used as alternative diagnostic method despite having lower sensitivity.

Introduction

Solitary fibrous tumors (SFTs) are extremely rare spindle-cell mesenchymal neoplasms expressing CD34 antigens that was first described as a tumor arising from the pleura.[1] SFTs have subsequently been found in many different locations, although SFTs involving the central nervous system (CNS) is very rare,[2,3] most likely because of the low content of true connective tissue elements in the CNS.[4] The first cases of intracranial solitary fibrous tumors (ISFTs) were reported by Carneiro et al. in 1996. They reported seven cases of meningeal SFT that could be distinguished from fibrous meningioma based on morphologic and immunohistochemical grounds.[5] Since then, there are less than three hundred cases of SFTs that have been reported at various sites within the CNS in the English literature,[3] and ISFTs was reported to account for ~0.09% of all meningeal tumors.[2]

Solitary fibrous tumors in the CNS can affect both cranial and spinal meninges and may involve spinal nerve roots. The tumors are seen primarily in adults and may show invasion of brain parenchyma or nerve roots as well as the skull base.[3] Most CNS SFTs are intracranial, and just over one-fifth of tumors involve the spine. In decreasing frequency, ISFTs involve the

supratentorial compartment, infratentorial compartment, pontocerebellar angle, sellar and parasellar regions, and cranial nerves. Intraspinal tumors are mainly located in the thoracic and cervical segments.[4,6]

Intracradial solitary fibrous tumors (ISFTs) are usually benign, however, a growing body of literature demonstrates an unpredictable clinical course and an uncertain prognosis, where anaplastic or malignant transformation of benign ISFTs resulting in multiple local and distant recurrences has been described.[4] There has been changes in WHO classification and diagnostic criteria for SFT over the years. Current WHO Classification of Soft Tissue and Bone Tumors has classified SFT as a fibroblastic neoplasm with intermediate (rarely metastasizing) behavior.[7] The knowledge of natural course and prognostic factors of ISFTs is still limited. ISFT has also often been easily misdiagnosed with other types of brain tumors given that it has a very low incidence in the CNS and shows resemblance to meningioma or hemangiopericytomas, and thus remains a diagnostic challenge.[8,9] For that reason, this article intended to contribute the pathologic findings and results of immunohistochemical studies of a 25-year-old woman with ISFT.

Case Report

Pathologic Findings

An intra-cranial extra-axial tumor tissue resection from a 25-year-old woman was evaluated in the Surgical Pathology Laboratory. Routine H&E staining, special staining and immunohistochemical studies were performed after formalin fixation and paraffin-embedding. Light microscopy examination of the sections showed a cellular spindle cell tumor with “patternless” pattern and staghorn blood vessels. The neoplastic short spindle cells featured elongated nuclei. There was extensive background cautery artefact, which hampers assessment of mitotic activity. Mitotic activity was not readily identified (less than 5 mitoses per 10 high-power field). No definite necrosis was identified. No heterologous cartilaginous or “grungy” calcified matrix identified.

Immunohistochemical studies found that the neoplastic cells were positive for CD34. The neoplastic cells were only weakly and focally positive for STAT6. The neoplastic cells were negative for AE1/AE3, CAM 5.2, ERG, TLE1, SOX10, EMA and PR stains. INI1 immunohistochemistry was non-contributory. However, while there was complete lack of expression in the neoplastic cells, there was also lack of expression in the internal control (such as smooth muscle cells and endothelial cells). Thus, the lack of INI1 expression in the neoplastic cells may be caused by poor specimen immunoreactivity, possibly due to cautery artefact and/or specimen fixation issue, rather than true aberrant loss of expression in tumor cells.

