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The Relationship of Body Mass Index with Length of Stay in Acute Appendicitis Patients Who Have Undergoing Open Appendectomy at RSUS Lippo Village Karawaci Hospital

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Abstract

Background : Appendicitis is an inflammation that occurs in the veriform appendix. The Indonesian Ministry of Health announced that the number of inpatients with appendicitis is the fourth most common disease in Indonesia. Open appendectomy is a procedure for treating appendicitis. Patients who have an open appendectomy procedure require hospitalization for the wound to heal. Various studies have been conducted to find a relationship between body mass index and length of stay in patients with appendicitis but have different results, besides that research on this topic is still minimal in Indonesia. Therefore, this study was conducted to analyze the relationship between body mass index and length of stay in acute appendicitis patients who had undergone open appendectomy.

Methods : This study used a cross-sectional study design with a sample population of acute appendicitis patients at Lippo Village Hospital Karawaci. 182 samples were selected using a purposive sampling technique. The research sample data was taken from the patient's medical records and will be tested for analysis using SPSS 25 with the Kruskal Wallis ANOVA method.

Result : From 182 research samples, it was found that the median length of stay of patients with different body mass indexes was 3 days. Based on the Kruskal Wallis ANOVA test, there was no significant elationship between gender and length of stay ($p > 0.05$).

Conclusions : This study shows that there is no relationship between body mass index and length of stay in acute appendicitis patients who have undergone open appendectomy.

Introduction

Appendicitis is inflammation that occurs in the vermiform appendix. Appendicitis is most often caused by obstruction of the lumen by faecolith and lymph tissue.[1] The Indonesian Ministry of Health announced that the number of inpatients with appendicitis is the fourth largest disease in Indonesia after dyspepsia, duodenitis and other digestive diseases with 28,949 inpatients and 34,386

outpatients. Additionally, appendicitis was one of the top 10 diseases in hospitalized patients in 2009, with 596,132 cases and at least 234 patient deaths.[2]

BMI is defined as a person's weight (in kilograms) divided by their height (in meters) squared (kg/m2).3 BMI consists of categories: underweight (<18.5 kg/m2), normal (18.5 – 24 .9 kg/m2), overweight (25 – 29.9 kg/m2), obese (>30 kg/m2).[3] Luke Frecelton et al. in his 2018 research at a hospital in South Wales entitled *"Impact of body mass index on utilization of selected hospital resources for four common surgical procedures"* found that 52 patients with obese BMI who underwent a laparoscopic appendectomy procedure had a longer hospital stay. longer (2 – 3.6 days) than in 78 patients with a normal BMI (1 – 2 days). The same thing was also found in patients who had an underweight BMI who had a longer hospital stay (1.4 – 3.6 days). from normal BMI.[4]

Research conducted by Eric Lorio et al. had different results from research conducted by Luke Frecelton.In his research entitled in 2021 with the title *"Appendectomy Hospital Stay: No Difference in Obese Adult or Pediatric Patient Length of Stay Compared to Nonobese Patients".* Eric Lorio studied 118 people adults and 38 children who underwent appendectomy. Patients were grouped into obese and non-obese, with obesity defined as a BMI of 30.0 kg/m2. In adults, there was no significant difference in length of stay between 45 obese and 73 non-obese patients. In children, there was also no significant difference in length of stay between 9 obese patients and 29 non-obese patients.[5]

One of the reasons researchers wanted to conduct this research was the relationship between the patient's length of stay and the costs incurred to care for the patient. Research conducted by Achmad Musa et al. shows that the cost of the length of stay required in one day at RSUD Dr. Moewardi amounting to Rp. 110,000.00. The author hopes that by conducting this research, health workers can estimate the costs needed to treat appendicitis patients who have different body mass indexes, furthermore. The difference in research results in these two studies and the small number of studies conducted in Indonesia on this matter caused the author to want to research this matter.

Material And Methods

This research was 3 groups unpaired numeric comparative analytic study with cross sectional study design, conducted from January 2023 to April 2023. The sample used in this research is 182 post open appendectomy patient with the inclusion of complete patient data in the medical record, namely height, weight, duration of hospitalization and diagnosis of acute appendicitis. Acute appendicitis patients undergoing open appendectomy at

RSUS Lippo Village Karawaci aged 18-60 years. Data was collected using purposive sampling from patient's medical record. Samples who fulfilled the exclusion criteria, namely Patients who have complicated appendicitis, Peritonitis, Patients who have comorbidities such as diabetes, hypertension, anemia, and smoking, etc, were removed from the research. With the classification of research variables in the form of independent variables, which were knowledge about open appendectomy and body mass index, and the dependent variable was length of stay, as well as confounding variables namely age and sex.

Obtained research data was processed and analysed using Statistical Package for the Social Sciences (SPSS) software version 25. Multivariate statistical analysis was performed using Kruskal Wallis when the data distribution was not normal and ANOVA when the data distribution was normal. The researcher also calculated the median, minimal value, maximal value, and 95% CI. Data analysis was then continued with multivariate analysis using the Linear regression test method. The variables used for the linear regression test were Body Mass Index (BMI), age and gender. This research has received approval from the ethical committee of the Faculty of Medicine, University of Pelita Harapan with the number 015/K-LKJ/ETIK/I/2023.

Result

According to table 1, From the 182 subject data processed, the characteristics of the subjects were obtained, consisting of 72 men and 110 women. After calculating the body mass index of the subjects, it was found that 23(12.6%) patients were underweight (BMI <18.5), 85(46.7%) patients had normal/adequate body weight (BMI 18.5 -22, 9), 34 (18.8%) patients were overweight (BMI 23 – 24.9), and 40 (22%) patients were obese based on Asia – Pacific criteria. Based on the data analysis carried out, it was found that the median age of subjects who underwent surgical procedures was 25 years with the youngest being 18 and the oldest being 18 years.

Table 1. Demographic of Samples

Variabel	BMI <18,5(%)	BMI 18,5 - 22,9 (%)	BMI 23 - 24,9 (%)	BMI>25 (%)
Total	23 (12,6%)	85 (46,7%)	34 (18,8%)	40 (22%)
Age				
Median (Min/Max)	22 (18/55)	25 (18/60)	25.5 (18/60)	27.5 (18/60)
Sex				
Male	9 (39,1%)	28 (32,9%)	17 (50%)	18 (45%)
Female	14 (60,9%)	57 (67,1%)	17 (50%)	22 (55%)

Based on the results analyzed using the SPSS program, it was found that the median length of stay in patients who had undergone appendicitis surgery who had a BMI <18.5 was 3 days with a minimum length of stay of 2 days and a maximum of 6 days. Patients who have a BMI of 18.5 – 22.9 have a median length of stay of 3 days with a minimum length of stay of 2 days and

a maximum of 6 days. Patients who have a BMI of 23 – 24.9 have a median length of stay of 3 days with a minimum length of stay of 2 days and a maximum of 6 days. Patients who have a BMI >25 have a median length of stay of 3 days with a minimum length of stay of 2 days and a maximum of 4 days. Tabulation result is shown in table 2.

The results of the Mann – U Whitney test found that the comparison results were not significant between BMI and length of stay (p> 0.05). In the bivariate calculation between age and length of stay, a correlation was found of r = -0.057 and there was no significant comparison between age and length of stay.

In bivariate calculations of the relationship between patient gender and length of stay, it was found that the median value for men - men was 2 days and women was 3 days with the shortest length of stay being 1 day and the longest being 6 days. Based on the p value found after calculations, there was no significant relationship between gender and length of hospitalization.

Table 2. Analysis of Subject Variables on Length of Stay

Variable	n	Median	Min/Max	P Value
BMI* **				
<18,5	23	3	2/6	0.760
18,5 -22,9	85	3	1/6	
23 - 24,9	34	3	1/6	
>25	40	3	1/4	
Age**	r = -0.057		18/60	0.446
Sex*				
Male	72	2	1/6	0.496
Female	110	3	1/6	

Data analysis was then continued with multivariate analysis using the Linear regression test method. The variables used for the linear regression test were Body Mass Index (BMI), age and gender. Based on the results of the confounding test, it shows a coefficient of determination with a value of 0.004. The R2 value explains that the independent variable is able to explain the influence on the duration of hospitalization by 0.4% and the remaining 99.6% is explained by other variables. The final regression model was shown in table 3.

Table 3. Multivariate Analysis of Independent Variable towards Length of Stay

Confounding Variables		No Confounding Variable	P Value
BMI	R square	0,001	0.810
Age	R square	0,003	0.464
Sex	R square	0,003	0.711

Discussion

Based on the results obtained from the research, it was found that the research subjects were dominated by women, totaling 110 people (60.4%). This is in accordance with the epidemiology of appendicitis patients where men suffer from appendicitis 1.4/1 more often than women, but women are more likely to have an appendectomy.

This is also in accordance with the journal conducted by Guss D et al. In this

study it was found that perforated appendicitis was found in 38.7 men and 23.5% of women. This can cause the number of male patients to be less than female because perforated appendicitis is included in the exclusion criteria.

The median length of stay in 182 subjects was 3 days, this is in accordance with the optimal length of stay for patients who have undergone an appendectomy procedure, namely 3 - 5 days. 43 The median age of patients who have had appendicitis is 25 years, this is in accordance with the explanation of Sellar et al. where the most common age for appendicitis is 20 – 30 years old.[1]

The results of the Kruskal Wallis test showed that the comparison results were not significant ($p > 0.05$) between Body Mass Index and the length of stay in patients who underwent open appendectomy surgery. The results of this study are in accordance with research conducted by Lorio E et al. in 2021 which shows that there is no difference in length of stay in obese or non-obese patients. However, my research has different results from research conducted by Marjolijn E. W. Timmerman et al.[5] in 2016 which stated that there was a significant relationship between patients who were obese and patients who were underweight in children.

This difference in results can be explained by the fact that perforations were more often found in children who were underweight, namely 31% when compared to children with normal weight, namely 20%.[6] In a journal conducted by Felix C Blanco et al. It was found that 45% of patients with obese body weight had perforation in appendicitis, while 30% of patients with normal body weight had perforation in appendicitis.[7] Patients who had perforation were included in the exclusion criteria in this study. This can help explain why Body Mass Index did not significantly influence patient length of stay in this study

The results of the Mann-U Whitney test which was carried out to determine the relationship between age and patient length of stay showed that the results were not significant ($p > 0.05$). This is in accordance with the journal conducted by Muhammad Sayuti et al. in Bali in 2022 where age does not significantly influence length of stay. Age can influence length of stay because as age increases, the likelihood of appendicitis perforation increases. In research conducted by Hanson K. A. et al. Patients over [8] years of age are 4 times more likely to suffer from perforated appendicitis.[9] In the elderly group it was also found that elderly women had a shorter hospital stay compared to men due to differences in hormones that can help wound healing. after operation.

Confounding tests were also carried out to determine whether age and gender played a role as confounding factors in this

study. For this reason, multivariate analysis was carried out using the linear regression method. R2 ≥ 10% and delta coef. B ≥ 10% indicates the confounding role of a variable. Because in the results of this confounding test it was found that R2 was <10% and delta coef. B < 10% for these two variables, it is considered that age and gender do not play a role as confounding factors in this study.

There are several shortcomings of this research such as limitations in the research sample resulted in having an abnormal sample in the Kolmogorov – Smirnoff test. Apart from that, there is a lack of factors studied by researchers that can influence the length of stay in patients undergoing open appendectomy surgery.

The obstacles experienced by researchers are the large amount of incomplete data which means researchers cannot have a normal data distribution and the large number of histopathology reports which are not listed in the patient's medical record so researchers cannot classify the type of appendicitis based on anatomical pathology, this research excels with The age limit for the subjects included is the adult age category, namely 18 – 60 years, so that confounding factors regarding age have been minimized.

Apart from that, patients who have complicated appendicitis are also excluded because various studies agree that the severity of appendicitis has a significant effect on the patient's length of stay and can be a confounding factor. 45-47 Different surgical methods are also excluded because the laparoscopic method has been proven to be significant. affecting length of stay, infection at the surgical site and lower pain scores when compared to the appendectomy method. 48 In this study patient comorbidities were also excluded to reduce confounding factors in this study because comorbidities can significantly influence the length of stay in appendicitis patients.

Conclusion

There is no significant relationship (p> 0.05) between body mass index and length of stay in acute appendicitis patients who have undergone open appendectomy at RSUS Lippo Village Karawaci. The median for the length of stay in all body mass index category is 3.

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Author's Statement

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The Relationship Between Big Five Personality Traits and Academic Performance of Asian Medical Students

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Abstract

Introduction : Personality traits have been shown to influence the individual's critical thinking, learning strategies, and motivation, resulting in the overall student's academic performance. Academic performance is an important factor among medical students to ensure their success in long-term medical education, training and work performance as medical doctors. This study aims to evaluate the relationship between personality traits and academic performance among medical students.

Methods : The study was conducted among preclinical medical students from the Medical Schools of Pelita Harapan University, Indonesia. The personality traits were assessed using the NEO Five-Factor Inventory-3 (NEO-FFI-3), which consists of 60 items assessing the five personality traits (neuroticism, extraversion, openness, agreeableness, and conscientiousness). The academic performance was evaluated using the cumulative grade point average (CGPA) score.

Results : A total of 224 participants were included in this study. The mean age of the participants was 19.8 years old (SD±1.3). Neuroticism was the predominant personality trait among medical students and was found to be negatively associated with CGPA in univariable and multivariable analyses ($p<0.05$).

Conclusion : This study reveals that neuroticism personality traits are prevalent among preclinical medical students and adversely affect their academic performance. Understanding the general personality traits present among medical students and its relationship with academic performance can provide valuable input for further medical education programme development.

Introduction

Academic performance relies on cognitive and non-cognitive attributes, including motivation, learning strategies and environments, socioeconomic status, health status, and personality traits.[1] Personality traits are one of the non-cognitive factors that stands out as a pivotal element that influences educational success.[2,3] Previous studies have underscored the substantial impact of personality traits on critical thinking abilities, learning strategies, and overall academic motivation.[4-7]

The Big Five model of personality traits has emerged as an international,

well-established framework for understanding the relationship between individual personality traits and various academic behaviours and educational outcomes.[2,3] Conscientiousness is a personality trait characterized by being self-disciplined, organized, and prioritizing learning tasks, and has consistently been shown as a stable predictor of academic performance.[2,3] The weak to moderate positive correlation of openness personality traits with academic performance has been shown in prior studies.[2,3] The findings for the other Big Five personality traits (agreeableness, extraversion, and neuroticism) are mixed and inconclusive for showing a significant correlation with academic performance.[2,3,8]

However, most previous studies examining the relationship between personality traits and academic performance were carried out in Western countries, in which differences in social, economic, and political contexts that have been known resulted in the geographical variation in personality traits.[2,9] Thus, the relationship between personality traits and academic performance in the Asian population is still unclear. In this study, we aim to explore the association between the personality traits of the Big Five model and academic performance among medical students at the University of Pelita Harapan, one of the prominent private medical schools in the Southeast Asia region, Indonesia.

Methods

Study design, participants, and procedure

This cross-sectional study was performed between December 2022 and May 2023. It was approved by the Pelita Harapan University research ethics committee (No: 197/K-LKJ/ETIK/XI/2022). Participants were preclinical medical students in the Faculty of Medicine of Pelita Harapan University. They were asked to complete the questionnaire disseminated through Google Forms or social media platforms like Line and WhatsApp.

