

Vol. 7 No. 7 October 2019 – January 2020

MEDICINUS

JURNAL KEDOKTERAN
UNIVERSITAS PELITA HARAPAN

Diterbitkan oleh Fakultas Kedokteran, Universitas Pelita Harapan, Indonesia

ISSN 1978 - 3094
E ISSN 2622 - 6995

MEDICINUS

Journal of Faculty of Medicine
University of Pelita Harapan

Vol. 7 No. 7
October 2019 – January 2020
ISSN 1978-3094
E-ISSN 2622-6995

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Publish

February – June – October

Preliminary Study Using Medical Student Stressor Questionnaire in Faculty of Medicine Pelita Harapan University.

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Abstract

Citation : Marlina Mona, Preliminary Study Using Medical Student Stressor Questionnaire in Faculty of Medicine Pelita Harapan University. *Medicinus*. 2019 October; 7(7):205–208
Keywords: Stressor domain, MSSQ, stress among medical student
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Background : Best teaching program for students is certainly the main focus of the faculty. However, we must consider from the student perspective, cause student in Faculty of Medicine is high risk of being stress. Prolonged stress could harm the student physically and or mentally and will disrupt the competencies achievement. One of the validated tools for identifying a group of stressors is Medical Student Stressor Questionnaire (MSSQ).

Methods : A cross-sectional univariate done within 30 medical students batch 2016. Age around 16-18 years old consist of 8 male and 21 female.

Result : The highest stressor facing by the student was interpersonal related stressors (IRS) mean 2.547, followed by teaching and learning-related stressors (TLRS) 2.485, academic related stressors (ARS) 2.304, group activities related stressors (GARS) 2.259, drive and desire related stressors (DRS) 2.195, and social related stressors (SRS) 2.173.

Conclusion : All the stressors domains were in a high level of stress. Further research needed in larger population and level of the study

Introduction

As a lecturer, one of our job is delivering a good content and material in our expertise. Sometimes we are too busy to find the best methods in teaching, so the student could achieve all the competencies needed. However, the student success is not only because of the lecture capability in teaching. There are many aspects that could influence the student achievement. One of the contribution aspect is the student capability in stress management.^{1,2}

Stress is a changing situations that makes a tension and will affect a person both in physically and or mentally. The impact of stress could be positive and negative. The positive site could encouragie someone to be better, but if the stress prolong and the person could not manage the stress will

leads to anxiety, depression, sleeping disorders, decreased attention, reduced concentration, conflicts, cynicism, academic dishonesty and even leads to burnout. Burnout is a disorder consists of 3 symptoms. The symptoms are emotional exhaustion, depersonalization, and low accomplishment. All the negative symptoms could make the student have low achievement and even ended in committed suicide.^{1,3,4,5,6}

Medical school is one of the stressful study programs among others. Including in Faculty of Medicine Pelita Harapan University (UPH). In UPH learning goes through 2 phases. First is bachelor program/academic/preclinical stage for 7 semesters and second phase is professional/clinical phase for 4 semester. The characteristic of student year one is

around age 17 to 18 years old and graduates students from 12th grade high school.

Lots of stressful things facing by the medical student. The stress factor divided into academic and non-academic factors. Academic stressors such as excessive material to learn, tight schedule, teaching-learning methods, lots of examination, grading method, bad score and remedial process, some competencies that must be achieved, and so on. Non-academic stressors such as conflict with peer group and other personnel in the faculty, peer group expectation, not interested in medical school cause parents/family member wishes, family/social relation factor, and other factors.^{5,7}

Aim of the study was to know the stressors domains that are facing by the student and the level stress in all stressors domain.

Method

A cross sectional univariate measurement using Medical Student Stressor Questionnaire (MSSQ). Total statements are 40 divided among 6 domains. Data was calculated manually.

Validated tools used for identifying a group of stressors in medical is Medical Student Stressor Questionnaire (MSSQ). The MSSQ develop by Muhamad Saiful Bahri Yusoff, and Ahmad Fuad Abdul Rahim from Malaysia. It is consists of 40 items representing the six stressor domains randomly. Domain 1 is Academic Related Stressors (ARS), domain 2 is Interpersonal & Intrapersonal Related Stressor (IRS), domain 3 is Teaching and Learning Related Stressor (TLRS), domain 4 is Social Related Stressor (SRS), domain 5 is Drive & Desire Related Stressor (DRS), last domain is Group Activities Related Stressor (GARS).⁵ The stressors domain and all the items can be seen in Table 1.

Table 1. MSSQ stressors domain and items:

Stressors Domains	Items number	Statements Example
I: Academic Related Stressor (ARS)	1, 4, 7, 10, 12, 17, 19, 23, 25, 27, 30, 33, 36	No.10: Heavy workload No.33: Large amount of content to be learnt
II: Interpersonal and intrapersonal Related Stressor (IRS)	3, 5, 9, 26, 28, 31, 39	No.3: Conflict with other students No.28: Verbal or physical abuse by teacher(s)
III: Teaching and Learning Related Stressor (TLRS)	8, 14, 16, 20, 22, 35, 37	No.14: Lack of guidance from teacher(s) No.35: Not enough feedback from teacher(s)
IV: Social Related Stressor (SRS)	2, 18, 21, 24, 29, 38	No.18: Lack of time for family and friends No.29: Frequent interruption of my work by others
V: Drive and Desire Related Stressor (DRS)	6, 32, 40	No.6: Parental wish for you to study medicine No.40: Family responsibilities
VI: Group Activities Related Stressor (GARS)	11, 13, 15, 34	No.11: Participation in class discussion No.15: Feeling incompetence

Each statement answered using rating scale from 0 to 4. 0 means causing no stress at all, 1 means causing mild stress, 2 means causing moderate stress, 3 means causing high stress, and 4 causing severe stress. From the final calculation from each domain we got the range of stress level. The scales are 0-1.00 cause mild stress, 1.01-2.00 cause moderate stress, 2.01-3.00 cause high stress, 3.01-4.00 cause severe stress.

Result

There are 30 medical students batch 2016 volunteered, with 8 males and 21 females. Age around 16-18 years old. When the research conducted, batch 2016 is in the first year of the study. One of the questionnaire excluded because not giving the answer as instructed. Result in orders shown in Chart 1

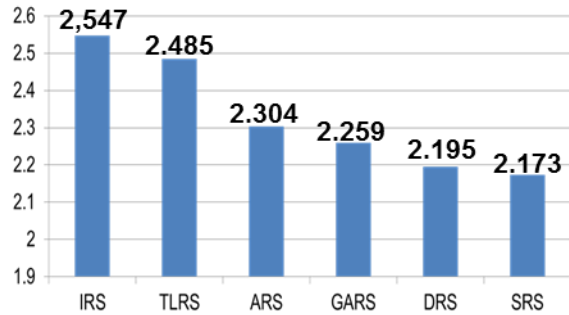


Chart 1. The highest stressors domain and the level of stress

Interpersonal & Intrapersonal Related Stressor (IRS) contributed as the highest stressor domain with 2.547, followed by Teaching and Learning-Related Stressors (TLRS), Academic Related Stressors (ARS), Group Activities Related Stressors (GARS), Drive and Desire Related Stressors (DRS), and Social Related Stressors (SRS) with 2.173 as the lowest score. The stress level in all stressors domain were high stress level with the range between 2.01-3.00.

Discussion

Although various studies provide different picture of the stressors domain but in the end, all the stressors will impact the academic domain. Highest stressors domain in UPH is dominated by IRS. This might be influenced by the process of adaptation that occurred during the early stages of education. In the other hands the academic stressors was not the highest domain because the learning material faced by the student when the research conducted not entered the medical core learning material yet.^{5,8,9}

Previous research also mention, the first year was the highest burden for the medical student, because the student needs to adapt from high school to new environment. Other research mention last year of study was the hardest, cause the learning environment was changing into doctor-patient interaction, work with other professions, and also thinking about career plan in the future. UPH don't have this data yet.^{10,11}

What we need to be considered is not only the highest stressors domain, but we must seek deeper the cause of high stress in all stressors domain. Cause low ability to adapt from various stressor domain in the first year will lead to poor academic achievement and will increase the dropout rates. Not only that, it will harm the student physically and or mentally. Good stress management will help student to cope the stressors.^{1,2}

This preliminary study give us the picture of what facing by the UPH medical student in the first year. We need to seek deeper with further study to help student achieve all the competencies. Next step of research will focus on bigger population, follow each step of every level of study, and bring along the qualitative research with students and education managers to find the cause of stress and solution.