Discussion

A diagnosis of intracranial solitary fibrous tumor WHO Grade II was suggested in a 25-year-old woman with an intracranial extra-axial tumor based on histologic findings and results of immunohistochemical studies. The majority of ISFTs are found in females. The tumors grow slowly, and certain patients may develop the symptoms of episodic headaches, gait imbalance, dizziness, sensory disturbance, hemiplegic paralysis or epileptic seizure, while other patients may be asymptomatic, with no distinctive local symptoms. Only when the lesions become large enough or infringe into the important functional areas, will clear clinical symptoms arise.[2]

Forming a pre-operative diagnosis for ISFTs is quite challenging due to the atypical symptoms and imaging manifestations. ISFTs are difficult to distinguish radiologically from meningiomas because of their overlapping imaging features.[10] Therefore, post-operative pathological examination and immunohistochemistry markers evaluations are the mainstay for diagnosis. The microscopic histology of ISFTs is similar to the SFTs in other parts of the body. The SFT tissue mainly exhibits a proliferation of spindle cells with a variety of growth patterns.[2] These spindle cells tend to be bundled in barely undulating fascicles and lack any specific arrangement, and thus often result in a “patternless pattern.” Deposition of collagen substance is increased in the cell sparse area. Crack or staghorn-like vascular is often prominent in the cell-intensive areas, characterized by small and/or large branching vascular spaces.[9] The current patient showed cellular spindle cell tumor with ‘patternless’ pattern and staghorn blood vessels.

The new World Health Organization Classification uses a 3-tiered grading system to help determine the prognosis of SFT. Grade I define benign lesions that correspond to the classic SFT pattern with relatively low cellularity, rich collagen, spindle cell lesion. Both Grades II and III define malignant lesions. Tumors with less collagen, more cellularity, hemangiopericytoma pattern and "staghorn" vasculature, with less than 5 mitoses per 10 high-power fields were defined as Grade II lesions, while Grade III lesions showed more than 5 mitoses per 10 high-power fields.[11] The lesions from this patient was classified as WHO grade II SFT because it showed cellular spindle cell tumor with “patternless” pattern, which was a storiform arrangement of spindle cells combined with a hemangiopericytoma-like appearance and increased vascularity of the lesion, staghorn blood vessels, and <5 mitoses per 10 hpf.

Immunohistochemical examinations are considered essential for proper diagnosis of ISFTs. The important immunohistochemical characteristics for successful diagnosis and treatment of SFTs include STAT6, CD34, CD31, ERG, Bcl-2 protein, and vimentin,[1,4] whereas it is usually negative for cytokeratin, EMA, SMA, PR, S-100 and GFAP.[9,12] Immunohistochemical studies in this patient found that the neoplastic cells were strongly and diffusely positive for CD34, whilst only weakly and focally positive for STAT6, and negative for ERG. The neoplastic cells were also found to be negative for AE1/AE3, CAM 5.2, TLE1, SOX10, EMA and PR stains, thus excluding the differential diagnosis such as metastasis and meningioma.[9,12-14]

Studies in molecular pathology have found that transcription repressor NAB2 and the transcription activator STAT6 are two adjacent genes located on the q13 band of 12th chromosome,[15] and furthermore, almost all SFTs have detected NAB2 and STAT6 fusion genes.[16] Over-expression of NAB2-STAT6 gene fusion was reported to induce cell proliferation, activates EGR1 target genes and their promoters, promotes gene expression, and disrupts EGR1-related metabolic balance, which is a decisive factor in the mutation process of SFT.[8] Accumulating evidence after the discovery of NAB2-STAT6 fusion gene has found that STAT6 nuclear staining is extremely sensitive and specific in ISFTs, which made STAT6 immunohistochemistry a powerful and key diagnostic modality for this neoplasm.[10] The STAT6 immunostaining can also help to exclude the possible diagnosis of meningiomas, because it is totally negative in this type of

intracranial tumor. However, absence of STAT6 nuclear expression by IHC staining may not exclude the possibility of ISFT.[17]

Combination with other immunohistochemistry markers might be helpful to establish a diagnosis in STAT6-negative ISFTs, although their specificities for ISFTs are not so high as STAT6.[18] Positive expression of CD34 was regarded as the most prominent characteristic of ISFTs and was often used for differential diagnosis before the discovery of STAT6-NAB2 fusion gene.[6] CD34 is a transmembrane glycoprotein that had been identified in endothelial cells, hematopoietic stem and progenitor cells, and fibroblast-related mesenchymal cells.[19] Previous studies reported that SFT had a diffuse and strong positivity for CD34 in 80% to 100% of cases,[20] whereas other studies also reported that 5%–10% of SFTs were negative for CD34.[17,21] However, the specificity of CD34 for ISFT is quite low,[13] and this marker can be also detected in other type of brain tumors.[17] The sensitivity of STAT6 for ISFTs was reported to be 96.6% in current literature,[17] whereas CD34 was reported to have 87.5% sensitivity.[8]