Data collection

The study sample size was determined using Slovin's formula, described as follows: $N/(1+Ne^2)$, where N is the population number and e is the margin of error in percentage value. According to the faculty's database, until January 2022, the total of preclinical medical students at the Faculty of Medicine of Pelita Harapan University was about 500 individuals. This number was used as the total number of populations in Slovin's formula, and the margin error was set as 5%. As a result, this study's minimum required sample size was 222 individuals. Convenience sampling was used to select the participants. Written informed consent was obtained from the

individuals who decided to participate in the study.

The academic performance was evaluated using the cumulative grade point average (CGPA) score. The CGPA score and demographic information were collected using a questionnaire. The individual's personality trait was evaluated using the NEO Five-Factor Inventory-3 (NEO-FFI-3) consisting of 60 items to assess the five personality traits according to the five-factor models, namely, neuroticism (N), extraversion (E), openness (O), agreeableness (A), and conscientiousness (C). The answer format for each item is scored on a five-point Likert scale response, ranging from 0-4 or 4-0 for reverse-scored items. The participants are instructed to circle the correct box for each item: SD if they strongly disagree, or the statement is definitely false; D if they disagree or the statement is mostly false; N if they are neutral on the statement; if they cannot decide, or if the statement is about equally true or false; A if they agree or the statement is mostly true; SA if they strongly agree, or the statement is definitely true. The score of each personality trait was calculated by summing the 12 items that were allocated to evaluate each personality trait and converted into standardized T-scores.

Statistical analysis

The numeric variables were described as mean with the standard deviations (SD), and the nominal variables were shown as counts and percentages. GraphPad Prism (version 9.0) was used for statistical analysis and graph drawing. In all analyses, a two-tailed p-value of less than 0.05 was considered statistically significant.

Results

A total of 224 participants were included in this study, consisting of 59 (26%) male and 165 (74%) female participants. The mean (SD) age of participants was 19.8 (1.3). The T-score results of five personality traits from all participants are shown in **Table 1**. Neuroticism was the predominant personality trait for this study participant, with the highest mean (SD) T-score results being 68.2 (5.1), and most participants (72.3%) were amongst the very high groups of T-score categories.

Table 1. The profile of participants' personality traits

NEO-FFI	T-scores categories	N (%)	T-scores
Agreeableness	Very low	0 (0)	59.9 (6.0)
	Low	4 (1.8)	
	Average	44 (19.6)	
	High	142 (63.4)	
	Very high	34 (15.2)	

Conscientiousness	Very low	0 (0)	59.7 (5.5)
	Low	0 (0)	
	Average	38 (17.0)	
	High	156 (69.6)	
	Very high	30 (13.4)	
Extraversion	Very low	0 (0)	60.3 (8.4)
	Low	10 (4.4)	
	Average	55 (24.6)	
	High	73 (32.6)	
	Very high	86 (38.4)	
Neuroticism	Very low	0 (0)	68.2 (5.1)
	Low	0 (0)	
	Average	3 (1.3)	
	High	59 (26.4)	
	Very high	162 (72.3)	
Openness	Very low	0 (0)	63.2 (5.4)
	Low	0 (0)	
	Average	14 (6.3)	
	High	135 (60.3)	
	Very high	75 (33.4)	

The difference in mean T-scores between females and males was analysed using the Mann-Whitney U test. Data are presented in mean (SD), **p<0.01, ns; not significant.

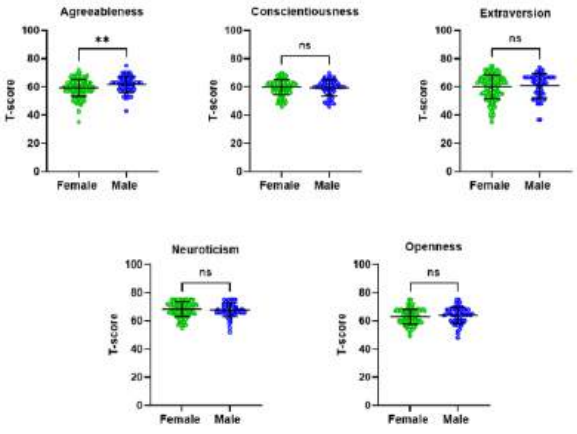

Figure 1. Comparison of personality traits between female and male

Male subjects had a higher T-score of agreeableness personality traits than female subjects (mean T-score: 61.8 vs. 59.2, p<0.01), and no significant difference between females and males was observed for the other T-score personality traits (**Figure 1**). Of 224 participants, 198 (88.4%) participants had a Cumulative Grade Point Average (CGPA) of 3 or higher, whereas 26 (11.6%) participants had a CGPA below 3.

The difference in mean T-scores between participants with CGPA<3 and CGPA≥3 was analysed using the Mann-Whitney U test. Numerical data are presented in mean (SD), *p<0.05, ns; not significant.

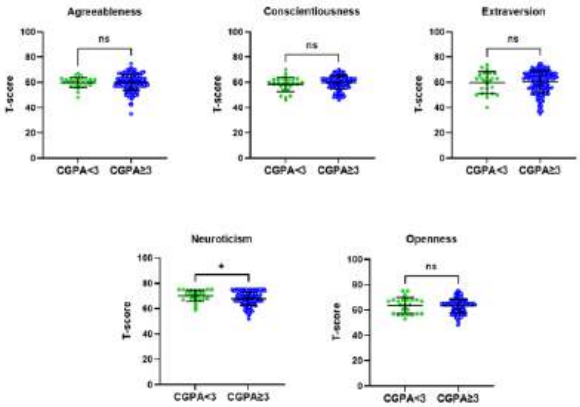

Figure 2. Comparison of personality traits according to Cumulative Grade Point Average (CGPA) results.

As shown in **Figure 2**, participants with CGPA<3 had a significantly higher mean T-score of neuroticism personality traits compared to participants with CGPA≥3 (70.2 vs. 67.9, P<0.05). No significant difference in the mean T-scores between participants with CGPA<3 and CGPA≥3 was observed for the

agreeableness, conscientiousness, extraversion, and openness personality traits (**Figure 2**). Furthermore, on the multivariable analysis, the higher T-score of neuroticism personality trait remained the significant independent factors associated with CGPA score <3 (**Table 2**).

Table 2. Univariable and multivariable analysis of variables associated with CGPA score <3

	Univariable			Multivariable		
Variables	OR	95% CI	p-value	OR	95% CI	p-value
Age	1.06	0.78-1.41	0.65	1.05	0.74-1.42	0.74
Gender (Female vs. male)	0.78	0.32-2.00	0.58	0.68	0.26-1.82	0.42
Personality traits						
Agreeableness	0.99	0.93-1.07	0.95	0.97	0.91-1.05	0.56
Conscientiousness	0.95	0.89-1.02	0.22	0.94	0.87-1.01	0.13
Extraversion	0.99	0.94-1.04	0.76	0.97	0.93-1.03	0.40
Neuroticism	1.10	1.01-1.21	0.03*	1.12	1.03-1.25	0.02*
Openness	1.01	0.94-1.09	0.71	1.02	0.94-1.11	0.51

Abbreviations: OR, odds ratio; CI, confidence interval; *p<0.05

Discussion

The present study evaluated the association between personality traits and academic performance among preclinical medical students. The academic performance was measured using the CGPA, which was calculated based on all GPAs obtained by the students throughout their learning process. This score will describe medical students' long-term academic performance that can be affected by their personality traits. The findings of this study support the hypothesis that personality trait is significantly associated with academic performance.[2,8,10,11] In line with previous studies,[10,11] our study found that the neuroticism personality trait was associated with lower academic performance. Additionally, we observed that many preclinical medical students had T-scores under very high neuroticism personality traits.

Several features of the neuroticism personality trait that adversely impact academic performance have been described. First, individuals with neuroticism are prone to emotional instability, characterized as being anxious, emotional, nervous, and jealous, resulting in difficulty in handling stress, concentrating during the learning process, and tend to procrastinate academically.[10, 12-14] Second, individuals with neuroticism are positively associated with the avoidance coping strategy, in which an individual tries to avoid or escape from a stressor rather than deal with it.[15,16] The avoidance coping strategy has been considered a maladaptive coping strategy because it often generates more significant psychological distress.[17] As a result, individuals with high neuroticism

are more prone to experience negative feelings, such as depression and anxiety, that interfere with their learning capacity, disrupt their ability to overcome obstacles or failures during the medical education process, and negatively impact their life quality.[18] Third, individuals with neuroticism tend to have low self-efficacy, possibly due to minimal confidence and low self-esteem, making them lack motivation to learn and participate in academic activities.[18-20]

Furthermore, due to emotional instability, poor coping strategy, and low self-esteem, individuals with neuroticism personality traits tend to avoid the risk of making mistakes in learning tasks. Therefore, they prefer the surface learning approach, which is characterized by minimal motivation to meet the requirement and memorization as a primary strategy to produce the results.[21] Since the problem-based learning (PBL) educational approach has been widely implemented in medical education and emphasizes the constructive, self-directed, collaborative, and contextual learning process, the PBL learning method will likely not greatly support the learning process for individuals with high neuroticism.[22, 23]

Although females have been found to score higher than men in neuroticism, [24, 25] we have not observed a significant difference between females and males in neuroticism personality trait scores. Moreover, in contrast with previous studies,[26, 27] the agreeableness personality trait related to behaviours of altruism was scored higher in men than women. The subtle impact of gender variations on personality traits has been reported,[28, 29] and external factors, such as environmental influences and parenting, more determined the personality trait development and stability.[30, 31]

Limitations in the current study can be attributed to the cross-sectional study design for establishing causal relationships between personality traits and academic performance. However, it is worth noting that the neuroticism personality trait consistently affects academic performance, as described in previous findings.[10, 11] The assessment of personality traits and academic performance is self-reported. These self-reported data are more likely to introduce potential response bias, as participants may offer socially desirable responses that are not actual and may recall the information inaccurately. Moreover, the current study does not evaluate factors that may impact academic performance more than personality traits, such as motivation, study habits, social environment, and cognitive factors. On the other hand, the strength of this study is that the homogenous samples, therefore, moderator variables like age and education level, may not interfere with the

association between personality traits and academic performance.

Conclusion

In conclusion, neuroticism personality traits have been found in a large number of preclinical medical students and negatively impact their academic performances. The findings of this study provide significant input for those involved in medical education to deliver the learning subjects, design a more conducive medical curriculum and develop the counselling program for preclinical medical students to improve their academic performance and well-being.

Conflict of interest statement

The authors have declared no conflicts of interest.

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Ratna Sari Wijaya

Pap Smear Practices among Female Healthcare Professionals in Indonesia and Their Associated Factors

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Abstract

Introduction : Cervical cancer is the fourth most frequent disease in women worldwide. However, pap smear coverage in Indonesia remains below the target. The purpose of this study was to describe pap smear practice among female healthcare professionals and its associated factors.

Methods : This cross-sectional study was conducted from August 2022 to June 2023 among married female healthcare professionals of reproductive age who worked in Kelapa Dua district, Tangerang, Banten, Indonesia. Three general hospitals, two primary clinics, and one community health center were involved in this study. Data was collected using a self-administered questionnaire and analyzed using a chi-square test.

Results : From 236 respondents, only 80 respondents (33.9%) had pap smear tests. The most common reasons for not doing the test were lack of time and having not experienced any of the symptoms. Those who were doing the pap smear tests were likely to be more than 40 years old (OR 29.900; 95% CI 9.595 – 93.172; p<0.001), married for more than 10 years (OR 28.737; 95% CI 9.955 – 82.955; p<0.001), multiparous (OR 6.941; 95% CI 2.706 – 17.805; p<0.001), and have higher economic income (OR 7.333; 95% CI 1.443 – 37.274; p=0.020). Female healthcare professionals other than medical practitioners, nurses, or midwives were less likely to do the pap smear tests (OR 0.370; 95% CI 0.167 – 0.823; p=0.02).

Conclusion: Pap smear practice among female healthcare professionals in Indonesia was inadequate. Age, marriage duration, parity status, types of healthcare professionals, and socioeconomic status were significantly associated with pap smear practice.

Introduction

Cervical cancer is the fourth most frequent disease in women worldwide with an estimated incidence of 604.000 cases and 342.000 deaths in 2020. In Indonesia, cervical cancer reached an estimated number of 36.600 new cases and 21.000 deaths in 2020, thus becoming one of the most common types of cancer in that year.[1] One of the global strategies to prevent the fatality of cervical cancer is early detection. Papanicolaou smear, shortened as pap smear, is an effective screening exam done by collecting samples of cervical cells using a brush or a spatula to identify cellular changes that

may lead to cervical cancer.[2] Based on a study by Najib et al., the sensitivity and specificity of pap smear tests in detecting premalignant cervical lesions were 47.19% and 64.79% respectively, while the sensitivity and specificity of pap smear tests in detecting high-grade lesions of the cervical intraepithelial neoplasia were 55.40% and 96.8% respectively. This reliable screening tool has been used since the 1940s and has been beneficial in detecting precancerous and cancerous cervical cells around the world.[3]

Pap smear tests have contributed to a decline in cervical cancer cases worldwide. The mortality rate of cervical cancer in some developed countries has been decreasing since the implementation of the pap smear national screening program. For instance, cervical cancer mortality rate in the United States of America and South Korea had decreased from 2.8 to 2.3 deaths per 100.000 women,[4] and 2.8 to 2.0 deaths per 100.000 women respectively in the span of 12 to 15 years.[5]

The Indonesian Ministry of Health recommends screening every 3 to 5 years if pap smear test results are normal and primarily targets married women between the ages of 30 and 50 years old.[6] However, pap smear coverage in Indonesia remains low. In 2018, only 7.34% of Indonesian women underwent cervical cancer screening including pap smear tests.[7] It underlines the urgency to implement national effective strategies to increase the uptake of pap smear screening. Female healthcare professionals have important roles in promoting pap smear tests and raising awareness among other women in their communities. They are more well-informed about pap smear tests and have more awareness about the screening. Studies assessing pap smear practice among female healthcare professionals in Indonesia are limited. Thus, the purpose of this study is to describe pap smear uptake among female healthcare professionals in Kelapa Dua District, Tangerang, as well as to investigate the associated factors.

Methods

This was a descriptive-analytical cross-sectional study conducted from August 2022 to June 2023. There were 236 married female healthcare professionals working at Siloam Hospital Lippo Village, Siloam General Hospital Lippo Village, Siloam Clinic Lippo Village, Siloam Hospital Kelapa Dua, Siloam Clinic Kelapa Dua, and Kelapa Dua Community Health Center included in this study. All healthcare facilities were in the district of Kelapa Dua, Tangerang regency, Banten, West Indonesia. Respondents with a history of abnormal pap smear test results or any other malignancies, those who were divorced, widowed, or already had menopause, were excluded from the study. Only those who provided consent

and filled out questionnaires completely were analyzed.

Respondents were given self-administered questionnaires through quota sampling. Questionnaires were distributed to each healthcare facility until the quota number of samples specified for each location was met. The questionnaire was used to obtain information on pap smear practice and socio-demographic data. Pap smear practice information was obtained through a dichotomous question with a “yes” or “no” answer. The socio-demographic data obtained were comprised of age, marriage duration, parity status, type of healthcare professionals, workplace, and socioeconomic status. The profession of respondents was classified into nurses, doctors, midwives, and others. Medical practitioners, specialists, and dentists were inserted into the ‘doctors’ group. Respondents in the ‘others’ group consisted of pharmacists, psychologists, physiotherapists, nutritionists, radiographers, medical laboratory analysts, medical record technicians, and health promotion staff. The workplace in this study refers to where the sample was taken of the respondent at the time or the place where the respondent works, this variable is classified into hospital and clinic/community health center. Socioeconomic status is classified into the lower, middle, and upper class. This classification is based on the 2022 Tangerang Regency minimum wage.