Conclusion

Medical student in the first year needs to learn stress management, so they could cope the stressor and have a healthy live.

Acknowledgement

Highly gratitude to Faculty of Medicine Pelita Harapan University and all the participant in batch 2016.

Note

This research has been displayed in the proceeding book and presented in the short communications session at the Asia Pacific Medical Education Conference (APMEC) on January 11, 2020 in Singapore.

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Role Of Span-75 In Determining Prognosis Of Non-Thrombolysis Acute Ischemic Stroke Patients

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Abstract

Citation : Sutanto Anyeliria, Simanungkalit Astra Dea, Role Of Span-75 In Determining Prognosis Of Non-Thrombolysis Acute Ischemic Stroke Patients

Medicinus. 2019 October; 7(7):209–215

Keywords : acute ischemic stroke, non-thrombolysis, prognosis, SPAN-75 index

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Introduction: The SPAN-75 index is a modification of the SPAN-100 index as a prognostic tool in acute ischemic stroke patients. Previous studies were using SPAN index in cases of ischemic stroke patients treated with rTPA and in cases of intracerebral hemorrhage.

Aim: To determine the role of the SPAN-75 index as a prognostic scoring in patients with acute ischemic stroke who did not get thrombolysis therapy.

Method: The subjects were acute ischemic stroke patients at Siloam Hospitals Lippo Village who were not treated with thrombolysis therapy and had no disability before stroke onset during January to April 2019. Subjects were classified into a positive and negative of SPAN-75 index group. Disability due to stroke was assessed with Modified Rankin Score (mRS) at the time of admission and discharged from the hospital. This prospective study was analyzed by the Kruskal-Wallis test.

Result: Forty subjects (average age of 57 years old) consisted of 31 negative and 9 positive of SPAN-75. Based on the Kruskal-Wallis test, the SPAN-75 index was positively associated with a more severe degree of stroke disability at the time of admission ($p = 0.002$), but not related to the change in the degree of disability when the patient was discharged from the hospital ($p = 0.807$). Age ($p = 0.445$) and gender ($p = 0.578$) had no significant relationship with the degree of disability of acute ischemic stroke.

Conclusion: The SPAN-75 index is related to the degree of disability of acute stroke patients at the time of admission

Background

Stroke is the second most common cause of death worldwide with annual mortality reaching 5.5 million people.¹ Stroke is caused by a multifactorial etiology, both modifiable and non-modifiable risk factors.² High degree of stroke severity (NIHSS > 8) and age over 65 years are the main predictors that cause poor outcome in patients with ischemic stroke.³ The scoring

system commonly used in assessing the severity of acute stroke is the NIHSS (NIH Stroke Scale), which consists of 11 variables, with each variables are assessed with a score of 0 - 4. The NIHSS classify strokes into 5 categories, (1) without symptoms of stroke, (2) minor stroke, (3) moderate stroke, (4) moderate-severe stroke, and (5) severe stroke.⁴ Stroke Prognostication using Age and NIH Stroke Scale (SPAN) was created in 2012 by

Saposnik et al.⁵ with the aim of being a prognostic tool in acute stroke patients who received intravenous thrombolysis therapy with rtPA (recombinant tissue plasminogen activator). The SPAN index is calculated by adding the age of patients with NIHSS scores, then classified into two categories, namely, SPAN-100 is positive in patients with SPAN-100 scores greater than or equal to 100, and SPAN-100 is negative if the SPAN score is below 100. The SPAN-Index 100 were created with the rationale: (1) age and severity of stroke are the two most important prognostic factors in acute stroke, (2) patients over 80 years of age and high NIHSS scores (≥ 20) have a worse prognosis, and (3) the need for a simple index that is easier to apply than the scoring that is now available.⁵ Several studies have shown that the SPAN-100 index can assess the prognosis of stroke patients receiving rtPA therapy.⁵⁻⁷

Stroke not only causes a high mortality rate but also causes significant morbidity, around 50% of stroke patients will experience chronic disability.¹ The degree of disability or dependence for carrying out daily activities in stroke patients is generally assessed using mRS (Modified Rankin Scale). The mRS degree consists values from 0 to 6 which represent degrees of disability from asymptomatic to death.⁸ Research conducted by Fabiana et al showed the SPAN-100 index could predicted functional output (mRS) in stroke patients receiving tPA intravenous thrombolysis.⁹ Based on previous research, a positive SPAN-100 index was very difficult to achieve, even with a high NIHSS score.⁷ Therefore in 2015 Escabillas et al modified the SPAN-100 index (modified SPAN-100 index) by lowering the positive threshold value from 100 to 75. The study showed a negative SPAN-75 index related to ICHS (Intracerebral Hemorrhage Score) and a lower amount of cerebral hemorrhage.¹⁰ Most studies focused more on examining the SPAN index on the output of stroke patients receiving rt-PA as well as in cases intracerebral hemorrhage^{10,11}, so the role of the SPAN index in determining the prognosis of patients not treated with rtPA remains unclear. Until now there has been no research that examines the role of SPAN-75 in determining the prognosis of acute stroke patients. In this study we assessed the role of the SPAN-75 index in

determining the prognosis in acute stroke patients who were not receiving rtPA therapy.

Methods

Study design and population

This study was an observational prospective cohort study in patients with acute ischemic stroke who did not receive rtPA at Siloam Hospitals Lippo Village during January-April 2019 timeframe. Severity of symptoms and disability were assessed twice with NIHSS and mRS within 5 to 10 days in-patient care on hospital admission and discharge. Exclusion criteria were patients who experienced hemorrhagic transformation, had a history of previous stroke, had a disability before the onset of stroke, and went home on their own request before the treatment period was completed. The diagnosis of acute ischemic stroke was established by a neurologist with clinical judgement and non-contrast brain CT scan. Patient with SPAN index more than 75 were considered SPAN-75 positive while less than 75 were considered SPAN-75 negative. In the statistical analyses, factors considered potential confounders were education, age, comorbidities and number of previous stroke.

Statistical analysis

Statistical analysis was performed using PASW (Predictive Analytic Software) Statistics 25 (SPSS Inc., Chicago, Ill., USA). All data were checked for normality. Categorical variables were presented as frequency and percentage, while continuous data were expressed as mean and standard deviation or as medians and interquartile distances accordingly. Bivariate analysis was carried out using Kruskal-Wallis H analysis test, p-values ≤ 0.05 were considered significant. Our missing data analysis procedures used missing at random (MAR) assumptions. We used the MICE (multivariate imputation by chained equations) method of multiple multivariate imputation in STATA.

Results

The number of research subjects in this study were 40 subjects with NIHSS values at admission in minor, moderate, moderate-severe, and severe strokes respectively were 8 (20%), 30 (75%), 1 (2.5%), and 1 (2.5%) subject. In addition, NIHSS scores at

discharges were 15 (37.5%), 24 (60%), 1 (2.5%), and 0 (0%). The mRS at admissions with scores of 0 to 6 in a row were 0 (0%), 9 (22.5%), 13 (32.5%), 11 (27.5%), 6 (15%), 1 (2.5%), and 0 (0%), while for MRS at discharge were 0 (0%), 10 (25%), 20 (50%), 7 (17.5%), 2 (5%), 1 (2.5%) and 0 (0%).

As many as 31 subjects (77.5%) were in the negative SPAN-75 group and 9 subjects (22.5%) were in the positive SPAN-75 group. Based on sex, the sample in this study consisted of 16 male (40%), (12 in the SPAN-negative group, 4 in the SPAN-positive group) and 24 female (60%) (19 in the SPAN-negative group, 5 in the group SPAN-positive). The average age of the total sample of the study was 57 years. In the SPAN-75 negative group, the average age was 51 years old, while in the SPAN-75 positive group the average age was 75 years old.