Conclusion

T Intracranial SFTs are an extremely rare mesenchymal neoplasms originating in the meninges. They have low incidence in the CNS and are difficult to distinguish radiologically from meningiomas, thus post-operative pathological examination and immunohistochemistry markers evaluations are the mainstay for diagnosis. STAT6 immunohistochemistry is considered as one of the most sensitive diagnostic methods, while the evaluation of CD34 expression can be used as alternative diagnostic method despite having lower sensitivity.

References

1. Suzuki SO, Fukui M, Nishio S, Iwaki T. Clinicopathological features of solitary fibrous tumor of the meninges: An immunohistochemical reappraisal of cases previously diagnosed to be fibrous meningioma or hemangiopericytoma. Pathol Int. 2000; 50(10):808-17. https://doi.org/10.1046/j.1440-1827.2000.01120.x

2. Wang ZY, Qiu K, Ma YH, Wang XT, Bao JJ, Zhang ZF, Liu XZ. Intracranial solitary fibrous tumors: A report of two cases and a review of the literature. Oncol Lett. 2016; 11(2):1057-1060. https://doi.org/10.3892/ol.2015.3985

3. Yang G, Deisch J. Intracranial Solitary Fibrous Tumor with Pseudopapillary Architecture: An Uncommon Tumor with Unusual Histopathology. N A J Med Sci. 2016 ;9(4):181-186. *10.7156/najms.2016.0904181]*

4. Gubian A, Ganau M, Cebula H, Todeschi J, Scibilia A, Noel G, Spatola G, Chaussemy D, Nannavecchia B, Gallinaro P, Coca A, Pop R, Signorelli F, Proust F, Lhermitte B, Chibbaro S. Intracranial Solitary Fibrous Tumors: A Heterogeneous Entity with an

Uncertain Clinical Behavior. World Neurosurg. 2019; 126:e48-e56. https://doi.org/10.1016/j.wneu.2019.01.142

5. Carneiro SS, Scheithauer BW, Nascimento AG, Hirose T, Davis DH. Solitary fibrous tumor of the meninges: a lesion distinct from fibrous meningioma. A clinicopathologic and immunohistochemical study. Am J Clin Pathol. 1996; 106(2):217-24. https://doi.org/10.1093/ajcp/106.2.217

6. Bisceglia M, Galliani C, Giannatempo G, Lauriola W, Bianco M, D'angelo V, Pizzolitto S, Vita G, Pasquinelli G, Magro G, Dor DB. Solitary fibrous tumor of the central nervous system: a 15-year literature survey of 220 cases (August 1996-July 2011). Adv Anat Pathol. 2011; 18(5):356-92. https://doi.org/10.1097/pap.0b013e318229c004

7. Demicco EG, Fritchie KJ, Han A. Solitary fibrous tumor. In: WHO Classification of Tumours Editorial Board, editor. WHO Classification of Tumours 5th Edition: Soft Tissue and Bone Tumours. 2020; 104–108.

8. Chenhui Z, He G, Wu Z, Rong J, Ma F, Wang Z, Fang J, Gao W, Song H, Zhang F, Di G, Jiang X. Intracranial solitary fibrous tumor/hemangiopericytomas: a clinical analysis of a series of 17 patients. Br J Neurosurg. 2021:1-8. https://doi.org/10.1080/02688697.2021.1944980

9. Cheng L, Ni H, Dai Y. Intracranial solitary fibrous tumor mimicking meningioma: A case report. Medicine (Baltimore). 2020; 99(50):e23504. https://doi.org/10.1097%2FMD.0000000000023504