The data was then analyzed using the Statistical Package for Social Sciences (SPSS) version 27. The chi-square test was performed to determine the association between age, duration of marriage, parity status, type of healthcare professionals, workplace, and socioeconomic status with pap smear practice. If the p-value is less than 0.05, the association is considered significant. The odds ratio was also calculated to measure the likelihood of undergoing Pap smear tests from each variable. This study had been approved by the Ethics Committee of Pelita Harapan University and received ethical clearance with approval number 035/K-LKJ/ETIK/I/2023.

Results

Table 1 shows the demographic characteristics of respondents. Most of the respondents were more than 30 years old, married for 5 – 10 years, and multiparous. More than 50% of the respondents were nurses. Other types of healthcare professionals who participated in this study were pharmacists, psychologists, physiotherapists, nutritionists, radiographers, medical laboratory analysts, medical record technicians, and health promotion staff. More than 90% of the respondents worked at hospitals. There were only 80 respondents (33.9%) who had done pap smear tests, while the remaining 156 (66.1%) had never done pap smear tests before.

Table 1. Distribution of demographic characteristics

Variable	N = 236	
	n	Percentage (%)
Age		
20 – 30 years	74	31.4
31 – 40 years	124	52.5
41 – 50 years	38	16.1
Duration of Marriage		
< 5 years	75	31.8
5 – 10 years	103	43.6
> 10 years	58	24.6
Parity		
Nullipara	42	17.8
Primipara	84	35.6
Multipara	110	46.6
Type of Healthcare Professionals		
Nurse	132	55.9
Midwive	18	7.6
Doctor	30	12.7
Others	56	23.7
Workplace		
Hospital	214	90.7
Clinic / Community Health Center	22	9.3
Socioeconomic Status		
Lower Class	13	5.5
Middle Class	181	76.7
Upper Class	42	17.8

The most common reasons for not doing the test were lack of time and having not experienced any of the symptoms. Other reasons were listed in Table 2.

Table 2. Reasons for no pap smear tests

Variable	N = 156	
	n	Percentage (%)
Time constraints	50	32.1
Have not experienced cervical cancer symptoms	37	23.7
No interest to be tested at this time	25	16.0
Feels embarassed / scared to get tested	15	9.6
Have been vaccinated against HPV	7	4.5
Recently married	5	3.2
Pap smear tests are costly	4	2.6
Will get tested in due time	3	1.9
In a long-distance relationship	2	1.3
Lack of pap smear knowledge	1	0.6

Bivariate analysis shown in Table 3 revealed significant associations between pap smear practice and age of respondents, duration of marriage, parity status, types of healthcare professionals, and socioeconomic status. Female healthcare professionals performing pap smear tests were likely to be older, married for a longer duration, multiparous, working in a hospital, and belonging to the upper class. Midwives were more likely to perform pap smear tests compared to other types of healthcare professionals.

Table 3. Bivariate analysis results

Variable	N = 236		Odds Ratio (95% CI)	P Value
	No n (%)	Yes n (%)		
Age				
20 - 30 years	69 (93.2%)	5 (6.8%)		
31 - 40 years	75 (60.5%)	49 (39.5%)	9.016 (3.396 – 23.939)	<0.001
41 - 50 years	12 (31.6%)	26 (68.4%)	29.900 (9.595 – 93.172)	<0.001
Duration of Marriage				
< 5 years	70 (93.3%)	5 (6.7%)		
5 – 10 years	67 (65.0%)	36 (35.0%)	7.522 (2.785 – 20.317)	<0.001
> 10 years	19 (32.8%)	39 (67.2%)	28.737 (9.955 – 82.955)	<0.001
Parity				
Nullipara	36 (85.7%)	6 (14.3%)		
Primipara	69 (82.1%)	15 (17.9%)	1.304 (0.466 – 3.650)	0.800
Multipara	51 (46.4%)	59 (53.6%)	6.941 (2.706 – 17.805)	<0.001
Type of Healthcare Professionals				
Nurse	87 (65.9%)	45 (34.1%)		
Midwive	7 (38.9%)	11 (61.1%)	3.038 (1.102 – 8.372)	0.050
Doctor	15 (50.0%)	15 (50.0%)	1.933 (0.868 – 4.307)	0.156

Others	47 (83.9%)	9 (16.1%)	0.370 (0.167 – 0.823)	0.020
Workplace				
Hospital	140 (65.4%)	74 (34.6%)		
Clinic / Community Health Center	16 (72.2%)	6 (27.3%)	0.709 (0.266 – 1.890)	0.651
Socioeconomic Status				
Lower Class	11 (84.6%)	2 (15.4%)		
Middle Class	127 (70.2%)	54 (29.8%)	2.339 (0.501 – 10.908)	0.009
Upper Class	18 (42.9%)	24 (57.1%)	7.333 (1.443 – 37.274)	0.020

Discussion

The results of the study showed a low prevalence of pap smear uptake among the respondents. Female healthcare professionals are assumed to have a higher level of awareness to receive pap smear tests due to being more knowledgeable and working in an environment which often promotes cervical cancer prevention efforts. Therefore, the low pap smear uptake results obtained from the respondents do not correspond to what is expected.

The reason for the low pap smear uptake can be attributed to one of the elements in the Health Belief Model, which is perceived barriers. The most common barriers obtained for not undergoing pap smear exams were time constraints and having not experienced any of the symptoms. The findings of this study were similar to studies done by Sari et al. and Suantika et al. where both studies also reported time constraints and feeling embarassed as some of the reasons hindering their willingness to receive pap smear tests.[8,9]

This study implied that there were many barriers to someone's willingness to receive pap smear tests, besides a lack of knowledge or facilities. Although healthcare professionals are considered to have higher knoweledge and attitudes regarding pap smear programs than the general population, it appears that pap smear tests are still not a health priority for them. Various reasons obtained from the respondents who did not perform the test indicated a lack of self-awareness regarding the importance of pap smear tests in cervical cancer prevention. The results acquired from this study and previous studies mentioned above concludes a lack of awareness among female healthcare professionals being a common issue.

Age and duration of marriage among the respondents were significantly associated with pap smear practice, these findings were also reported in a study by Sari et al [8]. Respondents who were older and in a longer marriage were also found to be more likely to receive pap smear tests. This is because older people are more likely to engange in beneficial practices, such as getting screened for cervical cancer. This behavior reflects how, as a person ages, their mindset matures, allowing them to make more informed decisions.[9] As for the correlation between duration of marriage and pap

smear practice, the reason is unclear, but it appears that female healthcare professionals who had been married for a longer period had greater awareness to influence their decision to receive a pap smear test.

Multiparous respondents were the most likely to perform pap smear tests. The reason for this finding could be attributed to women with lower parity perceiving themselves as having a low risk for cervical cancer and thus preferring not to get screened. Types of healthcare professionals among the respondents except for midwives and doctors were also significantly associated with pap smear practice. Other types of healthcare professionals (pharmacists, psychologists, physiotherapists, nutritionists, radiographers, medical laboratory analysts, medical record technicians, and health promotion staff) had lower odds than nurses, midwives, and doctors. This is due to other types of healthcare professions being less exposed to cervical cancer and pap smear-related information, causing them to be less aware.

Socioeconomic status among the respondents was found to be significantly associated with pap smear practice, respondents in the middle and upper class were found to be more likely to receive pap smear tests. These findings were in line with a study conducted by Rayhana et al. which shows respondents in the middle-upper class having higher odds than the respondents in the lower class.[10] The results might be attributed to the respondents in the middle and upper classes having more financial freedom, leading to a lower financial burden for pap smear test expenses. However, the workplace was not found to be significantly associated with pap smear practice. Although it was found that respondents working in the hospital were more likely to receive pap smear tests. This suggests that other factors such as age, duration of marriage, parity status, types of healthcare professionals, and socioeconomic status are more likely to influence pap smear practice than workplace.

Conclusion

The results of this study showed a higher number of respondents had not had pap smear tests performed, which was indicative of Indonesia's low pap smear coverage. The two most common reasons obtained from the respondents were time constraints and not having experienced cervical cancer symptoms, hence medical facilities are advised to make pap smear tests more accesible for female health care professionals by providing a designated time to get tested with no cost. Taking pap smear tests could also be made an obligatory requirement for work.

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Angelina

Relationship Between The Level Of Knowledge And Attitude Towards Maternal Behavior Of Stunting Prevention At Bojong Nangka Community Health Center In Tangerang District

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Abstract

Background: Stunting is one of the major health problems in Indonesia. In 2022, the prevalence of stunting in Indonesia was 21.6%, and there were still 9,200 cases of stunting in Tangerang District alone. Stunting prevention can be done since pregnancy. It is estimated that stunting prevention behaviors among pregnant women is related to their knowledge and attitudes. Puskesmas Bojong Nangka was a community health center in Tangerang that treated stunting but has no data on this matter.

Methods: This study used a cross-sectional study design. Data on the level of knowledge, attitudes, and behaviors in stunting prevention was collected using questionnaires and further was analyzed using the Chi-square test.

Result: From 96 respondents, it was found that the majority (63.5%) had a good level of knowledge on stunting prevention. Most respondents also had a good attitude towards stunting prevention (83.3%). There were 72 respondents (75%) who had recommended stunting prevention behaviors. Bivariate analysis showed that there was a significant relationship between knowledge level and stunting prevention behaviors (P value < 0.001; OR 7.29; 95% CI 2.6 – 20.39) but there was no significant relationship between attitudes and stunting prevention behaviors (P value = 1; OR 1; 95% CI 0.29 – 3.45).

Conclusions: There was a significant relationship between the level of knowledge towards stunting prevention behaviors among pregnant women at Bojong Nangka Community Health Center, Tangerang District.

Introduction

Stunting is a problem of impaired child growth and development due to chronic nutritional problems, characterized by height-for-age less than -2 standard deviations (SD) based on the World Health Organization (WHO) growth curve.[1] Stunting can occur due to inadequate nutritional intake and chronic infections that take place in the first 1000 days of life.[1] Stunting causes several long-term impacts, namely: impaired physical growth, suboptimal cognitive and motor development, and even metabolic

disorders in adulthood such as diabetes, obesity, stroke, and heart disease.[2] Based on the results of the Indonesian Nutrition Status Survey in 2022, the prevalence of stunting in Indonesia is 21.6%.[3] The government's target is to reduce the stunting rate to 14% by 2024 based on the National Medium-Term Development Plan.[4]

Prevention of stunting can be done since pregnancy by providing adequate and high-quality nutrition to pregnant women.[5] Another prevention of stunting is that routine checks of pregnancy conditions can be carried out with a doctor to detect possible infections experienced in order to prevent or treat infections that cause stunting.[6]

Behavior is closely related to knowledge and attitudes.[7] According to Bloom, one of the main factors of behavior change can be influenced by knowledge, and followed by changes in attitude.[8] Based on previous research on the relationship between knowledge, attitudes of pregnant women towards stunting prevention behavior, there is a contradiction between the knowledge and behavior of pregnant women towards stunting prevention.[9,10] This can be caused by several factors such as economic conditions, availability of health facilities, support from family, friends and health workers.[9] This study was conducted at the Bojong Nangka Community Health Center located in Tangerang District, where there were still 9,200 cases of stunting in 2022.[11] Therefore, this study reviewed the relationship between knowledge and attitudes of pregnant women towards stunting prevention behavior at Bojong Nangka Community Health Center.

Objectives

The aim for this study is to know more about the maternal level of knowledge, and attitude towards stunting prevention behavior at Bojong Nangka Community Health Center in Tangerang District

Material And Methods

Participants

The population in this study were pregnant women at the Bojong Nangka Community Health Center. There were 96 respondents who met the inclusion criteria which are: pregnant women who visited the Bojong Nangka Community Health Center during the study period and are residents of Tangerang District. The exclusion criteria in this study are: did not fill out the questionnaire completely and had difficulty to understand Indonesian language.

Study design

This study used cross-sectional design and was carried out from January to February 2024. It has received approval from the ethics committee of the Faculty of Medicine, Pelita Harapan University.

Research Instrument

Data were collected using questionnaires about knowledge, attitudes, and practices of stunting prevention. There are some additional questions regarding the demographic data of the respondents (name, age, education, job).

Statistical Analysis

Data was being analyzed using the Statistical Package for the Social Sciences version 26 (IBM, 2019). Chi-square test was used to determine the relationship between knowledge, attitude towards maternal stunting prevention with p-value < 0.05 as significance level.

Result

Respondent Characteristics

Table 1. Respondent Characteristics (N=96)

Respondent Characteristics	Number of Participants	Percentage (%)
Age		
<20 years	2	2.1%
20-35 years	84	87.5%
>35 years	10	10.4%
Education		
Elementary	7	7.3%
Middle School	28	29.2%
High School	47	49.0%
University	14	14.6%
Job		
Housewife	85	88.5%
Teacher	4	4.2%
Employee	6	6.3%
Midwife	1	1%
Knowledge		
Good	61	63.5%
Not good	35	36.5%
Attitude		
Good	80	83.3%
Not good	16	16.7%
Behavior		
Good	72	75%
Not good	24	25%
ANC clinic		
Aware	96	100%
Not aware	0	0%
Health Counselling		
Aware	96	100%
Not Aware	0	0%

There were 96 respondents who met all inclusion criteria for this study. The age demographics in this study were mostly in the age range of 20-35 years. The demographics of education in this study, most respondents have a final education of SMA / SMK with a total of 47 respondents (49%). In the demographics of the type of work of respondents in this study, most respondents were housewives with a total of 85 respondents (88.5%).

Most respondents had a good level of knowledge, namely 61 respondents (63.5%). and a good attitude towards stunting prevention, namely 80 respondents (83.3%). In the description of stunting prevention behavior, 72 respondents had good prevention behavior (75%). All pregnant women (96 respondents) also knew that there was a MCH clinic and health counseling at the Bojong Nangka Community Health Center (100%).

Stunting Prevention Facilities

The results of this stunting prevention facilities and infrastructure questionnaire addressed to the Head of Puskesmas Bojong Nangka, showed that Puskesmas Bojong Nangka has several programs that support the implementation of stunting prevention. Puskesmas Bojong Nangka has a maternal and child health clinic for pregnancy checks, counseling on healthy

food for pregnant women, and counseling on infection prevention.

Statistical Test Result

Table 2. Analysis of the relationship between knowledge and stunting prevention (N=96)

Knowledge	Prevention Behavior		P value	Ratio (OR)	CI (95%)
	Good n (%)	Not good n (%)			
Good	54 (88,5%)	7 (11,5%)	0,00*	7,29	2,60-20,39
Not good	18 (51,4%)	17 (48,6%)			

*significant

Based on the result on table 2, p value was <0.001. It showed that there was a significant relationship between the level of knowledge and stunting prevention behavior. The odds ratio (OR) value was 7.29; 95% CI 2.6 - 20.39. It can be concluded that someone with good knowledge has 7.29 times the odds of good stunting prevention behavior as well.

Table 3. Analysis of the relationship between Attitude and Stunting Prevention Behavior (N=96)

Attitude	Prevention Behavior		P value	Ratio (OR)	CI (95%)
	Good n (%)	Not good n (%)			
Good	60 (75 %)	20 (25%)	1	1	0,29-3,45
Not good	12 (75%)	4 (25%)			

*not significant

Table 3 showed the chi square test result for relationship between attitude and stunting prevention behavior. The p value was > 0.05 thus there was no significant relationship between attitude and stunting prevention behavior.