The median NIHSS scale at admission was 11 in the positive SPAN-75 group and 7 in the negative SPAN-75 group. The median value of mRS at admission was 3 at SPAN-75 positive and 2 at SPAN-75 negative. In both groups there were no subjects with a scale of mRS 0 and 6. In the SPAN-75 negative group, 9 subjects (29%) experienced improvement and 22 subjects (71%) with no changes, whereas in the positive SPAN-75 group, there were 3 subjects (33.3%) with improvement, and 6 subjects (66.7%) with no changes. No deterioration in the degree of mRS was found in either the negative or positive SPAN-75 group.

Discussion

The SPAN-100 index was introduced in 2013 by Saposnik et al⁵ to help determine the treatment of stroke patients. The SPAN-100 index is calculated by adding the patients' age with NIHSS, with a value above or equal to 100 is classified as positive SPAN-100 and a value below 100 is classified as negative SPAN-100.⁵ Although other scoring systems have better prognostic strength and accuracy,¹² the SPAN-100 index is more practically applied in helping determine which patients have a better prognosis if thrombolytic or endovascular therapy is performed. In 2017, Escabillas et al modified the SPAN-100 index to SPAN-75 on the basis of the

difficulty of achieving a positive SPAN-100 value even with a high NIHSS score.¹⁰

This study assessed the role of SPAN-75 in determining the prognosis of acute ischemic stroke patients who were not treated with rTPA. The results showed that SPAN-75 had no significant relationship to the disability of patients when they were discharged from hospitals, which were assessed with mRS ($p > 0.05$). This was probably due to the short duration of follow-up (5-7 days), so that the mRS tended to have not experienced changes in either the SPAN-75 negative group or the SPAN-75 positive group. This possibility is consistent with the study of Nedeltchev et al which showed that the degree of the new mRS would show a significant change within 3 months after the patient was discharged from the hospital.¹³ Research conducted by Abilleira et al also showed the SPAN-100 index showed a significant relationship with the degree of mRS after 3 months.⁶

In the other hand, the study result showed a significant relationship between positive SPAN-75 value and a higher degree of mRS ($p < 0.05$). This result was in accordance with several previous studies which showed that age and severity of stroke, the two variables that make up the SPAN-75 index, were the main factors which affect the disability of acute stroke patients.^{14,15} Previous studies have shown that age over 65 years significantly increased the rate of disability in acute stroke patients as measured by the degree of mRS.¹⁴ Demchuk et al conducted a study which showed that patients with mild strokes (NIHSS score 1-5) compared with more severe strokes (NIHSS scores 11-15, 16-20, > 20) were associated with milder degrees of mRS (0-5).¹⁵ Other research also shows that the transition of mRS degrees also correlates with changes in NIHSS scores.¹⁶

The results of the analysis in this study showed that age was not directly related to the degree of mRS at admission or the change in mRS when the patient was discharged, even if added to the NIHSS score variable, which formed the SPAN-75 variable, showed a significant relationship with mRS at admission. This result was likely due to the uneven distribution of subjects in which the subjects below the

age of 45 years old were only 25% (n = 10) of the total sample, compared to subjects aged over 45 years who fill 75% (n = 30) of the total sample. Sex was also not associated with the degree of mRS either at the time of admission or changes in mRS when the patient went home (p <0.05). This result was different from previous studies¹⁴, where female sex tended to have worse degrees of mRS (> 2). This result was likely due to a small sample (n = 40) and a too short degree of follow-up of mRS.

Limitations

Limitations of our study are the short duration of follow-up so that significant changes in mRS degrees might be difficult to be achieved. Our study did not examine factors that increase the risk of positive

SPAN-100 such as hypertension, atrial fibrillation,⁵ congestive heart failure, and smokers.

Fundings

None

Conclusion

The SPAN-75 index is related to the degree of stroke disability in patients with acute non-thrombolysis ischemic stroke at admission but is not related to changes in the degree of disability when the patient is discharged from the hospital. There is no significant relationship between age and sex with the degree of stroke disability at the time of admission or at discharge.

TABLES

Table 1. Characteristics of study subjects (n=40)

	n	%
Age (years)		
≤65	30	75
>65	10	25
Sex		
Male	16	40
Female	24	60
NIHSS (NIH Stroke Scale)		
Admission		
Minor stroke (1-4)	8	20
Moderate stroke (5-15)	30	75
Moderate-severe stroke (16-20)	1	2.5
Severe stroke (21-42)	1	2.5
Discharge		
Minor stroke (1-4)	15	37.5
Moderate stroke (5-15)	24	60
Moderate-severe stroke (16-20)	1	2.5
Severe stroke (21-42)	0	0
MRS (Modified Ranking Scale)		
Admission		
Score 0 (Without symptoms)	0	0
Score 1 (Without significant disability)	9	22.5
Score 2 (Mild disability)	13	32.5
Score 3 (Moderate disability)	11	27.5
Score 4 (Moderate-severe disability)	6	15
Score 5 (Severe disability)	1	2.5
Score 6 (Died)	0	0
Discharge		
Score 0 (Without symptoms)	0	0
Score 1 (Without significant disability)	10	25
Score 2 (Mild disability)	20	50
Score 3 (Moderate disability)	7	17.5
Score 4 (Moderate-severe disability)	2	5
Score 5 (Severe disability)	1	2.5
Score 6 (Died)	0	0

Tabel 2. Bivariat analysis at admission

	mRS at admission n(%)					Total n (%)	p value
	1	2	3	4	5		
Age (years)							
≤65	7 (17.5)	11 (27.5)	7 (17.5)	4 (10)	1 (2.5)	30 (75%)	0.146
>65	2 (5)	2 (5)	4 (10)	2 (5)	0 (0)	10 (25%)	
Gender							
Pria	2 (5)	7 (17.5)	3 (7.5)	3 (7.5)	1 (2.5)	16 (40%)	0.431
Wanita	7 (17.5)	6 (15)	8 (20)	3 (7.5)	0 (0)	24 (60%)	
SPAN-75							
Negative SPAN-75	9 (22.5)	12 (30)	7 (17.5)	3 (7.5)	0 (0)	31 (77.5%)	0.002
Positive SPAN-75	0 (0)	1 (2.5)	4 (10)	3 (7.5)	1 (2.5)	9 (22.5%)	

Tabel 3. Bivariat analysis at discharge

	mRS evaluation at discharge n (%)			Total n (%)	p value
	Improvement	No change	Deterioration		
Age (years)					
≤65	8 (20)	22 (55)	0 (0)	30 (75%)	0.445
>65	4 (10)	6 (15)	0 (0)	10 (25%)	
Gender					
Pria	4 (10)	12 (30)	0 (0)	16 (40%)	0.578
Wanita	8 (20)	16 (40)	0 (0)	24 (60%)	
SPAN-75					
Negative SPAN-75	9 (22.5)	22 (55)	0 (0)	31 (77.5%)	0.807
Positive SPAN-75	3 (7.5)	6 (15)	0 (0)	9 (22.5%)	

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Association of Quality of Sleep and Decreased Short Term Memory Function in Medical Students of Pelita Harapan University

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Citation : Budianto Stevanie , Siahaan Yusak M.T. Association of Quality of Sleep and Decreased Short Term Memory Function in Medical Students of Pelita Harapan University Medicinus. 2019 October; 7 (7):216–222

Keywords : Quality of sleep, short-term memory, students, Pittsburgh Sleep Quality Index, Digit span

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Online First : October 2020

Abstract

Background: Memory is a place where information is stored from the learning process or experience. There are several types of memory , one of them is short term memory. Declining sleep quality is directly proportional to the decrease in short-term memory. Poor sleep quality is often associated with medical student due to exams or vast amount of tasks. Therefore, researcher wants to see whether there is significant correlation between sleep quality and short-term memory function in students.

Aim: To assess the association of the quality of sleep towards short term memory function of medical student of Pelita Harapan University.

Methods: This study was conducted with a cross-sectional method, with taking sample using the method of a simple random sample. A total of 90 respondents at University of Pelita Harapan were taken. Data collected sorted out according to the inclusion and exclusion criteria. Quality of sleep assessed with PSQI questionnaire while short-term memory assessed by Digit span backward test. Results processed with SPSS version 24 and tested with Chi Square.