10. Liu J, Wu S, Zhao K, Wang J, Shu K, Lei T. Clinical Features, Management, and Prognostic Factors of Intracranial Solitary Fibrous Tumor. Front Oncol. 2022;12:915273. https://doi.org/10.3389%2Ffonc.2022.915273

11. Louis DN, Perry A, Reifenberger G, et al. The 2016 World Health Organization Classification of Tumors of the Central Nervous System: a summary. Acta Neuropathol 2016;131(6):803–20. https://doi.org/10.1007/s00401-016-1545-1

12. Gopakumar S, Srinivasan VM, Hadley CC, Anand A, Daou M, Karas PJ, Mandel J, Gopinath SP, Patel AJ. Intracranial Solitary Fibrous Tumor of the Skull Base: 2 Cases and Systematic Review of the Literature. World Neurosurg. 2021;149:e345-e359. https://doi.org/10.1016/j.wneu.2021.02.026

13. Tariq MU, Din NU, Abdul-Ghafar J, Park YK. The many faces of solitary fibrous tumor; diversity of histological features, differential diagnosis and role of molecular studies and surrogate markers in avoiding misdiagnosis and predicting the behavior. Diagn Pathol. 2021;16(1):32. https://doi.org/10.1186/s13000-021-01095-2

14. Kasper E, Boruchow S, Lam FC, Zinn PO, Anderson M, Mahadevan A. "Hitting all the right markers to save a life" Solitary fibrous tumors of the central nervous system: Case series and review of the literature. Surg Neurol Int. 2012;3:83. https://doi.org/10.4103%2F2152-7806.99173

15. Rekhi B, Shetty O, Tripathi P, et al. Molecular characterization of a series of solitary fibrous tumors, including immunohistochemical expression of STAT6 and NATB2-STAT6 fusion transcripts, using reverse transcriptase (RT)-polymerase chain reaction (PCR) technique: an Indian experience. Pathol Res Pract 2017; 213(11):1404–11. https://doi.org/10.1016/j.prp.2017.08.011

16. Robinson DR, Wu YM, Kalyana-Sundaram S, et al. Identification of recurrent NAB2-STAT6 gene fusions in solitary fibrous tumor by integrative sequencing. Nat Genet. 2013; 45(2):180–5. https://doi.org/10.1038/ng.2509

17. Yamashita D, Suehiro S, Kohno S, Ohue S, Nakamura Y, Kouno D, Ohtsuka Y, Nishikawa M, Matsumoto S, Bernstock JD, Harada S, Mizuno Y, Kitazawa R, Ohnishi T, Kunieda T. Intracranial anaplastic solitary fibrous tumor/hemangiopericytoma: immunohistochemical markers for definitive diagnosis. Neurosurg Rev. 2021; 44(3):1591-1600. https://doi.org/10.1007/s10143-020-01348-6

18. Macagno N, Figarella-Branger D, Mokthari K, Metellus P, Jouvet A, Vasiljevic A, Loundou A, Bouvier C. Differential Diagnosis of Meningeal SFT-HPC and Meningioma: Which Immunohistochemical Markers Should Be Used? Am J Surg Pathol. 2016; 40(2):270-8. https://doi.org/10.1111/j.1750-3639.2011.00552.x

19. Sidney LE, Branch MJ, Dunphy SE, Dua HS, Hopkinson A. Concise review: evidence for CD34 as a common marker for diverse progenitors. Stem Cells. 2014 Jun;32(6):1380-9. https://doi.org/10.1002%2Fstem.1661

20. Cummings TJ, Burchette JL,McLendon RE. CD34 and dural fibroblasts: the relationship to solitary fibrous tumor and meningioma. Acta Neuropathol 2001; 102(4):349–54. https://doi.org/10.1007/s004010100389

21. Dermawan JK, Rubin BP, Kilpatrick SE, Gjorgova Gjeorgjievski S, Fritchie KJ, Goldblum JR, McKenney JK, Billings SD. CD34-negative Solitary Fibrous Tumor: A Clinicopathologic Study of 25 Cases and Comparison with Their CD34-positive Counterparts. Am J Surg Pathol. 2021; 45(12):1616-1625. https://doi.org/10.1097/pas.0000000000001717