Discussion

Relationship between knowledge and maternal stunting prevention at Bojong Nangka Community Health Center

This study found there was a significant relationship between knowledge level and stunting prevention behavior (P value = 0.000; OR 7.29 CI 2.60 - 20.39). This result was in line with the results obtained by Lasarus et al. (2022) in Locus village, East Nusa Tenggara that showed there was significance between poor maternal knowledge and a high risk of stunting.[12] The study had 166 mothers-children aged 24–59-month dyads. Based on Bloom's theory, an action is carried out based on knowledge, and a person can be said to be knowledgeable when applying this knowledge based on the six levels of knowledge that apply.[13]

Good knowledge possessed by respondents in this study can be supported by accessibility to the Bojong Nangka Community Health Center, so that they get education from a team of medical officers from the Bojong Nangka Health Center. Accessibility also accompanied by educational support will likely increase a person in making prevention efforts, while people who lack health accessibility will cause ignorance and unconsciousness in stunting prevention efforts.[14]

Relationship between attitude and maternal stunting prevention at Bojong Nangka Community Health Center

In this study, it was found that there was no significant relationship between the level of attitude and stunting prevention behavior (P value = 1; OR 1 CI 0.29 - 3.45) These results indicate that the behavior of pregnant women at the Bojong Nangka Puskesmas in preventing stunting is not influenced by their attitudes.

The results in this study are not in accordance with previous research, which in a study conducted by Arnita et al. (2020) showed that there was a significant relationship between attitudes and behavior to prevent stunting in toddlers at Puskesmas Simpang Kawat, Jambi City in 2019.[10] In this study there was no significant relationship between the attitudes of pregnant women and stunting prevention behavior. This can happen because behavior is not influenced by attitude alone, but knowledge also plays an important role. A person can be said to be knowledgeable if they apply what they know.

Conclusion

The study concludes that most pregnant women at Bojong Nangka Health Center have good knowledge about stunting prevention (63.5%), while 36.5% have poor knowledge. Additionally, the majority of these women demonstrate a good attitude toward stunting prevention (80%). Furthermore, the findings reveal a significant relationship between knowledge and stunting prevention behavior in pregnant women, whereas no significant relationship is observed between attitude and stunting prevention behavior at Bojong Nangka Health Center.

Limitation

This study was using cross-sectional method that cannot determine the existence of other confounding factors not examined in this study such as economic status, emotions, experience, and information from other media regarding stunting prevention which can affect the level of knowledge, attitudes, and stunting prevention behavior. The sample selection also has weaknesses where random sampling is not carried out.

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(Dwi Savitri Rivami)

Characteristics of COVID-19 Therapy Based on Disease Severity at Siloam Kebon Jeruk Hospital

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Abstract

Introduction : COVID-19 is an infectious disease that can cause acute respiratory syndrome by droplet transmission. Along with the very fast spread of the virus which occurs in almost all countries, it is necessary to have therapies that can reduce the morbidity and mortality of patients infected with COVID-19. Various factors affect the administration of therapy so a management guideline is needed for medical personnel so that the administration of therapy can be consistent and efficient in accordance with scientific evidence. This study aims to determine the characteristics and therapeutic options of COVID-19 patients based on the severity of the disease so it can be an evaluation for policymakers and health workers in providing COVID-19 therapy.

Methods : This type of research is descriptive, and the research design is cross-sectional with a total population sampling. The study was conducted at Siloam Kebon Jeruk Hospital with a total of 135 respondents from secondary medical record data.

Results : The observed data include the characteristics of the respondents and the therapies for COVID-19 patients, which consist of antiviral, anti-inflammatory, and anticoagulant treatments. Based on the collected data, COVID-19 patients were predominantly male (55.6%) with an average age of 55 years. Many patients presented with moderate severity without requiring oxygen (34.1%) and were classified as having referred outcomes (47.4%). Antiviral therapy using favipiravir was predominantly administered to patients with mild to moderate severity, while remdesivir was mostly given to those with moderate to severe severity. Corticosteroids, such as dexamethasone and methylprednisolone, were the preferred choice for anti-inflammatory therapy (72.2%). Heparin was the most commonly used anticoagulant therapy across all severity levels, and antibiotics were administered to the majority of patients infected with COVID-19 (73.3%).

Conclusions : Evaluation of the low rate of use of corticosteroids and anticoagulants in COVID-19 patients is needed.

Introduction

The World Health Organization (WHO) officially classified the Coronavirus outbreak as a pandemic on March 11, 2020, due to its rapid global spread.[1] By July 6, 2021, Indonesia had reported 2,379,397 confirmed COVID-19 cases, with 62,908 deaths (2.6%). DKI Jakarta accounted for the highest number of cases,

totaling 482,264 (23.9%) and 7,922 deaths.[2] COVID-19 primarily affects the respiratory system and poses a significant health risk due to severe complications, including pneumonia.[3,4] The clinical manifestations of COVID-19 include fever, cough, malaise, dyspnea, fatigue, anorexia, sneezing, and rhinitis.[5] The disease is categorized into four levels of severity: asymptomatic, mild, moderate, and severe.[6]

The therapeutic approach to managing COVID-19 patients varies according to the severity of the disease and the treatment guidelines in use. Several factors influence the selection of therapy, including ethical considerations, medical professionalism, research evidence, a comprehensive understanding of the patient's condition, the identification of potential treatment options, patient consent to proposed interventions, implementation of the treatment plan, and evaluation of outcomes. Non-clinical factors, such as the patient's economic status, racial and cultural background, attitudes, beliefs, and the availability of healthcare resources, also play a critical role in clinical decision-making, adding layers of complexity.[7,8]

Given the variability in therapeutic approaches, standardized clinical guidelines are essential to promote consistent and efficient treatment while reducing the gap between practice and evidence-based medicine.[9] This study seeks to analyze the characteristics of therapies provided to COVID-19 patients and their alignment with disease severity. The investigation focuses on evaluating therapy patterns for COVID-19 patients at Siloam Kebon Jeruk Hospital

Material And Methods

This study employs a descriptive observational design with a cross-sectional approach, utilizing secondary data from the medical records of COVID-19 patients treated at Siloam Kebon Jeruk Hospital. The sample consists of COVID-19 patients aged ≥18 years who received treatment at the hospital between December 2020 and August 2021. The collected data will be analyzed using statistical software.

Result

From a total of 135 respondents, the age distribution showed a mean of 55 years (SD ±1.42). The majority of the sample comprised male patients, totaling 75 individuals (55.6%). The most prevalent severity level was moderate without oxygen support, with a proportion of 34.1%. Diabetes mellitus was the most common comorbidity, affecting 30.7% of patients, followed by hypertension at 27.4%. Additionally, 32 respondents (23.7%) presented with ≥2 comorbidities. The detailed characteristics of the respondents are presented in **Table 1**.

Table 1. Respondent Characteristics

Characteristic	Number (N = 135)
Gender	
Male	75 (55.6%)
Female	60 (44.4%)
Severity Level	
Mild	29 (21.5%)
Moderate without oxygen	46 (34.1%)
Moderate with oxygen	41 (30.4%)
Severe	19 (14.1%)
Comorbidities	
Diabetes mellitus	41 (30.4%)
Hypertension	37 (27.4%)
Heart disease	11 (8.1%)
Chronic kidney disease	11 (8.1%)
Asthma	7 (5.2%)
Chronic obstructive pulmonary disease (COPD)	2 (1.5%)
Cancer	2 (1.5%)
Autoimmune disease	0 (0%)
≥ 2 comorbidities	32 (23.7%)
Others	19 (14.1%)

Table 2 outlines the therapeutic interventions employed for COVID-19 patients included in the study. The data indicate that the most frequently utilized antiviral agent was favipiravir (48.9%), predominantly administered to individuals with mild to moderate disease severity who did not require oxygen supplementation (36%). Conversely, remdesivir emerged as the preferred antiviral for patients with moderate disease severity requiring oxygen support and severe cases, with a usage rate of 48.3%. Corticosteroids, serving as anti-inflammatory agents, were the second most common therapeutic choice (23.7%). Their application was most pronounced in patients with moderate disease necessitating oxygen support. Within this category, dexamethasone was the predominant choice for patients with moderate disease requiring oxygen and for severe cases, whereas methylprednisolone was more frequently administered to patients with moderate disease not requiring oxygen supplementation. Additional anti-inflammatory interventions, including IL-6 receptor antagonists and intravenous immunoglobulin, were primarily reserved for patients with severe disease. Among anticoagulants, heparin was overwhelmingly the most utilized agent (87.5%), surpassing enoxaparin and rivaroxaban in frequency, with its use being highest among patients with moderate disease requiring oxygen support. Specific interventions such as spironolactone and convalescent plasma were exclusively administered to patients with moderate disease requiring oxygen support. Antibiotic therapy was implemented in 73.3% of cases, with the highest prevalence observed in moderate cases without oxygen supplementation (34.3%). N-acetylcysteine demonstrated the highest usage in moderate cases requiring oxygen, while the administration of hydroxychloroquine was evenly distributed among mild and moderate cases without oxygen support.

Table 2. Therapies Based on COVID-19 Disease Severity

Therapeutic Type	Mild (n=29)	Moderate w/o Oxygen (n=46)	Moderate w/ Oxygen (n=41)	Severe (n=19)	Total (n=135)
Antiviral Therapy					
Favipiravir	13 (27.1%)	14 (29.2%)	16 (33.3%)	5 (10.4%)	48 (35.6%)
Remdesivir	0 (0.0%)	13 (31.0%)	17 (40.5%)	12 (28.6%)	42 (31.1%)
Oseltamivir	4 (50.0%)	3 (37.5%)	1 (12.5%)	0 (0.0%)	8 (5.9%)
Anti-inflammatory Therapy					
Corticosteroids	2 (6.3%)	9 (28.1%)	11 (34.4%)	10 (31.3%)	32 (23.7%)
Dexamethasone	1 (3.8%)	5 (19.2%)	10 (38.5%)	10 (38.5%)	26 (19.3%)
Methylprednisolone	1 (16.7%)	4 (66.6%)	1 (16.7%)	0 (0.0%)	6 (4.4%)
IL-6 receptor antagonist	0 (0.0%)	0 (0.0%)	1 (14.3%)	6 (85.7%)	7 (5.2%)
Intravenous immunoglobulin	0 (0.0%)	0 (0.0%)	1 (25.0%)	3 (75.0%)	4 (3.0%)
Ivermectin	0 (0.0%)	0 (0.0%)	1 (100.0%)	0 (0.0%)	1 (0.7%)
Anticoagulant Therapy					
Heparin	1 (4.8%)	2 (9.5%)	12 (57.1%)	6 (28.6%)	21 (15.6%)
Enoxaparin	0 (0.0%)	0 (0.0%)	1 (50.0%)	1 (50.0%)	2 (1.5%)
Rivaroxaban	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	1 (0.7%)
Angiotensin-Converting Enzyme II and RAAS Inhibitors					
Spironolactone	0 (0.0%)	0 (0.0%)	1 (100.0%)	0 (0.0%)	1 (0.7%)
Convalescent Plasma Therapy	0 (0.0%)	0 (0.0%)	2 (100.0%)	0 (0.0%)	2 (1.5%)
Antibiotic Therapy	14 (48.3%)	34 (34.3%)	33 (33.3%)	18 (18.2%)	99 (73.3%)
N-acetylcysteine Therapy	3 (8.6%)	12 (34.3%)	15 (42.9%)	5 (14.3%)	35 (25.9%)
Hydroxychloroquine Therapy	1 (50.0%)	1 (50.0%)	0 (0.0%)	0 (0.0%)	2 (1.5%)

Discussion

Data from the COVID-19 Task Force in Indonesia indicates that individuals aged 46–59 years and those over 60 years constitute the two largest age groups with the highest mortality rates among COVID-19 patients. This trend can be attributed to age-related degenerative processes that compromise immune function, rendering older individuals more vulnerable to COVID-19 and increasing their risk of developing Acute Respiratory Distress Syndrome (ARDS).[10] The higher prevalence of COVID-19 cases among males may be explained by various factors, including hormonal differences, behavioral patterns, lifestyle choices, and physiological disparities in immune system

responses between males and females, all of which influence susceptibility to SARS-CoV-2 infection.[11–13] Regarding disease severity, findings are consistent with research by Kusumawardani, which identified moderate severity as the most common clinical presentation among COVID-19 patients.[14] In terms of comorbidities, a similar pattern was observed in a study conducted at a hospital in Surakarta during the period from March to December 2020, where diabetes mellitus was the most frequently reported comorbidity, followed by hypertension.[15]

Favipiravir was predominantly used in mild to moderate cases. Based on reviews, favipiravir demonstrated a tolerable safety profile with manageable side effects, improved viral clearance within seven days, and clinical improvement during the first 14 days in mild to moderate cases. Its oral formulation facilitates easy administration.[16] However, studies show no benefit in administering favipiravir to severe cases, highlighting the need for caution in its use for such patients. Furthermore, adding favipiravir to the standard care for severe cases does not improve clinical outcomes.[17,18] In this study, five severe patients received favipiravir therapy, underscoring the need for further investigation into its efficacy in severe cases.

Oseltamivir, while more cost-effective than favipiravir for moderate COVID-19 cases, has demonstrated limited effectiveness.[19] Recent in vitro studies and clinical usage showed that oseltamivir is ineffective against SARS-CoV-2, does not improve symptoms, and does not slow disease progression. Consequently, oseltamivir is unsuitable for COVID-19 treatment and is no longer recommended in the 2022 COVID-19 management guidelines.[20,21]

Remdesivir was commonly used in moderate cases requiring oxygen and in severe cases. Current COVID-19 management guidelines recommend remdesivir for moderate and severe patients. Research indicates that remdesivir accelerates clinical recovery, reduces recovery time, and has an acceptable safety profile based on clinical trials.[22]

Combination antiviral therapies were also noted. While some studies suggested that combining favipiravir and oseltamivir could expedite clinical recovery in severe influenza cases, there is no supporting evidence or recommendation for such combinations in COVID-19 management, especially given oseltamivir's ineffectiveness against SARS-CoV-2.[23]

Corticosteroids, with their anti-inflammatory and immunosuppressive effects, were used to modulate immune response.[15] Research shows that corticosteroids can reduce mortality among hospitalized COVID-19 patients, but their

benefits are limited to those requiring supplemental oxygen or mechanical ventilation. Their use in patients not requiring supplemental oxygen does not improve outcomes and may pose risks, leading to their exclusion from recommendations for such cases.[24] However, this study observed corticosteroid use in mild cases, contrary to COVID-19 management guidelines. This may reflect attempts to alleviate systemic symptoms and reduce the risk of COVID-19-induced ARDS. Further evaluation of this practice is necessary.[25]

There is a hypothesis suggesting that methylprednisolone has higher pulmonary penetration compared to dexamethasone, alongside a trend towards lower mortality rates in patients receiving methylprednisolone, albeit without statistical significance.[26] Studies on the efficacy of dexamethasone versus methylprednisolone have demonstrated their significant effectiveness in controlling inflammatory markers and improving the PaO2/FiO2 ratio in moderate to severe COVID-19 cases.[27] However, this study found that only 31% and 34% of moderate and severe cases, respectively, received corticosteroid therapy, highlighting low usage and emphasizing the need to evaluate corticosteroid administration in these patients.