Results: Data analyzed by Chi square test showed there are 33 students (58.9%) have poor sleep quality and short term memory function. There are also significant association between the quality of sleep and short term memory function (p value = 0.026)

Conclusion: There is significant association between the quality of sleep and short term memory function of medical student of Pelita Harapan University

Introduction

Memory is one of the most important aspect that can affect students performance in learning activities. It's definition is the process by which information obtained through learning activities or experiences, is stored and can be reused in the future.¹ Memory can be classified into three, which are short term memory, medium memory and long term memory.² Short term memory consists of a few chunks of information which will be stored in a coded form.³ Those information will be kept for a limited capacity and time. There are several factors that can affect memory, one of them is sleep quality.

Sleep is defined as the state of unconsciousness, but become aware when there is stimulus.² During sleep, the brain activity, which is an active process, will continue to run.⁴ The restoration of the body's energy is a function of sleep. This is needed by everyone to achieve optimal body condition for the next day. The need for optimal sleep duration for each person is different. It is influenced by many factors, one of them is age. For example, babies or toddlers need more sleep duration than adults. For young adults, the duration of sleep needed generally around 7 to 8 hours per day.⁵

A good sleep quality can be seen when someone has a good night's sleep or there were no distractions and difficulties during sleep until he wakes up. The quality of sleep can be assessed from several component in the Pittsburgh Sleep Quality Index (PSQI) measurement. There are seven indicators of sleep quality, which are subjective sleep quality, latency or difficulty when starting to sleep, duration, efficiency of sleep, sleep disturbances, use of sleeping pills and presence of disturbances during daytime activities.⁶

Based on the research conducted by Ajeng Hana Anjani Djajaatmadja in 2016, there was a positive correlation between poor sleep quality and decreased short term

memory in the elderly.⁷ This study shows that having a poor sleep quality tend to result to a decreased short term memory function. Another research by Weizhen Xie, Anne Berry, Cindy Lustig, Patricia Deldin and Weiwei Zhang in 2019 showed a similar result. This study had concluded that poor sleep quality was highly correlated with reduced working memory capacity in college students from University of California.⁸ However, contrary to the two previous studies, a research titled "Effects of sleep deprivation on cognitive and physical performance in university students" by Yusuf Patrick, Alice Lee, Oishik Raha, et al, which was conducted on 2017, showed that there was no correlation between sleep deprivation and cognitive performance.⁹ Negative correlation was also found in a study titled "The relationship between subjective sleep quality and cognitive performance in healthy young adults: Evidence from three empirical studies" by Zsofia Zavecz, Tamas Nagy, Adrienn Galko, Dezso Nemeth & Karolina Janacsek in 2020.¹⁰

Poor sleep quality is often associated with medical students, due to the large number of tasks or study material that has to be learned. This reason and inconsistency result among previous studies about sleep quality and short term memory function, drives the researcher to conduct a study to know whether there is a relationship between poor sleep quality and decreased short term memory function in medical students.

Materials And Method

This analytical study is an unpaired comparative analytic cross-sectional study design, which was carried out for 4 months, starting from January 2019 to April 2019. This study was conducted at the Faculty of Medicine of Pelita Harapan University. Minimum sample size estimation was calculated by a simple random sample method. The result was a total of 51 samples. Data was obtained through the filling out of the Pittsburgh Sleep Quality

Index (PSQI) questionnaire and Digit span test.

The materials used in this study include the following. Informed consent sheet, to indicate that the respondent agreed to be a sample in this study. Faculty of medicine of Pelita Harapan University demographic information as the list of sample for this study. PSQI questionnaire, which had been translated into Bahasa Indonesia, to assess respondent's sleep quality. Digit span test, to assess respondent's short term memory. Lastly, Depression, Anxiety and Stress Scales (DASS-42) questionnaire, which had been translated into Bahasa Indonesia, to determine whether the sample is under stress or not.

Faculty of Medicine of Pelita Harapan University students, class of 2016, 2017 and 2018 were taken as the subject for this study. Firstly, the researcher explained the purpose of the study and provided a DASS-42 questionnaire to determine whether the sample is stressed or not. Those who falls into the stress category were excluded from the study, while those who are not were continued to the next stage. This was because psychological conditions such as depression and anxiety may impair quality of sleep or short term memory functions. Therefore, this questionnaire made sure subjects that falls on stress or depression category was not included in this study. There were 3 aspects being monitored in this questionnaire, which are stress, depression and anxiety, that were assessed in DASS-42 questionnaire. If the subjects scored 0-14 in stress category, 0-9 in depression category and 0-7 in anxiety category, they were included in the study. A total score achieved above those range, shows that the subjects were under stress, depressed or anxiety. By this process, the researcher can filter the subjects before proceeding to the next process.

Later on, informed consent was given. After the subject agreed to participate in the study, their personal data, filled out PSQI

questionnaire and digit span test result were collected.

The total score obtained from PSQI questionnaire will give two results, which are good and poor sleep quality. A total score of < 5 indicate a good sleep quality, while ≥ 5 signify a poor sleep quality. There are 2 types of digit span test, which are forward and backward digit span test. In this study, backward digit span test was performed. It is said that short term memory performance is poor when the total score obtained < 6 , while ≥ 6 indicate a good short term memory performance.

All data that had been obtained then processed using SPSS software version 24.0 and tested with Chi square.

Results

Over 4 months of study, there were 90 students from Faculty of Medicine at Pelita Harapan University who met the inclusion and exclusion criteria. There were 39 male students (43.3%) and 51 female students (56.7%). The age varied from 18 to 25 years old and median value at the age of 19. The average body weight was 58.43 ± 8.00 , height was 165.31 ± 7.84 and body mass index was 21.28 ± 1.47 .

There were 56 students (62.2%) had poor sleep quality, while 34 students (37.8%) had good sleep quality. The result of short term memory function of the students, based on Backward digit span test, were 44 students (48.9%) had poor short term memory function and the other 46 students (51.1%) had good short term memory function.

Table 1. Subjects Characteristics

Subject Characteristics (n=90)	n
Gender	
Male	39 (43.3%)
Female	51 (56.7%)
Age (years)	
Mean ± SD	19.33 ± 1.08
Median	19
Min	18
Max	25
Weight (kg)	
Mean ± SD	58.43 ± 8.00
Median	57.50
Min	44.00
Max	87.00
Height (cm)	
Mean ± SD	165.31 ± 7.84
Median	165.0
Min	150.0
Max	192.0
Body Mass Index (BMI)	
Mean ± SD	21.28 ± 1.47
Median	21.88
Min	18.56
Max	23.60
Quality of Sleep	
Poor	56 (62.2%)
Good	34 (37.8%)
Short term memory function	
Poor	44 (48.9%)
Good	46 (51.1%)

Gender and Sleep Quality

In this study, there were 15 male and 19 female students who had good sleep quality, while there were 24 male and 32 female students with a poor sleep quality. The relationship between gender and sleep quality was insignificant because the p value obtained was 1.000 (p value >0.05).

Table 2. Association of Gender and Sleep Quality

	Quality of Sleep		Total	OR (95% CI)	P value
	Good	Poor			
Male	15 (38.5%)	24 (61.5%)	39 (100.0%)	0.950 (0.402- 2.243)	1.000
Female	19 (37.3%)	32 (62.7%)	51 (100.0%)		
Total	34 (37.8%)	56 (62.2%)	90 (100.0%)		

Gender and Short Term Memory

On table 5, there were 19 male and 27 female students had a good short term memory, while 20 male and 24 female

students had a poor short term memory. The relationship between gender and short term memory was also insignificant, as the p value was 0.854 (p value >0.05).

Table 3. Association of Gender and Short Term Memory Function

	Short Term Memory		Total	OR (95% CI)	P value
	Good	Poor			
Male	19 (48.7%)	20 (51.3%)	39 (100.0%)	1.184 (0.514- 2.728)	0.854
Female	27 (52.9%)	24 (47.1%)	51 (100.0%)		
Total	46 (51.1%)	44 (48.9%)	90 (100.0%)		

Sleep Quality and Short Term Memory

The relationship between sleep quality and short term memory function was tested with Chi square in SPSS program. The result obtained indicate that there is significant relationship between the two, as the p value was 0.026 (p value <0.05). Poor sleep quality result to a decrease in short term memory function. This can be seen through the presence of 33 students with poor sleep quality had a poor short term memory function, while there were only 11 students with good sleep quality and poor short term memory function.