COVID-19-induced pulmonary symptoms are associated with a hyperinflammatory response and cytokine storm involving interleukin and chemokine dysregulation. The cytokine storm leading to acute respiratory distress syndrome (ARDS) is a major cause of respiratory and lung damage in severe cases. IL-6 receptor blockers play a pivotal role in mitigating hyperinflammation, with IL-6 cytokine receptor blockade emerging as a promising therapy for severe SARS-CoV-2 cases.

The cytokine storm triggered by COVID-19 can lead to hyperinflammation and hypercoagulability due to dysregulated coagulation cascades. Pro-inflammatory activation, as part of cytokine release syndrome during SARS-CoV-2 progression, initiates a coagulation cascade that can result in thrombosis and widespread intravascular clot deposition. This disrupts organ blood supply, causing organ failure and death. Hence, anticoagulant therapy is crucial for preventing coagulopathies leading to thrombosis and thromboembolism, providing a favorable prognosis for COVID-19 patients. This study observed low anticoagulant use (33.3%) among moderate cases requiring oxygen and severe cases, warranting further investigation into its implementation.

Intravenous immunoglobulin is thought to be most beneficial when administered early, as patients begin to deteriorate but before respiratory failure occurs.[28,29] Research indicates IVIG can

improve clinical outcomes, reduce disease duration, enhance oxygen saturation, and prevent the progression of lung lesions in severe COVID-19 cases refractory to standard treatment.[30,31] However, in this study, only two patients received convalescent plasma therapy, likely due to the difficulty in obtaining plasma donors during the pandemic. While systematic reviews have shown convalescent plasma therapy offers no clear benefits, does not improve clinical recovery, and fails to reduce mortality risk in moderate or critical cases, further studies are required.[32] The use of antibiotics in COVID-19 patients remains controversial, as bacterial co-infections in COVID-19 are relatively rare. Excessive antibiotic use poses risks, including increased resistance rates and higher mortality.[33–35] This underscores the need for careful evaluation before administering antibiotics in COVID-19 management. N-Acetylcysteine, an antioxidant with antidotal properties, shows promise as both a therapeutic and preventive agent for COVID-19. Studies indicate that NAC significantly reduces the duration of extracorporeal membrane oxygenation (ECMO) use, shortens hospital stays, suppresses pro-inflammatory cytokine production, inhibits viral replication, and acts as an antioxidant. These properties make NAC effective in reducing inflammation caused by COVID-19 infection.[36]

Conclusion

The study results indicate that antiviral therapy was administered to 72.6% of COVID-19 patients, predominantly those with severe cases and moderate cases requiring oxygen. Anti-inflammatory therapy was given to 32.6% of patients, primarily those with severe disease, while anticoagulant therapy was administered to 17.8%, again mostly to those with severe conditions. This study emphasizes the importance of clinicians adhering to established guidelines when prescribing COVID-19 therapies. The findings can serve as a foundation for institutions to conduct further research on therapeutic approaches for COVID-19 patients, given the need for a thorough review of appropriate treatment strategies. Large-scale studies are needed to better understand the characteristics of therapy administration across different severity levels, which could guide the development of education and outreach programs aimed at ensuring healthcare professionals make informed and precise therapeutic decisions.

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(Teddy Tjahyanto)

Predictive Value of Optic Nerve Sheath Diameter in Subarachnoid Hemorrhage: A Systematic Review and Meta-Analysis

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Abstract

Introduction : Optic nerve sheath diameter (ONSD) is a promising non-invasive marker for elevated intracranial pressure (ICP), potentially aiding in the prognostication of subarachnoid hemorrhage (SAH) outcomes. This study aimed to evaluate the predictive value of ONSD for poor outcomes in SAH patients, defined by the Glasgow Outcome Scale (GOS).

Methods : A systematic review and meta-analysis were conducted, including studies from 2010 to 2021 that examined the relationship between ONSD and outcomes in SAH patients. A total of 615 patients were analyzed, with mean ages ranging from 54.1 to 58.8 years, and a predominance of males (38.2%). SAH severity was stratified using the Hunt and Hess classification, ranging from Grade 1 to Grade 5. The QUADAS-2 tool assessed the risk of bias, and the GRADE framework evaluated evidence certainty.

Results : The pooled analysis revealed moderate predictive accuracy for ONSD in determining poor outcomes, with a pooled proportion of 0.70 (95% CI: 0.61–0.78). Significant heterogeneity (I^2 = 77.4%, p = 0.004) was observed, likely due to variability in ONSD thresholds, measurement techniques, and timing. Funnel plot analysis suggested potential publication bias, although further statistical testing is needed.

Conclusions : ONSD demonstrates potential as a non-invasive tool for predicting poor outcomes in SAH patients. However, significant heterogeneity and moderate accuracy highlight the need for standardization of ONSD thresholds and measurement protocols. Further multicenter studies are required to validate its clinical utility and integrate it into comprehensive prognostic models.

Introduction

Subarachnoid hemorrhage (SAH) is a life-threatening neurological emergency with high rates of morbidity and mortality.[1] Timely identification and management of complications, particularly elevated intracranial pressure (ICP), are essential to improving outcomes. Traditional methods of ICP monitoring, such as invasive devices, are considered the gold standard but are associated with significant risks, including infection and hemorrhage, and may not be feasible in all clinical settings.[2] This limitation highlights the need for reliable, noninvasive alternatives.

Optic nerve sheath diameter (ONSD) has emerged as a promising noninvasive surrogate marker for ICP.[3] Due to the continuity between the intracranial subarachnoid space and the optic nerve sheath, changes in ICP are reflected in the ONSD. Studies demonstrate a strong correlation between ONSD and ICP, with reported correlation coefficients ranging from 0.59 to 0.91.[4] In patients with SAH, a linear relationship between ONSD and ICP has been observed, with a correlation coefficient of $r = 0.525$ ($p = 0.036$).[5] Additionally, the mean ONSD in SAH patients is significantly higher compared to healthy controls (6.6 ± 0.8 vs. 5.1 ± 0.47 mm), reinforcing its relevance in detecting elevated ICP.

Beyond diagnostic value, ONSD also holds prognostic significance in SAH. Studies report that SAH patients with poor neurological outcomes exhibit larger ONSD measurements, and a cutoff value greater than 6.22 mm is associated with a sensitivity of 70.3% and specificity of 80.7% for predicting poor outcomes.[5] Furthermore, the predictive value of ONSD for neurological prognosis, as reflected by C-statistics ranging from 0.735 to 0.812, highlights its utility as a tool for risk stratification. Integrating ONSD with clinical grading scales, such as the Hunt and Hess scale, has further enhanced prognostic accuracy, underscoring its potential in clinical decision-making. Among a study population of 223 SAH patients, 90.6% survived until discharge, with 83.4% demonstrating favorable neurological outcomes on the Glasgow Outcome Scale (GOS).[5] However, patients with elevated ONSD were more likely to have poor outcomes, emphasizing the importance of this measure in guiding clinical management.

This systematic review and meta-analysis aim to determine the outcomes of patients with SAH in relation to ONSD measurements. By synthesizing existing data, this study seeks to clarify the diagnostic and prognostic value of ONSD in SAH and evaluate its potential role in improving patient management strategies

Material And Methods

This systematic review and meta-analysis was conducted following a predefined protocol to ensure methodological rigor and transparency. Studies were included if they evaluated ONSD in patients with SAH and reported diagnostic or prognostic outcomes, such as correlations with ICP or neurological status. Eligible study designs included randomized controlled trials, cohort studies, and case-control studies published in peer-reviewed journals. Studies without full-text availability, those not reporting ONSD measurements, or conducted in populations other than SAH patients were excluded.

The literature search was performed in PubMed, EMBASE, and Scopus databases to identify relevant studies published up to August 1, 2024. The search strategies were tailored to each database, combining Medical Subject Headings (MeSH) terms and keywords such as *"optic nerve sheath diameter," "ONSD," "subarachnoid hemorrhage," "SAH," "intracranial pressure,"* and *"prognosis."* Boolean operators (*AND*, *OR*) were used to refine results, and filters for human studies and English language articles were applied (**Table 1**). Reference lists of included articles and relevant systematic reviews were screened for additional studies.

Table 1. Comprehensive Search Strategies Employed Across Databases

Scholar Repository	Search terms
PubMed	("optic nerve"[MeSH Terms] OR ("optic"[All Fields] AND "nerve"[All Fields]) OR "optic nerve"[All Fields]) AND ("foreskin"[MeSH Terms] OR "foreskin"[All Fields] OR "sheath"[All Fields] OR "sheath s"[All Fields] OR "sheathed"[All Fields] OR "sheathes"[All Fields] OR "sheathing"[All Fields] OR "sheaths"[All Fields]) AND ("diameter"[All Fields] OR "diameters"[All Fields]) AND ("subarachnoid haemorrhage"[All Fields] OR "subarachnoid hemorrhage"[MeSH Terms] OR ("subarachnoid"[All Fields] AND "hemorrhage"[All Fields]) OR "subarachnoid hemorrhage"[All Fields])
Scopus	optic AND nerve AND sheath AND diameter AND subarachnoid AND hemorrhage OR subarachnoid AND haemorrhage
EMBASE	(((optic nerve sheath diameter and subarachnoid hemorrhage) or subarachnoid haemorrhage) and outcome).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]

The population includes adult patients diagnosed with SAH, encompassing varying degrees of severity as classified by clinical grading systems such as the Hunt and Hess scale. The intervention involves the measurement of ONSD, regardless of the specific imaging modality or method used, provided that each study explicitly specifies the measurement technique. The comparison is implicit in the context of patients with differing GOS-defined outcomes, comparing those with favorable neurological recovery to those with poor outcomes. The outcome of interest is the incidence of poor neurological outcomes, specifically assessed using GOS scores, to determine the prognostic utility of ONSD in this population.

Studies were included if they evaluated the predictive value of ONSD in adult patients diagnosed with SAH, provided a clear definition of poor neurological outcomes based on the GOS, and explicitly reported the method of ONSD measurement, regardless of the imaging modality used. Both prospective and retrospective observational studies published between 2010 and 2021 were considered, provided they presented original data. Exclusion criteria included

studies involving pediatric populations, those without a clear definition of poor outcomes, studies that did not specify ONSD measurement techniques, conference abstracts without full text, case reports, reviews, and studies not published in English.

Two independent reviewers (TT and MS) screened the titles and abstracts of all identified records. Full-text articles were retrieved for studies that appeared to meet the inclusion criteria or where eligibility was uncertain. Disagreements during screening and selection were resolved by discussion. No automation tools were used in this process to ensure a thorough and unbiased review.

Data extraction was conducted independently by two reviewers (TT and MS) using a predesigned data extraction form. Extracted data included study characteristics (author, year, design, and population), ONSD measurement details, outcomes (e.g., ICP correlation, neurological prognosis), and statistical measures (e.g., c-statistics). Any discrepancies in extracted data were resolved through consensus.

The risk of bias in included studies was assessed using the QUADAS-2 tool, justified by its relevance for diagnostic accuracy studies. QUADAS-2 evaluates study quality across domains such as patient selection, index test, reference standard, and flow and timing.[6] Additionally, the GRADE approach was used to assess the certainty of evidence, as it provides a structured and transparent framework for rating the quality of evidence and strength of recommendations in systematic reviews.

Data synthesis was performed using RStudio with the *meta* package. Statistical analysis included pooling c-statistics to evaluate the diagnostic and prognostic value of ONSD in SAH patients. Heterogeneity was assessed using the I^2 statistic, and random-effects models were applied to account for variability across studies. Data were described using 95% confidence intervals (CI), and statistical significance was defined as a p-value < 0.05.

Result

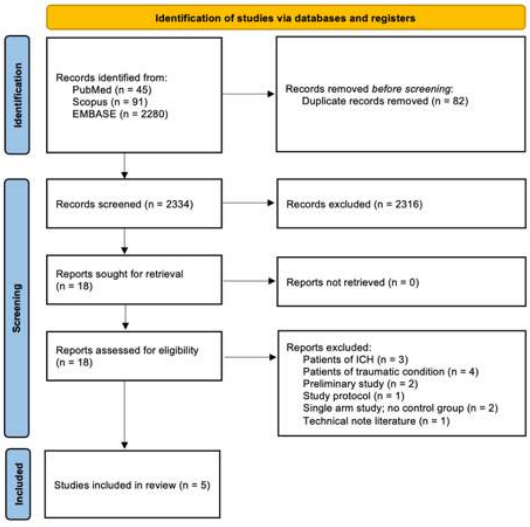

Figure 1. Screening of potential studies in adherence to the PRISMA guideline.

During the identification phase (**figure 1**), records were gathered from three databases: PubMed (45 records), Scopus (91 records), and EMBASE (2280 records), resulting in a total of 2416 records. After removing 82 duplicate entries before screening, 2334 unique records were left for further review. In the screening phase, these 2334 records underwent evaluation, and 2316 records were excluded for not meeting the inclusion criteria. Eighteen reports were sought for retrieval, all of which were successfully retrieved without any missing documents. These reports were then assessed for eligibility. Following the eligibility assessment, thirteen reports were excluded for various reasons. Specifically, three reports involved patients with ICH, four focused on patients with traumatic conditions, two were preliminary studies, one was a study protocol, two were single-arm studies without a control group, and one was technical note literature. This process left five studies that were ultimately included in the review.[5,7–10]

Table 1. Demographic characteristics of the included studies (n = 615)

Study ID, cutoff ONSD	Study duration	Total cohort, n	Age, years	Male, n	GCS	Hunt Hess Classification
Lee 2019, 6.22 mm	January 2012 and June 2017	223	58 ± 13 years	84	11.2 ± 4.4	Grade 1: 100 Grade 2: 100 Grade 3: 40 Grade 4: 36 Grade 5: 47
Yesilaras 2017, 5.76 mm	January 2010 - December 2014	61	56 (IQR = 25, min: 24, max: 90) years	24	GCS 14–15: 32 GCS 9–13: 13 GCS < 9: 15	Grade 1: 31 Grade 2: 5 Grade 3: 11 Grade 4: 7 Grade 5: 6
Cenik 2021, 4 mm	March 2019 and September 2019	56	58.8 ± 15.1 years	16	GCS 14–15: 42 GCS 9–13: 5 GCS < 9: 9	Grade 1: 20 Grade 2: 16 Grade 3: 5 Grade 4: 7 Grade 5: 8
Kim 2023, 4.78 mm	January 2015 and December 2021	171	54.1 ± 12.1 years	60	12.5 ± 3.9	Grade 1: 60 Grade 2: 40 Grade 3: 30 Grade 4: 34 Grade 5: 7
Zhu 2021, 6.4 mm	August 2015 to November 2020	104	58.8 ± 17.4 years	51	GCS 3: 27 GCS 4: 4 GCS 5: 8 GCS 6: 4 GCS 7: 4 GCS 8: 7	n/r
		615		235		

The included study period was between 2010 and 2021, encompassing a total of 615 patients diagnosed with SAH. The mean age of participants ranged from 54.1 to 58.8 years, with a predominance of males (235 patients, 38.2%) with different ONSD threshold. GCS scores varied widely across the studies, reflecting the spectrum of neurological severity at presentation. The Hunt and Hess classification, used to assess the severity of SAH, revealed the following totals across the included studies: Grade 1 (211 patients), Grade 2 (161 patients), Grade 3 (91 patients), Grade 4 (84 patients), and Grade 5 (68 patients). These distributions underscore the variability in clinical presentation, ranging from mild to severe cases, and highlight the heterogeneity in patient populations assessed across studies. According to the QUADAS-2 assessment (**figure 2**), the studies were classified as having a low risk of bias, while the GRADE evaluation indicated that the studies provided evidence of high certainty.