Table 4. Association of Sleep Quality and Short Term Memory Function

Variable	Short Term Memory		Total	OR (95% CI)	P value
	Good	Poor			
	Quality of Sleep	23 (67.6%)			
	Good	Poor			
	23 (41.1%)	33 (58.9%)	56 (100.0%)		
Total	43 (47.8%)	47 (52.2%)	90 (100.0%)		

Discussion

This study aims to determine the association between sleep quality with a decrease in short term memory function of medical students at Pelita Harapan University. Based on the result that had been obtained, the p value was 0.026, indicating that there was a strong relationship between the two variables. There was a significant difference in total number of students who had poor short term memory function on a good sleep quality and poor sleep quality. There were 11 students (32.4%) and 33 students (58.9%) respectively.

The result obtained was in line with the research conducted by Ajeng Hana Anjani Djajaatmadja (2016) entitled "Relationship between Sleep Quality and Short-term memory in Non-dementia Elders" with p value 0.001 (p value <0.05). This study stated that disturbances in sleep result in poor sleep quality and eventually causes a decrease in short term memory function.⁷ It was supported by another study by Ady Nugroho Solikhin et al (2016) entitled "The Relationship between Sleep Duration and Short term memory of students at Darul Hikam middle school in Bandung Academic Year of 2015-2016". Analysis between the two variable had a p value of 0.042 (p value <0.05).¹¹ Similar result was also obtained by a study conducted by Ayesha Uddin (2015) entitled "Effects of Sleep on Vigilance, Short Term Memory, and Learning in College Students" with a p value of 0.008 (p < 0.05).¹²

Poor sleep quality can cause a decrease in short term memory function. This is due to the presence of neural activation in the prefrontal and parietal cortex during sleep, especially in slow-wave sleep. Neural activity affects the anterior cingulate cortex (ACC), which has an important role in regulating level of attention. According to stages of memory formation, in order for information to enter short term memory, a good attention is needed. This will allow information from sensory, auditory or visual stimulus can be forwarded from ACC to

enthorinal cortex (EC) in the hippocampus, which is a short term memory storage. Poor sleep quality interfere this process, resulting a decrease of neural activation in ACC and disturbing the function of EC. As a result, short term memory function will also decrease.^{13,14} In addition, memory storage process is said to be more efficient during sleep, therefore sleep deprivation will also affect memory function.¹⁵

Based on the discussion above, it can be concluded that there is significant association between sleep quality and a decrease in short term memory function on medical students of Pelita Harapan University.

In this study, Chi square test was also performed to test between the variable of gender and sleep quality. This test was carried out to see whether or not gender has an association with sleep quality. The p value result was 1.000 (p value > 0.05). This shows gender has insignificant relationship with one's sleep quality. However, this result was contrary from previous study by Yaqoot Fatima et al (2016), which stated that women have a greater predisposition to poor sleep quality compared to men.¹⁶

In addition to seeing the relationship of gender with sleep quality, its relation with short term memory was also seen. The p value obtained was 0.854 (p value > 0.05), so it can be concluded that there was insignificant relationship between gender and short term memory. This too, contrary to the research conducted by Dr. Selwin Gabriel et al (2016), which states that there was a meaningful relationship between the two variable. Dr. Selwin's research used Word list recall to assess short term memory function¹⁷, while this study use Backward digitspan test. The difference of measurement tool use may be the cause of different results obtained.

There were several limitations in this study. This research does not discuss other factors that might affect sleep quality or short term

memory function, such as dwelling, diet and others. Data taken on subjects was only once, therefore increasing the risk of invalid result. Therefore, further research is needed by including other confounding factors, and if possible, data collecting process could be done more than once to get a more valid result.

Conclusion

There is a significant relationship between sleep quality and short term memory function among medical students of Pelita Harapan University.

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Management of Autoimmune Hemolytic Anemia in the Midst of Coronavirus Disease 2019 Pandemic: A Case Report

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Citation : Kurniawan Andree , Halim Devina Adella. Management of Autoimmune Hemolytic Anemia in the Midst of Coronavirus Disease 2019 Pandemic: A Case Report
 Medicinus. 2019 October; 7(7):223–228
Keywords : -
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Online First : October 2020

Abstract

Introduction : The novel coronavirus disease 2019 (COVID-19) has become a pandemic COVID-19 has involved all people, it can be severe and life-threatening in a certain population such as those with comorbidity. Autoimmune hemolytic anemia (AIHA) is an autoimmune hematologic disease characterized with antibodies production that binds to red cell surface antigens. In this pandemic, several concerns have been raised by autoimmune disease clinicians and patients regarding the use of immunosuppressive drugs. In this case report, we illustrate the problems of autoimmune hemolytic anemia patient when she got active case.

Case Illustration : A 28 years old lady was admitted to the hospital owing to fatigue and tired during exercise for two weeks. She had been diagnosed with autoimmune hemolytic anemia before and was not comply with the treatment. This patient has been reevaluated of having AIHA from the symptoms of fatigue, enlarged spleen, low hemoglobin, increased reticulocytes, signs of hemolytic in blood smear examination, increased indirect bilirubin, LDH and the Combs' test result was given positive. She received methylprednisolone 2 mg/kg of body weight intravenously, washed packed red cells (PRC), calcium and proton pump inhibitor. She was discharged at the seventh day since admission and she was prescribed oral methylprednisolone equal to 1 mg/kg body weight.

Conclusion

This is an educated case of non-compliance of AIHA that should be given high dose steroid and blood transfusion during hospitalization amid the COVID-19 pandemic. The recommendation of treatment for AIHA was still the same as before the pandemic occur.

Introduction

The novel coronavirus disease 2019 (COVID-19) has become a pandemic since it was announced by World Health Organization (WHO) at the end of January 2020. The COVID-19 pandemic is worsening globally. Nowadays, the virus has rapidly spread around the world. Until this article was written, the positive cases

have increased to 4,524,679 and 303,345 deaths worldwide. In Indonesia there were 16,006 positive cases and 1,043 death cases.¹ According to the current literature, COVID-19 has involved individuals aged 30-80 years and has low mortality in healthy individuals but it can be severe and life-threatening in certain population such as those with comorbidity.²

Autoimmune hemolytic anemia (AIHA) is the clinical condition in which antibodies of immunoglobulin G (IgG) and/or immunoglobulin M (IgM) bind to red cell surface antigens and initiate red cell destruction via the complement system and the reticuloendothelial system. AIHA is characterized by the production of autoantibodies directed against red blood cells (RBC). The treatment of AIHA depends on the type of antibodies and the course of the disease. Steroid and immunosuppressant agent were the mainstay of treatment beside splenectomy. In certain cases, the autoimmune hemolytic anemia needs blood transfusion for patient with extremely severe anemia.³

During the pandemic, several concerns have been raised by hematologist, autoimmune disease clinicians, and as well as autoimmune patients who took immunosuppressive drugs. There is a concern whether immunosuppressant treatment might increase the risk of severe COVID-19.⁴ The other concern was on the blood availability in the community. The blood supply from the donor was decreased during the pandemic.⁵ In this case report, we illustrated the problems of autoimmune hemolytic anemia patients when they got active case. As the COVID-19 cases had unfolded worldwide, the information would be so crucial for patients and clinicians to make evidence-based decision in how we should manage AIHA during the pandemic.

Case illustration

A 28 years old lady admitted to the hospital owing to fatigue and tired during exercise for two weeks. She was diagnosed autoimmune hemolytic anemia one year ago. She was hospitalized three times with the similar complaints, fatigue and

tiredness. She took prednisone 50 mg daily with other vitamins. However, she frequently stopped to consume it when there were no symptoms felt. Her condition had ever been complicated with tuberculosis peritoneal and she took the tuberculosis drugs for 9 months. There is no history of blood transfusion in one month before.

When she arrived in the emergency ward, firstly, she was screened for COVID-19 and the result was negative. The vital signs were stable. The eye looked pale and slightly icteric. The spleen was enlarged with the size of *schuffner* 4. The others physical examination was unremarkable. The initial hemoglobin was 3.2 g/dl, normal leucocyte and low platelet 99,000/mcL. The mean corpuscular volume was 120 fl and the reticulocyte was increased to 3.5%. The blood smear showed normocytic anemia, spherocyte, and helmet cells. Both indirect bilirubin and lactate dehydrogenase (LDH) was increased to 3mg/dL and 1027 U/liter, respectively. The combs test showed autoantibodies to red blood cells with positive IgG and complement 3 (C3).