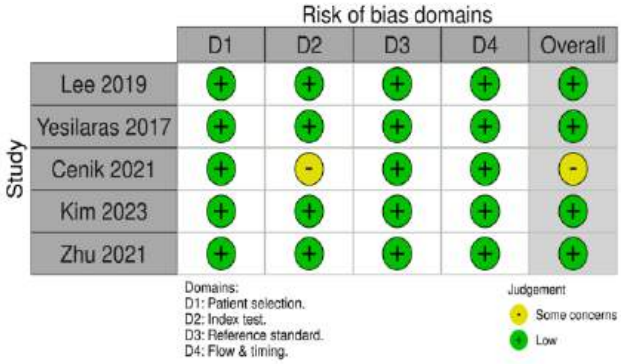

Figure 3. QUADAS-2 assessment of the included studies

The pooled analysis (**figure 2**), incorporating data from four studies, demonstrates a moderate predictive accuracy with a pooled proportion of 0.70 (95% CI: 0.61–0.78). However, significant heterogeneity (I^2=77.4, p = 0.004) highlights variability across studies, likely due to differences thresholds for ONSD. The funnel plot suggests potential publication bias, though further statistical testing is necessary for confirmation.

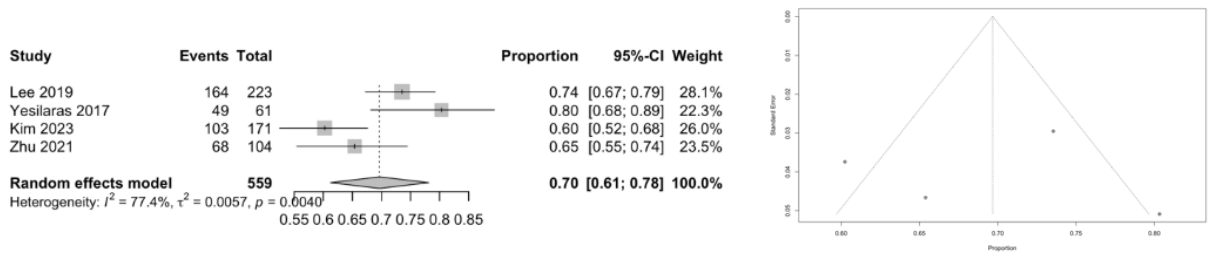

Figure 2. Pooled analysis of the concordance value of ONSD for predicting poor outcome in patients with SAH.

Discussion

The ONSD has been increasingly studied as a non-invasive marker for assessing ICP, a critical determinant of outcomes in patients with SAH. Elevated ICP is strongly associated with poor neurological outcomes, positioning ONSD as a potentially valuable prognostic tool in clinical settings.[11] This study aimed to evaluate the predictive value of ONSD for poor outcomes in SAH patients, as defined by the GOS. The variability in clinical presentations and the inherent challenges of early risk stratification in SAH underscore the importance of identifying reliable, non-invasive prognostic markers. A marker such as ONSD could contribute to improved decision-making and better patient outcomes.[12]

The analysis of four included studies, encompassing 615 SAH patients, demonstrated moderate predictive accuracy for ONSD, with a pooled proportion of 0.70 (95% CI: 0.61–0.78). These findings suggest that ONSD is capable of identifying patients at higher risk of poor outcomes. The robustness of the evidence was supported by high-certainty ratings from the GRADE assessment and a low risk of bias according to QUADAS-2.

The use of the Hunt and Hess classification in stratifying SAH severity highlighted the broad applicability of ONSD across different clinical grades.[13] The inclusion of patients with varying levels of severity, ranging from mild to severe (Grades 1 to 5), emphasized the potential utility of ONSD in diverse clinical scenarios. Additionally, the non-invasive nature of ONSD measurement presents significant advantages over invasive ICP monitoring, particularly in resource-limited healthcare settings.[14] The inclusion of studies conducted over an 11-year period, with mean participant ages ranging from 54.1 to 58.8 years, also ensured a representative sample for evaluating the clinical relevance of ONSD.

Despite the promising results, significant heterogeneity ($I^2 = 77.4\%$, $p = 0.004$) was observed among the included studies, which limits the generalizability of the findings. Variations in ONSD thresholds, the timing of measurements relative to SAH onset, and differences in imaging modalities likely contributed to this inconsistency.[15,16] For instance, some studies used ultrasound for ONSD measurement, while others relied on computed tomography (CT) or magnetic resonance imaging (MRI), potentially affecting the precision and comparability of results.[17]

The funnel plot revealed a possible risk of publication bias, suggesting that studies with predominantly positive findings might have been overrepresented. Additionally, the moderate predictive accuracy of ONSD indicated that it might not account for all factors influencing patient outcomes. Confounding variables,

such as comorbidities, variations in treatment strategies, and individual patient trajectories, could also affect the reliability of ONSD as a standalone prognostic marker.[18]

Some studies have further suggested that while ONSD correlates with elevated ICP, it might lack specificity in predicting long-term outcomes. Transient increases in ICP or other pathophysiological mechanisms unrelated to ONSD could diminish its prognostic value in some cases.

Limitations and Implications of Heterogeneity

Significant heterogeneity across studies warrants further investigation to identify underlying sources. Factors such as differences in ONSD measurement techniques, timing of assessment relative to SAH onset, and variability in patient management strategies could contribute to this variability.[19] Standardizing ONSD thresholds and measurement protocols may improve consistency and enable broader clinical implementation. The potential publication bias, as suggested by the funnel plot, raises additional concerns.[20] While the implications of bias cannot be fully ascertained without further statistical testing, it underscores the need for transparency and inclusion of negative or inconclusive findings in future research.

Integration into Clinical Practice

The findings underscore the promise of ONSD as a non-invasive, rapid, and accessible tool for early risk stratification in SAH patients. When used alongside traditional clinical and radiological markers, ONSD could enhance prognostic accuracy and guide management decisions, such as the allocation of intensive monitoring or timely interventions.[21] However, given the moderate predictive accuracy observed, ONSD should not be used in isolation but as part of a comprehensive assessment.

Future Directions

Future studies should aim to standardize ONSD measurement techniques and establish evidence-based thresholds tailored to SAH severity grades. Additionally, larger multicenter studies with diverse patient populations are needed to validate these findings and explore the potential influence of demographic and clinical variables. Addressing heterogeneity through subgroup analyses and harmonized methodologies could further refine the utility of ONSD in clinical practice.

Conclusion

This study provides evidence supporting the utility of ONSD as a moderate predictor of poor outcomes in SAH patients. While promising, the heterogeneity across studies and the moderate predictive accuracy highlight the need for further standardization and validation before routine clinical implementation.

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(Teddy Tjahyanto)

Bereavement as A Risk Factor for Depression in The Elderly: An Evidence Based Case Report

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Abstract

Background: Depression disorder among the elderly population is a serious issue that is often underdetected and undertreated. Depression can lead to functional impairments, which are comparable to or even worse than those in individuals with chronic conditions such as heart and lung diseases. Bereavement is believed to be one of the risk factors for depression in the elderly. This literature search aims to explore bereavement as an etiology of depression in the elderly.

Method: A structured search was conducted using the PubMed, Cochrane, and Science Direct databases, using tailored keywords aligned with the clinical question to obtain relevant results.

Results: The search and selection process yielded one selected article that was deemed relevant to the case. This article provided a summary of evidence concerning the relationship between bereavement and the emergence of depression diagnosis in the elderly.

Conclusion: The results of this systematic review and meta-analysis indicate that bereavement increases the risk of depression in the elderly. However, further studies are still needed to elucidate the mechanisms underlying depression in the elderly**.**

Introduction

Depression is categorized as an affective disorder, characterized by three typical symptoms: a depressed mood, loss of interest and pleasure, and reduced energy leading to increased fatigue and decreased activity. These symptoms persist for at least two weeks, with distinct changes in affect, cognition, and individual functioning. Careful consideration is necessary to differentiate between normal sadness and grief-related bereavement.[1] Bereavement can cause significant suffering, yet it is not immediately labeled as a depressive disorder. Bereavement and depression co-occur, depressive symptoms and impaired functioning tend to be more severe, with a worse prognosis compared to bereavement without concurrent depression.[2] Bereavement can disrupt sleep in the elderly who have lost their partners, which is not correlated with the length of time since the loss but is related to the level of perceived sadness. Bereavement-related sadness exhibits

depressive symptoms such as decreased functioning, sleep disturbances, and withdrawal from usual activities. Monk et al. noted in their study that 28% of cases of bereavement progress into depression among the elderly.[3]

Prevalence data indicates that depression can occur in 1-3% of the general elderly population, with 8-16% exhibiting significant functional impairments. Findings from studies highlight that depression in the elderly is a serious issue, with less than 20% of those experiencing depression receiving a diagnosis and undergoing therapy. A meta-analysis study conducted over a 24-month follow-up period found that among depressed elderly individuals, 33% fully recovered, 33% remained in a depressive state, and 21% passed away.[4] A program designed to prevent delirium in elderly patients during hospitalization was proven effective. It is expected that depression prevention in the elderly would yield similar effectiveness, yet risk factors associated with depression need to be identified for targeted prevention, including bereavement.[4]

The author draws attention to bereavement as an etiology of depression in the elderly, given the number of geriatric patients diagnosed with depression following a bereavement. The outcomes of this literature review are anticipated to provide conclusions, insights, and an overview of the risk factors linking bereavement to depressive disorders in the elderly. Ultimately, this could aid in the prevention and management of depression in the elderly population.

Case Illustration

A 68-year-old female patient arrived alone at the Primary Care Clinic. Occasionally, tears welled up in her eyes as she recounted the passing of her husband, who had died about 1.5 years ago. She had four children with varying personalities, including how they reacted when she talked about her late husband in front of them. Some remained silent and indifferent, while others became angry and scolded her, saying it was pointless to speak of him since he had been gone for a long time. The patient lacked a space to share her memories of her late husband.

Her sleep was disrupted; if she totaled it up, she managed to sleep for only about 30-60 minutes a day. Her mind was consumed by many thoughts, such as her eldest unmarried daughter, who was 42 years old. Every night she thought that God was unfair for taking her husband before her. Her husband's death had been caused by a malignancy. He had been under treatment for several months in a hospital until the malignancy spread to his brain, resulting in behavioral changes that eventually led to his demise. During his treatment, the patient revealed

that she had mentally prepared herself for the possibility of his condition deteriorating and his passing. At that time, she felt and expressed to the medical team that she had come to terms with and was ready for whatever might happen. She felt strong back then, knowing her husband would eventually pass away. She even considered that perhaps this was for the best. If she were to die first, there would be no one to care for her husband, who was bedridden. The situation would be better this way. Despite these thoughts, in reality, she still cried every day whenever she remembered her late husband. She also struggled with concentration, frequently forgetting things, having a loss of appetite, losing interest, and feeling a lack of energy.

The patient was a retired midwife. She understood that she needed to eat even when her appetite was gone and sleep even when sleep evaded her. She inquired whether the grief she was experiencing was causing the symptoms she currently felt, even though over a year had passed since her husband's death.

Method

The question under consideration is whether the elderly population that undergoes bereavement is more susceptible to experiencing depression in the future. To address this query, the clinical framework is structured using the PECO format. The patients in question are elderly individuals, the exposure involves the experience of bereavement, the comparison entails those without bereavement, and the primary outcome of interest is the occurrence of depression disorder. This framework will guide the exploration of the potential association between bereavement and heightened risk of depression among the elderly.

The search was conducted using keywords formulated based on Boolean operators. The evidence searches engines employed included Pubmed, Cochrane, and Science Direct, illustrated in Table 1.

Table 1. Results of journal article search

Search Engine	Keywords	Result
Pubmed	(((elderly[Title/Abstract]) AND(depression[Title/Abstract])) AND (risknfactors[Title/Abstract])) OR (bereavement[Title/Abstract])	50
Cochrane	(elderly) AND (risk factors) AND (depression) OR (bereavement)	12
Medline	elderly AND risk factors AND depression OR bereavement	27

The article selection process was carried out in stages. In the first stage, keywords were utilized, while in the second stage, screening was performed for meta-analyses and systematic reviews. Further filtering was then conducted according to the inclusion criteria: 1) Written in English; 2) Full-text format; 3) Human studies; 4) Elderly subjects. Articles obtained were

screened based on their titles and abstracts, aligning them with the clinical question. Subsequently, after the selection process from 3 databases, a systematic review and meta-analysis article was selected:

1. Cole MG, Dendukuri N. *Risk factors for depression among elderly community subjects: a systematic review and meta-analysis*. Am J Psychiatry. 2003 Jun;160(6): 1147-56. doi: 10.1176/appi.ajp.160.6.1147. PMID: 12777274. PMCID: PMC7862357

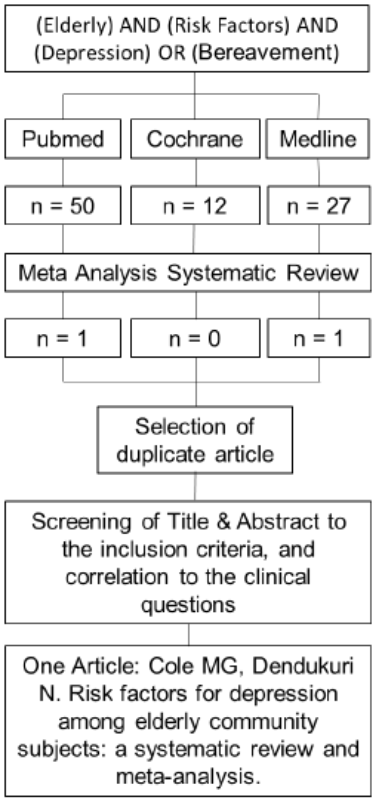

Figure 1. Results of journal article search

Results

The process of critical appraisal was conducted by assessing the validity, importance, and applicability of the selected articles using the meta-analysis appraisal sheet provided by the Centre for Evidence-Based Medicine.[5]

The objective of this systematic review and meta-analysis by Cole and Dendukuri is explicitly stated: to investigate the association between risk factors and depression in the elderly. This systematic review and meta-analysis detail the search for relevant studies. The study utilizes multiple databases, namely MEDLINE and PsychINFO. In addition, the study outlines inclusion and exclusion criteria. The individual studies have been thoroughly assessed for their validity, and there is a summary presented in tabular form.

The researchers present individual studies that yielded results regarding risk factors for depression in the elderly. Participants were older adults, and the outcomes were presented as odds ratios, enabling meta-analysis. A forest plot can be provided, facilitating the measurement of the magnitude of risk factors in the occurrence of depression among the elderly.

From the study findings, the elderly are at a 3.3-fold increased risk of experiencing depression in the presence of bereavement. Therefore, when clinicians identify the risk of bereavement in the elderly, periodic support can be provided to help patients prepare for and navigate through the grieving process. If symptoms meeting the criteria for depression are

detected, early intervention can be initiated promptly. For other family members such as children, education on preventing depression in the elderly who have lost significant individuals in their lives can be imparted. In cases of depression, family members can also be educated about providing social support for elderly individuals dealing with depression.

In the discussion of the study, limitations are acknowledged. Nevertheless, the researchers remain hopeful that risk factors that haven't been successfully identified can be further investigated, potentially serving as valuable insights for developing depression prevention programs for bereaved elderly individuals.