She was diagnosed warm type autoimmune hemolytic anemia with severe anemia. She was given methyl prednisolone 2 mg/kg body weight intravenously, calcium tablet 500 mg three times daily, and proton pump inhibitor omeprazole 20 mg daily. She was planned to receive washed packed red cells (PRC), but there was a delay and given on the second day after admission. A total of 5 unit washed PRC with furosemide prophylaxis were given, the hemoglobin was increased to 6.8 g/dl in the day four. She was discharged at the seven day of admission with hemoglobin 13 g/dl, and she was prescribed daily with methyl prednisolone equal to 1 mg/kg body weight, calcium, omeprazole and folic acid orally. The detail of hemoglobin results can be seen in figure 1.

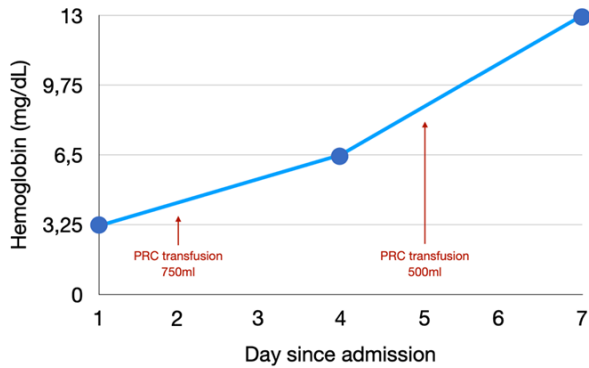


Figure 1. The hemoglobin results

Discussion

The diagnosis and management of AIHA continued to be challenging in current practice. It was related to an incomplete

understanding of the pathophysiology of disease process, complexity of initiating factors and lack of evidence in the standardized therapy. However, it became more complicated throughout the pandemic era. This patient had been reevaluated of having hemolytic anemia from her complaints of fatigue, enlarged spleen, low hemoglobin, increased reticulocytes, signs of hemolytic in blood smear examination, increased indirect bilirubin and LDH. The Coombs test result confirmed her of having AIHA warm type. The algorithm of AIHA diagnosis can be seen in figure 2. The low platelet should be thought several differential diagnoses such as thrombotic microangiopathy or Evan syndrome.⁶

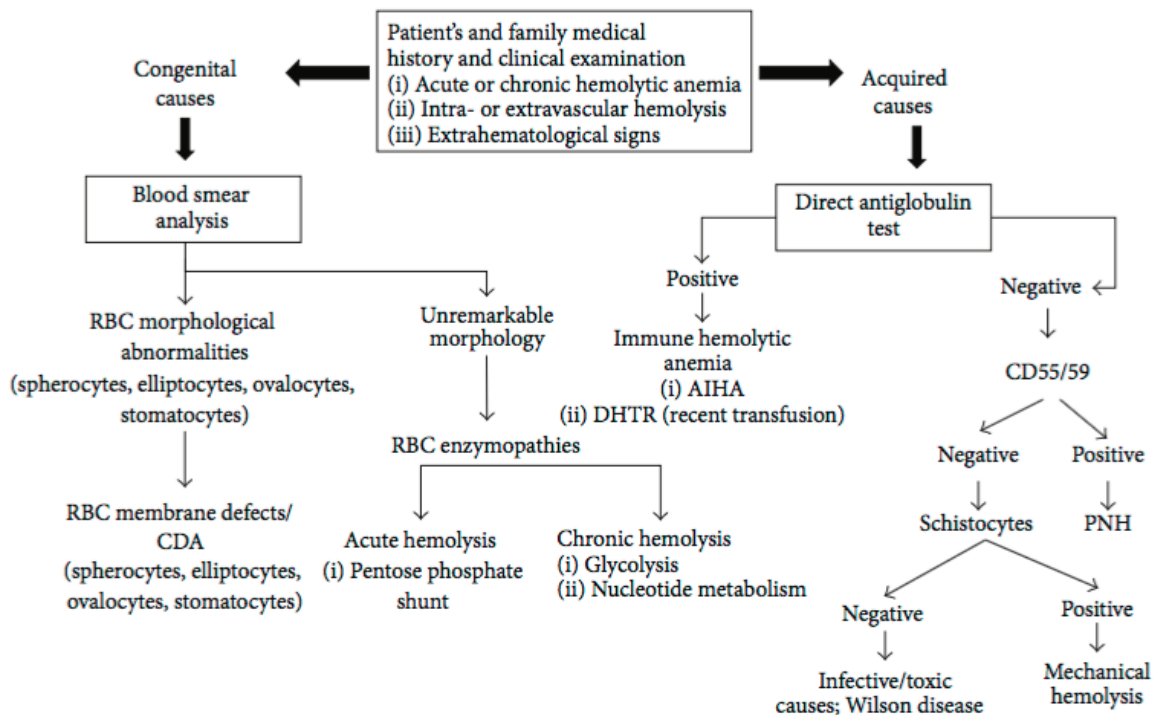


Figure 2. Diagnostic algorithm of hemolytic anemia.⁶ RBC: red blood cells; AIHA: autoimmune hemolytic anemia; DHTR: delayed hemolytic transfusion reactions; CDA: congenital *dyserythropoetic* anemia; PNH: paroxysmal nocturnal hemoglobinuria

She was planned on the first day of hospital stay to received blood transfusion of washed PRC due to her condition, severe anemia. Unfortunately, there was limited supply of blood in the red cross society. Thus, she was transfused in the second day. The challenges faced by the blood banks were to secure and protect the blood supply while the demand for blood and blood product my decrease during a pandemic due to postponement of elective surgeries, measures such as physical distancing and a large scale social restricted policy in the city may result in a larger decline in blood supply and an overall shortage of blood products.⁵

The patient was given high dose of steroid due to severe acute of AIHA. The first line treatment of warmed type AIHA was steroid with immunosuppressant dose. The patient had previous three episodes of severe anemia in the past year. Evaluation of refractory of AIHA should be in a consideration. Barcelini et al proposed the definition of refractory AIHA in the following scenarios: (1) Requirement of >20 mg of prednisone daily (or equivalent corticosteroid) to maintain hemolysis control; (2) Clinically significant relapse (hemoglobin <11 g/dl or symptomatic anemia with ongoing evidence of hemolysis); or (3) Intolerance to a currently effective treatment. If the hemolysis continued when the prednisone was being tapered, the second-line treatment with immunosuppressant can be considered.⁷

The dose of steroid was tapered after the hemoglobin value increased in day 5 of hospitalization. The increasing of hemoglobin might be due to the blood transfusion. The steroid would work after 5-7 days of administration. After the fifth day of given high dose steroid, the steroid was tapered to 1 mg/kg body weight dose. On the seventh day, the patient's hemoglobin became normal 13 g/dl. She was discharged on day seven of hospitalization with orally steroid equal to 1 mg/kg body

weight dose. Although steroid had led good response in warmed type AIHA, the complication of the treatment especially, the risk of infections remained as major area of concern. When it was used as pulse or high dose therapy, steroid might cause side effects on cardiac. This concern became even more pronounced during the COVID-19 pandemic. Existing clinical data have not confirmed the use of corticosteroid towards the risk of COVID-19 infection and manifest as more severe case.⁸ The universal precaution related to the prevention of contracting the disease should be done, such as using face mask, physical distancing and hand washing with soap and water regularly.⁹

The patient was educated to discuss any further complaints by teleconference with the physician. The dose of steroid was planned to be tapered at home after three weeks of treatment with a stable hemoglobin value. In many locations, going to a health care facility might increase the risk of being contracted by COVID-19. Most autoimmune disease patients should therefore be managed by phone, text, or email to follow-up their symptoms and should have less frequent blood counts. Nonetheless, certain condition who was unstable may need monitoring by regular check of blood counts. The patients should be educated to decrease the steroid dose weekly and called the healthcare if they develop symptoms of fatigue.⁸

AIHA patients, like other hematologic autoimmune disease who were stable on low dose of immunosuppressive drugs, should be maintained without treatment adjustment during COVID-19 pandemic. Changing the treatment were requiring increased in monitoring and could potentially result in relapse, thus it might be riskier than making no changes. For patients on higher doses of corticosteroid or immunosuppressive drugs, there were still no data to decrease or change to alternative

treatment because of limited options of treatment.⁸

Conclusion

This is an educational case of non-compliance patient in AIHA treatment that should be given high dose steroid and in need of blood transfusion during hospitalization during the COVID-19 pandemic. There was still a scarce evidence to associate between high dose steroid consumption and the risk of severe COVID-19 infection. The recommendation of treatment of AIHA was still the same as before the pandemic occurred. Further study is needed to be done for evaluating the risk of using high dose steroid regarding the risk of COVID-19 infection.

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Natural History and Risk Factors of Infantile Atopic Dermatitis: A Case Report and Literature Review

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Citation : Christopher Paulus Mario , Hung Maggie Stella. Natural History and Risk Factors of Infantile Atopic Dermatitis: A Case Report and Literature Review
Medicus. 2019 October; 7(7):229 – 235
Keywords : Atopic dermatitis, infant, risk factors
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Online First : October 2020

Abstract

Atopic dermatitis (AD) or atopic eczema is one of the most common forms of pediatric dermatological skin conditions, primarily beginning in childhood with a variable natural course characterized by intense pruritus and eczematous lesions. This condition requires multifactorial interplay and risk factors to explain the pathogenesis. We hereby report a case of a two-month-old male who presented with widespread erythematous lesions, excoriations, and dry skin since one day before admission. The antenatal history showed use of antibiotics during pregnancy, familial history of atopy, and non-exclusive breastfeeding which are all known risk factors. Dermatological examination revealed skin phototype III with diffuse erythematous patches scattered on the face, trunk, upper and lower limbs, and groin followed with excoriations and palmar hyperlinearity. Further laboratory and histopathological examinations were not conducted. The patient was treated with topical corticosteroid and emollients, resulting in a notable improvement without any further flares. A thorough history taking and physical examination must be conducted to establish the diagnosis based on the Hanifin and Rajka criteria and identify risk factors such as genetic factors, impaired skin barrier, and environmental factors and microbial exposure, which may play a protective or harmful role in AD development. Holistic treatments consist of pharmacological and non-pharmacological treatments, with significant emphasis on education to the patient and caregiver(s) to improve quality of life and prevent exacerbations and infectious complications while minimizing potential medication side effect

Introduction

Atopic dermatitis (AD) is a chronic, relapsing-remitting inflammatory skin disease characterized by pruritic eczematous lesions. The pathogenesis of AD is multifactorial consists of immune dysregulation, genetic susceptibility, environmental factors, and impaired barrier function.¹ With an estimated global prevalence of nearly 230 million, AD is considered one of the most common chronic conditions.² AD affects 10-20% of children and roughly 60% of cases manifested during the first year of life, posing a significant burden on health-care resources and patients' quality of life.³ In developing countries, AD prevalence appears to be increasing, likely due to an increase in urbanization, pollution, Western diet consumption, and obesity.⁴

This report describes a case of a two-month-old male with a diagnosis of AD. Owing to the peculiarity and risk factors of the case, it serves as a unique opportunity to present the risk factors interplaying in the pathogenesis leading to the development of the disease.

Case Illustration

A two-month-old male brought to the emergency department presented with generalized erythematous macules, excoriations, and dry skin first appeared one day before admission. The macules started on the patient's cheeks spreading to the trunks, upper and lower limbs, and groin area. The patient cried inconsolably during

scratching episodes, particularly during night time. The patient was born full-term at 40 weeks and two days by vaginal delivery with a birth weight of 3000 grams. Pregnancy was complicated due to intrauterine infection necessitating the use of oral antibiotics. Nutritional history revealed non-exclusive breastfeeding with the use of formula milk due to parents' concern of inadequate breast milk. Growth and development and immunization history were unremarkable. He has non-consanguineous Balinese parents and there was a history of similar illness in the family from the mother (atopic dermatitis). The personal hygiene of the baby was maintained with regular twice-daily baths with baby soap.

The physical examination comprising of vital signs and general examination were within normal limit. Nevertheless, dermatological examination showed skin phototype III with diffuse erythematous patches scattered on the face, trunk, upper and lower limbs, and groin followed with excoriations and palmar hyperlinearity (Figure 1). A skin biopsy and laboratory examinations were not performed due to the disapproval of the parents.

Diagnosis of infantile AD was concluded based on the history taking and physical examination following Hanifin and Rajka criteria. The patient was given hydrocortisone 2.5% cream q12hr and emollient of urea 10% q12hr. Appropriate education was discussed with the patient's family. After one week of treatment, the condition has improved and resolved with no further flare noticed.

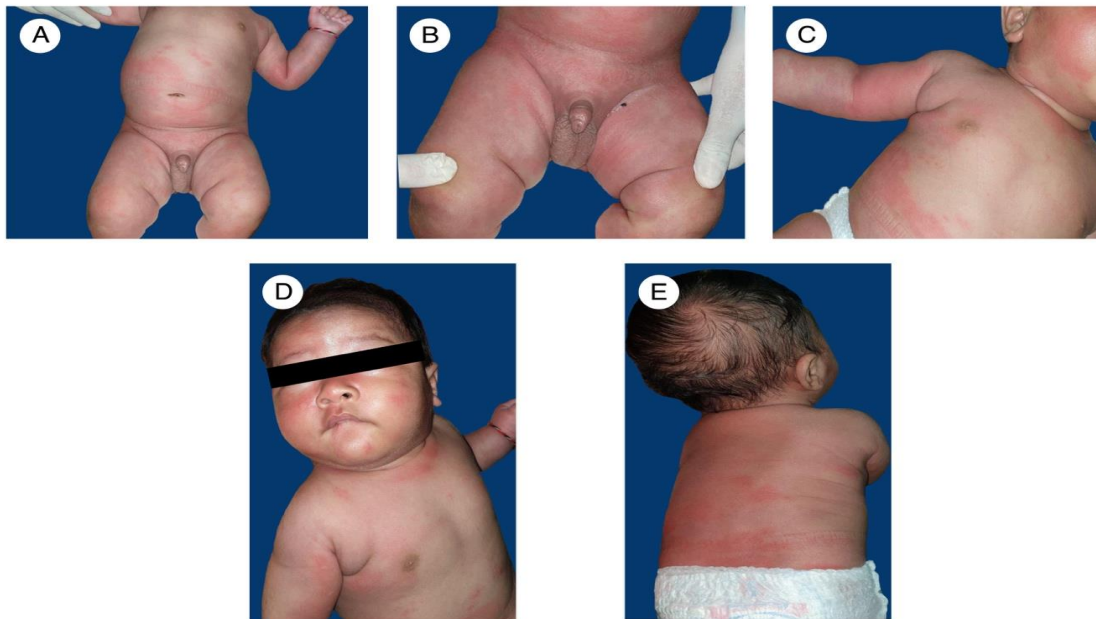


Figure 1. Clinical appearance and dermatologic findings of the patient where diffuse erythematous patches were observed over the face, trunk, upper and lower limbs, and groins area (A-E)

Discussion

In this case, we presented a case of the first flare episode of AD in a previously healthy young baby. The case represented several proposed risk factors of developing atopy,

subsequently manifesting as AD. These risk factors are 1) genetic factors, 2) impaired skin barrier function, and 3) environmental factors and microbial exposure (Figure 2).^{5, 6}