Discussion

Bereavement is the period of mourning and grieving following a death. When someone experiences grief, it's a normal process of reacting to loss. Grief can manifest mentally, physically, socially, or emotionally. Mental reactions can trigger anger, guilt, anxiety, sadness, and despair. Physical reactions may include disrupted sleep, changes in appetite, other physical health issues, or illness. The duration of grieving varies based on the closeness to the deceased and whether the death was anticipated. Friends, family, and faith can serve as sources of support. Grief counseling or therapy can also be beneficial for some individuals.[6]

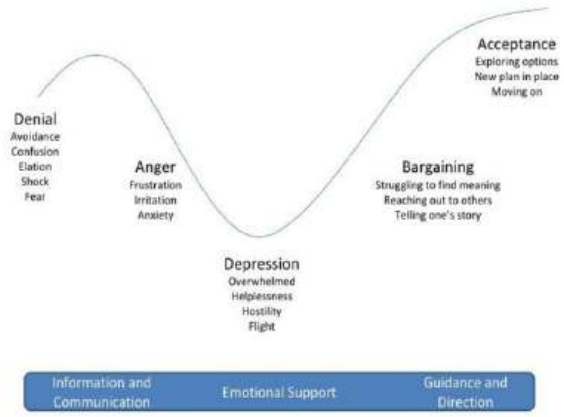

Figure 2. Kubler-Ross Grief Cycle

In a state of bereavement, the grieving process needs to be navigated for individuals to come to terms with their loss. Kubler-Ross proposed the theory of the grief cycle, consisting of five stages.[7]

The grief process comprises several stages. Initially, there's denial, where an individual refuses to believe in the permanence of the loss, often accompanied by avoidance, confusion, shock, and fear. This leads to anger, where frustration and irritability arise due to the loss, often mixed with anxiety. Following that is depression, a phase marked by a sense of helplessness, desperation, and withdrawal. Bargaining ensues as the bereaved seeks meaning, attempting to find solace by sharing memories and seeking support from others. Finally, there's acceptance, as the individual gradually plans for their future, embraces new experiences, becomes self-reliant, and emerges stronger and more resilient.

The progression through these stages doesn't always follow a linear path from step 1 to step 5; it can involve back-and-forth movement, revisiting previous stages. Moreover, there's no specific timeframe for transitioning between these phases. When providing support during the denial and anger stages, a therapist can convey information while employing communication techniques that consider the client's emotional state. During the depression phase, emotional support becomes crucial. As the journey reaches the bargaining and acceptance phases, therapists can accompany and guide clients in making forward-looking decisions.

In the depicted case illustration, the patient is currently experiencing the anger stage. They feel resentful towards God, perceiving an injustice due to their spouse's premature passing. As per the literature, they are undergoing a depressive disorder. Notably, the patient possesses risk factors including bereavement (3.3-fold increased risk), sleep disturbances (2.6-fold increased risk), and a previous history of depression (2.3-fold increased risk). These factors, in sequence, contribute to the risk of depression in the elderly, necessitating comprehensive management for addressing the patient's depression in a holistic manner.

Conclusion

The conclusion drawn from the evidence-based review conducted is that bereavement is one of the etiological risk factors for depression in the elderly. Bereavement potentially increases the risk of depression in the elderly by 3.3 times. Further studies are still needed to explore the etiology and risk factors associated with depression in the elderly, in order to facilitate the effective and comprehensive implementation of depression prevention programs for the elderly.

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(Dewanto Andoko)

Clivus Chordoma: Case Report and Current Considerations on Endoscopic Endonasal Trans-Sphenoid Surgery with Neurosurgeon-Otolaryngologist Collaboration

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Abstract

Chordomas, infrequent malignancies primarily located along the craniospinal axis, showcase gradual growth and localized bone destruction, with the clival region involved in approximately 25-35% of cases. Headaches accompanied by neurological deficits are the typical clinical presentations. Complete surgical resection is the mainstay, with recent collaborative efforts between otorhinolaryngologists and neurosurgeons leading to a positive shift from traditional craniotomic procedures to endoscopic endonasal approaches, fostering minimally invasive techniques and utilizing endoscopy for primary visualization across the neuraxis. Furthermore, the concept of team surgery has been introduced, involving simultaneous contributions from ENT surgeons and Neurosurgeons at all stages of the procedure, including the approach, resection, and reconstruction phases. This report presents a series of two successful cases of clival chordomas managed using the endoscopic endonasal approach at Siloam Hospital Lippo Village This indicates its potential as a viable surgical choice, particularly within medical centers that possess the necessary specialties. Successful implementation is notably enhanced through collaborative efforts between otolaryngologists and neurosurgeons, underscoring the significance of interdisciplinary teamwork.

Introduction

While a spectrum of immune and endocrine neoplasms can also occur, chordomas and chondrosarcomas are the most frequently encountered neoplastic pathologies involving the clivus.[1] Characterized as rare tumors (with an incidence of 0.08 per 100,000), chordomas originate from embryonic notochordal tissue and tend to exhibit slow growth, often forming within the bone. Although they can affect individuals of all ages, chordomas most commonly emerge during the third to the fifth decade of life, with a slight predominance in males.[2] The tumors in question display a low to intermediate malignancy and are characterized by their tendency to show local aggression.

Metastases are rare, usually occurring after recurrence. Primarily localized in the sacrum, clivus, or cervical vertebrae, these lesions often affect the distal and proximal ends of the spine. Caudal chordomas are observed in about 50% of cases, while a third of cases involve cranial chordomas affecting the clival region. These cranial chordomas typically appear as extradural midline masses and may involve cranial nerves, particularly the abducens nerve, during the initial presentation. [2] The incidence of chordomas varies depending on the anatomical location, with the sacrococcygeal region being the most common site (50-60%), followed by the spheno-occipital region (25-35%), and the vertebral column (10%).[3] Moreover, chordomas occur more frequently in males compared to females, highlighting a higher incidence in the male population. [4]

Chordomas in the cervical spine usually originate from parapharyngeal or paravertebral masses, accounting for approximately 3 to 7% of cases.[5] These chordomas develop from residual fetal or embryonic notochord remnants, which normally contribute to the formation of the nucleus pulposus in intervertebral discs. However, in the cephalic region of the notochord, these remnants differentiate into precursor cells responsible for forming the sella, the posterior body of the sphenoid, and the basiocciput bone.[6] The malignant transformation typically occurs in individuals aged between 50 and 60 years, with a relatively low incidence rate observed before the age of 40.[7] Chordomas in children tend to exhibit aggressive behavior. Surgical resection is the primary treatment objective, as it offers the most favorable prognosis. Patients who undergo complete tumor resection have a more optimistic outlook. The surgical challenge presented by the clivus arises from its intricate anatomy and its proximity to critical neurovascular structures.[8] Its anatomical structure is divided into three distinct regions: the upper clivus, mid clivus, and lower clivus. Traditionally, these regions have necessitated distinct surgical approaches, such as the orbito-zygomatic and transsphenoidal routes. [9]

The sphenoid sinus, positioned posterior to the ethmoid sinuses, carries significant anatomical importance for both neurosurgeons and ENT surgeons. [10] The evolution of the endoscopic endonasal approach (EEA) to the sphenoid sinus has taken distinct paths in neurosurgery and otolaryngology. Initially introduced in the early 1990s for pituitary lesion skull base surgeries, the endoscope emerged as a collaborative creation between otolaryngologists and neurosurgeons.[11] Collaboration between these two specialties proves vital for endoscopic endonasal transsphenoidal approaches due to the potential challenges and complications inherent in these procedures. This need for collaboration

arises from the structural variations, abnormalities, and complexities that neurosurgeons encounter during EEA to the sphenoid sinus.[12] Recent innovations, particularly within the realm of EEA, have revolutionized access to the clivus. This technique not only reduces complications but also enables local reconstructive flaps. EEA not only plays a pivotal role in managing chronic sinusitis and accessing the clival region but also empowers otolaryngologists to address a range of sinonasal disorders, even those involving complex sphenoid sinus lesions. The positive outcomes achieved through endoscopy further motivate neurosurgeons to embrace endoscopic techniques for clival procedures, drawn by the improved visualization they offer. [13,14] The triumph of endoscopic transsphenoidal approaches hinges on dynamic collaboration between neurosurgeons and ENT specialists.[12,15] Such collaboration proves indispensable when navigating through nasal variations, intricate skull base lesions, and multifaceted surgical interventions. In cases involving intrasellar lesions, neurosurgeons frequently take the lead in procedures at low-volume centers, with ENT surgeons playing a pivotal role in extended approaches.[12]

The emphasis on minimal invasiveness in the endoscopic approach not only facilitates the realization of "four hands" surgery but also confers notable advantages.[14] Collaborative endeavors between neurosurgeons and otorhinolaryngologists yield distinctive benefits, including heightened spatial orientation within the nasal cavity, simultaneous management of pathologies, and time savings in surgical procedures due to the specialized expertise each specialist contributes.[14] This has been further enhanced by the introduction of the team surgery concept, wherein ENT surgeons and neurosurgeons work in tandem across all stages of the procedure (approach, resection, and reconstruction).[16] This paradigm shift has also reshaped the surgical landscape, elevating the endonasal route to the primary approach for treating such lesions in carefully selected patients, relegating external approaches to a secondary option. The endonasal approach has indeed revolutionized skull base surgery, enabling less aggressive procedures that reach deep-seated structures without necessitating craniotomy and brain retraction. [16]

Case Report

We present two cases of clival chordomas that were observed between 2022 and 2023. In both cases, the surgical resection of the tumor was performed using an endoscopic endonasal approach, with collaboration between neurosurgeons and otolaryngologists.

First, a 20-year-old female who has been experiencing limited eye movement and double vision in the right eye for the past 3 years, accompanied by associated

pain. Initially, the double vision only occurred during lateral gaze, but gradually extended to straight-ahead vision. The left eye showed no complaints, and there was no history of prior illness. Neurologically, there was evidence of paresis in the right V1 cranial nerve and diplopia. Histopathological examination revealed multilayered columnar epithelial tissue, loose and dense connective tissue, atypical stellate-shaped nuclei, some with red cytoplasm, and myxoid stroma. There were also areas of necrosis, hemorrhage, trabecular bone, and granulation tissue, consistent with chordoma.

Second, a 21-year-old female patient who presented with blurred and unfocused vision in her left eye, accompanied by intermittent headaches over the past 2 years. The intensity of the headaches has been progressively increasing, along with worsening of her visual symptoms. Neurologically, there was evidence of paresis in the left VI cranial nerve and the right V cranial nerve. Other examination results were within normal limits. One year prior, the patient had been diagnosed with chordoma. MRI of the head revealed a contrast-enhancing, inhomogeneous, and destructive mass involving the clivus, intrasellar, suprasellar, and left parasella, extending into the sphenoid sinus and left prepontine cistern, measuring approximately +/- 4 x 3.1 x 2.6 cm, with a suggestion of chordoma.

The two patients were subsequently scheduled to undergo a resection procedure through collaborative efforts between an otolaryngologist and a neurosurgeon, using Endoscopic Endonasal Transsphenoidal Surgery (EETS). Both procedures followed the same approach, adhering to the principles of the binostril four-hand technique. The otolaryngologist initiated the procedure by creating a Hadad-Bassagasteguy flap. Subsequently, they established a path leading to the clivus through the sphenoid sinus. This involved performing a sphenoidotomy and a posterior septectomy to ensure more adequate access. Following this phase, the neurosurgeon proceeded with the surgical drilling towards the clivus, performing a subtotal removal of the chordoma. Upon its completion, the otolaryngologist took over to close the defect using a fibrin glue flap.

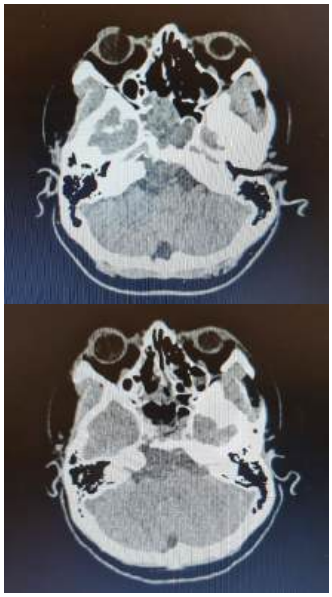

Figure 1. Image of chordoma size on pre- and post-operative non-contrast CT scans, showing a reduction in size on case 1

The CT scan (**figure 1.**) and contrast/non-contrast head MRI examinations in both cases revealed a significant decompression of the chordoma tumor mass following the endoscopic endonasal transsphenoidal surgery. In the first case, the dimensions were reduced to 3.3 x 5.9 x 2.8 cm, while in the second case, they were approximately +/- 2.6 x 1.5 x 1.8 cm.

After the operation, the first patient still complained of persistent shadowing vision and limited right eye movement, but some improvement was observed. Additionally, the patient had complaints of nasal congestion. 5 days later the patient was discharged and received prescribed medication upon returning home. For the second case, histopathological examination of the tissue obtained during the procedure showed a lobulated tumor mass composed of round nuclei resembling clustered epithelioid cells. These epithelioid cells exhibited pleomorphic nuclei with cytoplasm resembling physaliphorous cells. Necrosis and hemorrhage were also evident, consistent with a diagnosis of chordoma. Consequently, both patients were scheduled for multisession gamma knife treatment.

Discussion

Clival chordoma is a midline tumor known for its locally aggressive behavior at the spheno-occipital synchondrosis.[17] The concept of this tumor originating from remnants of the notochord was initially proposed by Muller, and later in 1894, Ribbert provided support for this theory after reviewing 5 cases.[18] Clival chordomas gained recognition as malignant tumors following the first reported mortality case in 1903.[18] In patients afflicted with clival chordomas, the typical presentation involves intractable headaches accompanied by neurological deficits, predominantly cranial nerve neuropathy.[19] Clival chordomas often manifest with abducens nerve involvement, resulting in diplopia, which is a common complaint. Additionally, rare symptoms and signs such as intracranial hemorrhage, epistaxis, and, in more uncommon cases, hearing loss, vertigo, and facial paralysis may present depending on the tumor's extent of growth.[20]

The narrow window of the clivus poses a challenging operative field for neurosurgeons. Adding to this complexity is the lack of clear protocols for managing clival chordomas, mainly due to its rarity. [17] Consequently, most reported cases exist in case series, resulting in limited literature and a scarcity of evidence-based treatment strategies for clival chordomas.[17] Nonetheless, it is established that the 5-year survival prognosis for treated clival chordomas falls between 50% and 85%, with the most favorable outcomes observed in cases where complete resection was achieved.[20] In the early

twentieth century, open approaches like transoral and transpalatal methods were the preferred means to access the clivus. [18] However, these approaches posed significant risks of morbidity, particularly cranial nerve injuries, as surgeons had to meticulously dissect around the delicate cranial nerves and vascular structures to reach the midline. [22] Furthermore, the open approaches showed high recurrence rates in clival chordoma surgeries due to the challenge of dealing with the lateral boundaries bounded by the cranial nerves and vascular system.

The advancement of endoscopic technology has significantly benefited surgeons in accessing the central part of the skull base, particularly the clivus. The direct anterior approach to the clivus offers several advantages, including the ability to avoid neurovascular structures at the lateral boundaries, resulting in a less invasive and lower morbidity procedure for patients. The continuous evolution of the endoscopic endonasal technique has enabled successful complete resection of clival chordomas. The integration of neuronavigation has become an essential tool in assisting surgeons to confirm vital landmark structures during dissection. [20] By combining MRI and CT scan data, the surgeon gains a comprehensive understanding of the operative field, including both bony structures and surrounding soft tissues.[23] The synergy between endoscopic endonasal methods and neuronavigation enhances safety and precision during surgery. Notably, virtual reality imaging has demonstrated an average shortest distance of 18.0 ± 1.8 mm between bilateral boundaries, with neuronavigation allowing for lateral extension of drilling in the superior and middle clivus, safeguarding the internal carotid artery from potential injury.[24] Nevertheless, some complications have been reported with this method, including persistent CSF leakage, hypopituitarism, temporary diabetes insipidus, and meningitis. Studies by Alessandro Paluzzi et al. have revealed promising results, recording a gross total resection rate of 83% for new chordomas and 44% for recurrent cases using the endoscopic transnasal method.[25] Following gross total or near-total resection of chordomas with endoscopic transnasal surgery, patients are typically recommended for radiochemotherapy to minimize the likelihood of recurrence and complete the comprehensive treatment approach.