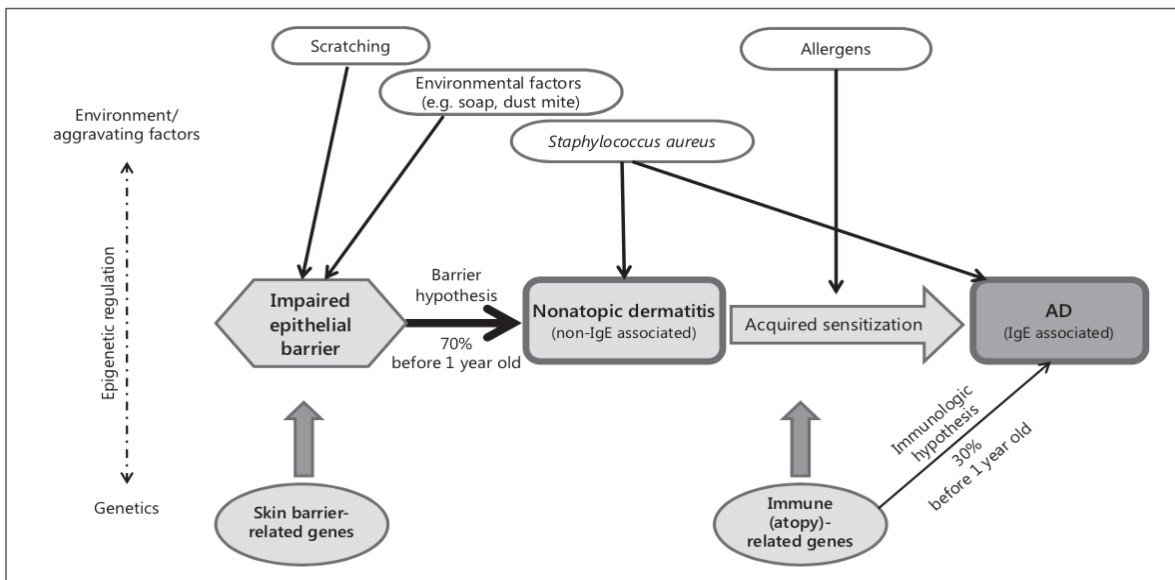


Figure 2. Risk factors contributing to the natural history of AD⁵

Genetic factors serve as an essential risk factor for AD in which positive parental history in AD patients and in twin studies showed a higher concordance rate in monozygotic twins compared to dizygotic twins. Genetics also plays a role in filaggrin (FLG) gene encoding the epidermal barrier protein, filaggrin, in which it is reported that loss-of-function mutations and downregulation of FLG lead to impairment of barrier function.^{6,7}

Essentially, an intact epidermal is needed for the skin to function as a physical and chemical barrier. The genetically altered epidermis or lipid composition prevented the skin barrier function leading to dysfunction and inflammation. Additionally, altered epidermal barrier allows easier and complemented environmental allergen penetration through the skin,

facilitating the recognition of the allergens with the local antigen-presenting cells and immune effector cells leading systemic immunoglobulin E sensitization and transition from the non-atopic state to the atopic state of the disease. The defective skin barrier in AD also predisposes to colonization or infection by pathogenic microbes whose exogenous proteases can also further damage the skin barrier^{5,7}

Lastly, environmental factors and microbial exposure shared its role as a risk factor in which it was found that environmental risk factors such as climate, urban versus rural setting, diet, breastfeeding and time of weaning, obesity and physical exercise or tobacco smoke and pollution have been proposed (**Table 1**).⁵

Table 1. Environmental risk factors for AD⁵

Factor	Associated Effect
Climate	
Low outdoor temperature	Increased risk
UV light exposure	Protective
Urban vs. rural setting	
	Increased risk
Diet	
Fresh fruits	Protective
Fish (During pregnancy)	Protective
Fast-food	Increased risk
Breastfeeding	
	Protective
Delayed weaning	
	Increased risk
Obesity	
	Increased risk
Pollution/tobacco smoke	
	Increased risk

Exclusive breastfeeding and avoidance of complementary feeds during the first 3-4 months of life have shown a protective risk against atopic dermatitis during infancy and childhood asthma, but not in later life.⁸ Association between atopy and exposure of cigarette smoke during in utero and early childhood is not yet clear, but exposure to parental smoking increase risk of AD and early childhood wheeze.⁸⁻¹⁰ Obesity plays a role in the immune system that modulates the severity of the atopic disease. The retrospective case-control pediatric cohort study demonstrated that obesity persisting more than five years and starting early in life (before 5) is associated with increased risk for AD and AD severity.⁶

Studies also suggested that microbial exposure could play its part in the development of AD. Antenatal antibiotics exposure associated with increased risk of AD in a dose-related manner.¹⁰ Postnatal antibiotics exposure in a meta-analysis study estimated increased odds of AD in children. It also plays a role in microbiota changes, knowing that the microbiota takes part in the immune response. In addition, skin microbiota is also found to be involved in the homeostasis of the immune system of skin and may also have an impact on AD.⁵ While a study suggests an association between the skin microbiome and AD, it remains unknown whether dysbiosis of the skin directly causes AD or simply reflects the impaired epidermal barrier and immune dysregulation of AD.¹⁰ These risk factors further support the underlying immune mechanisms in AD.

Immunopathogenesis of AD involved alteration of the innate and adaptive immune system. In AD, a decrease in the antimicrobial peptides has been observed and may contribute to the susceptibility towards infections in AD patients. A biphasic inflammation also characterizes immune response in AD, in which a Th2-

biased immune response (Interleukin [IL]-4, IL-13, thymic stromal lymphopoietin [TSLP], and eosinophils) is predominant in the initial and acute phase of AD. In contrast, in chronic AD skin lesions, a Th1/Th0 dominance has been described (interferon [IFN]- γ , IL-12, IL-5, and granulocyte-macrophage colony-stimulating factor [GM-CSF]). Additionally, a lesional and healthy skin of AD patients is frequently colonized with *Staphylococcus aureus* which exacerbates or aggravates skin lesions.⁵

Dermatological manifestations of AD are characterized by multiple erythematous papulovesicles with distribution varying following with the patient's age and disease activity. Based on age, AD can be classified into three groups, infancy (0-2 years), older childhood (2 years-puberty), and adulthood. Collectively, with the history taking, dermatological manifestation, age of manifestation, and/or supportive examinations and in unison based on Hanifin and Rajka criteria, AD can be diagnosed.⁷

Management of AD is based on the five pillars of therapy constituting of 1) education and empowerment of patients and caregiver(s), 2) avoidance and modification of environmental trigger factors, 3) rebuilding and maintenance of optimal barrier function, 4) clearance of inflammatory skin disorders and 5) control and elimination of the itch-scratch cycle.¹¹

Education plays a vital role in the management of AD in which physicians must emphasize the importance concerning the disease, therapy (why and how to take care of the skin), trigger factor, and prognosis. AD skincare routine involved bathing using lukewarm water, no longer than 10 minutes, using non-soap cleansers (low pH, hypoallergenic, and fragrance-free). Moisturizers should be applied soon after bathing to improve skin hydration as the application of moisturizers showed strong evidence that their use can reduce disease severity and the need for pharmacologic intervention. Type of moisturizers contained humectant(s),

emollient(s), and occlusive(s) or newer generation containing anti-inflammation and anti-pruritus (glycerrhectinic acid, temestein, and vitis vinifera) or containing physiological component (lipid, ceramide, natural moisturizing factor).¹¹⁻¹⁴

Avoidance of triggering factors based on history taking (irritant(s), allergen(s), extreme temperature, food, stress), clinical manifestation, and allergic panel test results. Rebuilding and maintenance of optimal barrier function can be achieved through the application of moisturizer after bathing, carried out throughout every phase of the disease.^{11, 13}

Clearance of inflammatory skin disorders can be achieved through the application of corticosteroid. Corticosteroids can be prescribed for manifesting AD as reactive therapy (twice-daily application) or for subclinical AD as proactive therapy. As for maintenance therapy, the corticosteroid can be applied to hot spots as weekend therapy (1-2 times per week). Nevertheless, care should be appropriately addressed to

the potential side effects for both topical and systemic corticosteroids, including possible hypothalamic-pituitary-adrenal axis suppression, particularly in children with AD in whom corticosteroids are used. Control and elimination of the itch-scratch cycle can be managed through the use of sedative antihistamine for babies and children, or non-sedative antihistamine as adjuvant therapy for life pruritus.¹¹⁻¹³ Nevertheless, the prognosis of AD is unpredictable due to the nature of the disease and the risk factors interplaying in its course.^{15, 16}

Conclusion

Atopic dermatitis is a multifactorial, chronic inflammatory and heterogenous dermatological disorder resulting from the interplay between genetic, immune, and environmental factors. Advancement in the understanding between risk factors, pathogenesis, and five pillars of AD therapy expectantly will aid for a better holistic and comprehensive approach among physicians treating AD.

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