In this case report, we present the successful management of 2 patients diagnosed with clival chordoma utilizing the endoscopic endonasal resection method with the collaborative efforts of neurosurgeons and otolaryngologists. Prior to the surgical procedure, prophylactic antibiotics were administered to both patients to prevent the occurrence of meningitis. Following the surgical intervention, both patients underwent

gamma knife therapy as an additional treatment to address the residual tumor and enhance local tumor control. The utilization of gamma knife therapy aimed to further reduce the tumor burden and improve the overall treatment outcome. In both of these cases, the chosen therapeutic approach involved the utilization of Endoscopic Endonasal Transsphenoidal Surgery (EETS) in a collaborative effort between otolaryngologists and neurosurgeons. This decision was made after carefully considering the manifold merits of skull base surgery in contrast to external surgical procedures such as craniotomy. The location of clival chordomas, situated within the midline of the skull base and surrounded by a multitude of intricate neurovascular structures, engenders a heightened risk of morbidity when managed via an external approach. EETS, on the other hand, offers a less invasive surgical intervention. Collaborative efforts between otolaryngologists and neurosurgeons span the entirety of the procedural spectrum, encompassing the approach, resection, and reconstruction phases.

Employing the "four-hand" concept, neurosurgeons in these cases benefit significantly in terms of enhanced visualization and orientation during tumor resection. This advantage is attributable to the prior assistance provided by otolaryngologists in facilitating improved access to the clivus. This is achieved through their extensive expertise in navigating the intricacies of nasal cavity structures and intervening in nasal cavity anatomy, particularly when confronted with variations or pathological features. This yields a distinct advantage, as the time required to access the sphenoid sinus is generally expedited when under the purview of otolaryngologists, with a concomitant reduction in endonasal complications. Neurosurgeons also enjoy greater procedural flexibility compared to undertaking EETS in isolation. The collaborative decision-making process fosters cross-fertilization of ideas, ultimately resulting in the selection of the optimal course of action. Additional advantages encompass a diminished incidence of morbidity, the absence of visible scarring, reduced surgical durations, and shorter postoperative convalescence periods.

In these specific cases, postoperative patients exhibited a swift recovery, necessitating only a brief 5-day hospital stay with minimal discomfort. Furthermore, patients were able to swiftly resume their daily activities. These outcomes underscore the inherent advantages of EETS over craniotomy, particularly when executed through direct collaboration between otolaryngologists and neurosurgeons.

Following the treatment, all patients underwent neuro-radiological imaging to

monitor their progress, considering the known high recurrence rate of clival chordoma. Both patients were kept under close follow-up, and subsequent MRI scans revealed a reduction in the size of the residual tumors, with the patients experiencing full restoration of their daily activities. These favorable results demonstrate the effectiveness of the endoscopic endonasal method in managing clival chordomas and achieving sustained remission in the long term. The successful outcomes further support the use of this approach as a viable treatment option for clival chordomas, emphasizing its potential for favorable long-term prognosis and improved patient quality of life.

Conclusion

Prior to the development of the endoscopic endonasal method, the resection of clival chordomas was exclusively performed by neurosurgical teams using open approaches. However, this approach was associated with a high incidence of recurrence and significant morbidity. With the introduction of endoscopic endonasal surgery, the quality of life for patients with clival chordomas can now be better maintained.

Extended Endonasal Transsphenoidal Surgery is a collaborative endeavor that goes beyond individual expertise. Collaboration between neurosurgeons and ENT surgeons is indispensable even for simpler approaches. The practical implications of endonasal structural variations underscore the importance of thorough preoperative assessments to minimize surgical complications. Additionally, the stepwise surgical approach to the sphenoid sinus highlights the significance of collaborative interventions in addressing complex anatomical challenges. EETS thrives on the unity of medical disciplines, utilizing collective expertise to optimize patient outcomes and surgical success.

Nevertheless, the limitation of this case series lies in its small sample size, which is a consequence of the rarity of this disease. Future innovations in this method should be pursued to further enhance and optimize the resection of clival chordomas, ensuring better outcomes for patients in the long run. Continued research and advancements in the field hold the promise of improving the management and prognosis of this challenging condition.

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(Michael Lekatompessy)

Identification and Interpretation of Spinal Cord Injuries in Robbery Victims: A Forensic Review

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Abstract

Robbery is intrinsically a violent crime and is defined as the original criminal plan of the perpetrator by committing robbery, by force committed on occasion or with the pretext of robbery. Strangulation by ligature occurs when an external force is applied to the neck causing various traumatic pathologies. If the injury is severe enough, cerebral perfusion and oxygen delivery are compromised and can lead to asphyxia and rapid neuronal death. These injuries can be encountered in a variety of clinical scenarios and may be present in suicide attempts, sports injuries, motor vehicle trauma, and may have implications in the fields of criminology and forensic pathology. In this case, a 66-year-old woman who was a victim of a robbery suffered a neck injury. After examination, there was a fracture in the cervical spine and was diagnosed with spinal cord trauma. As a result of this injury, the victim suffered permanent paralysis. The perpetrators of the robbery are threatened with criminal penalties under 364 KUHP and/or Article 351 No 3 KUHP.

Introduction

Ligature strangulation is a traumatic condition resulting from external pressure exerted on the neck and its adjacent structures. This form of asphyxia occurs due to impaired oxygen delivery, typically caused by the compression of cervical blood vessels or obstruction of the trachea.[1,4]

In cases of ligature strangulation, death is primarily attributed to cerebral hypoxemia, which progresses to cerebral ischemia. Four principal mechanisms contribute to mortality in such cases. First, compression of the jugular veins impairs venous return from the brain, elevating intracranial pressure and causing loss of consciousness, brainstem dysfunction, asphyxia, and ultimately death. Second, obstruction of the carotid arteries restricts the delivery of oxygenated blood to the brain, resulting in asphyxia and death. Third, compression of the larynx can obstruct oxygenation of pulmonary vessels,

leading to fatal hypoxia. Lastly, although uncommon, bilateral carotid artery compression may induce cardiac dysrhythmias, culminating in cardiac arrest.[1,3,4]

Robbery is intrinsically a violent offense, characterized as a criminal act where the primary intent is theft, with murder occurring either incidentally or as a direct consequence of the act. A criminal act refers to an unlawful behavior that contravenes societal norms and established regulations. Criminologists emphasize the importance of understanding crimes within the broader framework of societal structures, particularly the disparities in power and wealth, as well as the effects of economic and political transitions. Criminal cases are widespread in Indonesia, occurring at both high and moderate levels. Victims of crime encompass individuals across all income groups, including high-, middle-, and low-income communities. These victims frequently endure the loss of property, physical and psychological harm, and long-term trauma. Economic challenges, such as unemployment, inadequate wages, or job loss, often motivate individuals to engage in criminal behavior. Furthermore, limited educational attainment restricts their access to better employment opportunities, perpetuating economic hardship and increasing the likelihood of criminal activity.[2,3,15]

Crimes are broadly classified into four categories: (1) Property-related offenses, including robbery, theft, arson, and embezzlement; (2) Crimes targeting individuals, such as murder, rape, and assault; (3) Socially deviant behaviors, including gambling, prostitution, and substance abuse; and (4) Regulatory violations, such as participation in riots and traffic infractions.[10]

Table 1. Crime Rates in Indonesia from 2016 to 2021

Year	Crime Rate (per 100,000 people)
2016	140
2017	129
2018	113
2019	103
2020	94
2021	90

According to Table 1, which utilizes data from the Central Bureau of Statistics spanning 2016 to 2021, the crime rate in Indonesia exhibited a fluctuating pattern, declining from 140 crimes per 100,000 individuals in 2016 to 90 crimes per 100,000 individuals in 2021. Analyzing the causes of crime through an economic perspective provides deeper insights into the underlying factors.[7]

Central Sulawesi Province reported the highest average crime rate, with 303 cases, while Central Java Province recorded the lowest, with 43 cases. In terms of unemployment rates, Aceh Province had the highest rate at 9.53%,

whereas East Nusa Tenggara (NTT) Province had the lowest, at 3.33%.[7]

Murders occurring during robberies and those with unidentified motives present unique challenges for law enforcement in uncovering facts and determining motives. A significant proportion of these cases involve victims and perpetrators with no prior connection. These crimes frequently lack third-party witnesses, requiring investigators to infer violent motives from limited evidence. As a result, a substantial number of robbery-related murders appear to arise from instances where the motive remains unclear, rather than from any simplistic assumptions or projections.[10]

Case Report

A 66-year-old woman presented to the Emergency Department of Siloam Hospital Lippo Village on December 15, 2022, with complaints of bilateral leg paralysis. She was referred from the North Jakarta Regional General Hospital. According to her medical history, the paralysis occurred following a robbery incident in which the perpetrator forcibly twisted her neck. At the formal request of the Indonesian National Police, North Jakarta Metro Police, Tanjung Priok Sector, dated January 20, 2023, a medical examination was conducted to assess her condition.

On physical examination, the patient was alert but exhibited moderate discomfort. Her blood pressure was significantly elevated at 175/57 mmHg. She had a normal pulse rate of 64 beats per minute and a normal body temperature of 36°C. However, tachypnea was noted, with a respiratory rate of 25 breaths per minute.

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For diagnostic evaluation, imaging studies were performed, including a non-contrast MRI of the cervical spine, a chest X-ray in the posteroanterior (PA) view, and cervical spine X-rays in anteroposterior (AP) and lateral views.

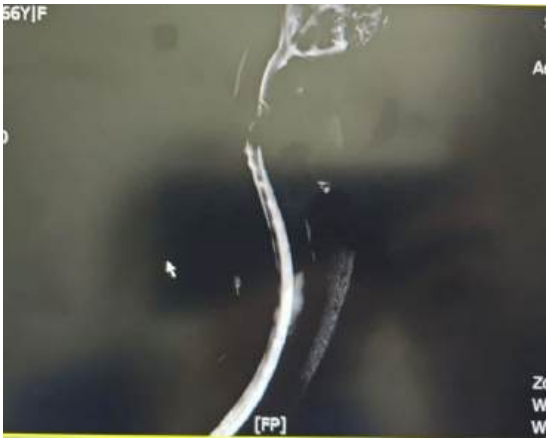

Figure 1. MRI of the Cervical Spine Without Contrast

Figure 2. MRI of the Cervical Spine Without Contrast

Figure 3. MRI of the Cervical Spine Without Contrast

MRI imaging of the cervical spine without contrast revealed several findings, including cervical reverse lordosis, thoracic scoliosis to the left, mild osteopenia, intervertebral disc degeneration, and cervical spondyloarthrosis. Compression of the C4-C6 vertebral bodies with associated bone edema was noted. Myelopathy and spinal cord edema extended from C3 to T1, along with tears in the interspinous ligaments at the C3-C6 levels. Paraspinal soft tissue edema was observed from C2 to T5, and fluid intensity was noted in the prevertebral soft tissues at these levels. At the C3-C4 level, there was bulging of the intervertebral disc, indenting the thecal sac without compressing the nerve roots. At the C4-C5 level, mild posteromedial disc protrusion was noted, predominantly on the left side, with hypertrophy of the left facet joint, causing compression of the thecal sac and impingement of the left C5 nerve root. At the C5-C6 level, there was posteromedial disc protrusion, mainly on the right side, along with retrolisthesis, thickening of the ligamentum flavum, and hypertrophy of the right uncinate process, leading to compression of the thecal sac and the right C6 nerve root. At the C6-C7 level, there was posteromedial disc protrusion, accompanied by thickening of the ligamentum flavum and bilateral hypertrophy of the uncinate processes, resulting in compression of the thecal sac and bilateral C7 nerve roots.

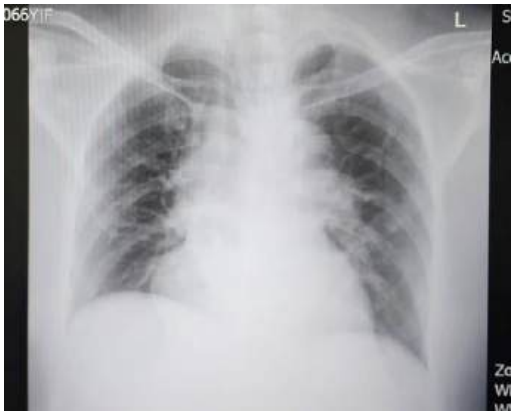

Figure 4. Chest X-ray PA View

The chest X-ray revealed minimal opacities in both the hilar and paracardiac regions. The Cardio-Thoracic Ratio (CTR) was measured at 60%, and there was evidence of calcification in the wall of the aortic arch.

Figure 5. Cervical X-ray AP View

Figure 6. Cervical X-ray Lateral View

The cervical X-ray revealed the presence of spur formations on the surface of the cervical spine. Additionally, a plate and screws were noted to have been installed at the C3 to T1 vertebral bodies.

Following the imaging examination, the patient was diagnosed with spinal cord trauma and epidural hemorrhage. Consequently, the patient underwent decompression laminectomy and stabilization. A tracheostomy was also performed, and the patient was subsequently admitted to the Intensive Care Unit (ICU) for further management.

Discussion

Trauma can result from violence associated with criminal acts, such as robbery, murder, or traffic accidents. In cases involving injuries due to criminal acts, investigators may seek assistance from medical professionals, as outlined in Article 133, Paragraph 1 of the Indonesian Criminal Code (KUHP). This provision states: "In instances where an investigator is handling a victim—whether injured, poisoned, or deceased—who is suspected of being involved in a criminal act, they are authorized to request expert testimony from a forensic doctor or another medical expert."[7] Examinations conducted by experts, including forensic doctors, general practitioners, or other specialists, are carried out under oath to ensure that the procedures adhere to the proper legal authorities at both the investigative and trial stages. This oath guarantees that the examination is conducted in accordance with established protocols, and that the information provided is truthful, accurate, and grounded in professional knowledge.[10]

In assessing the severity of an injury, the doctor must determine the source of the trauma and evaluate its impact on the body. It is essential to establish whether the injury resulted from sharp force trauma, blunt force, electrical trauma, thermal injury, chemical trauma, or other causes. Understanding the extent of the injury's effect on the victim is critical, as it directly influences the criminal penalty that may be

imposed on the perpetrator. The Criminal Code outlines three classifications for the consequences of abuse: (a) maltreatment that does not cause disease or impair the ability to perform tasks, hold a position, or sustain a livelihood, as described in Article 352 (minor assault); (b) abuse causing disease and impairment in work and livelihood, as defined in Article 351, Paragraph (1) (assault); and (c) torture resulting in severe injury, as specified in Article 351, Paragraph (2) and Article 90. Article 90 of the Criminal Code defines severe injuries as: (a) injuries or illnesses with no prospect of recovery or that pose a life-threatening risk, (b) incapacity to continue working or earning a living, (c) loss of one of the senses, (d) severe disability, (e) paralysis, (f) mental disturbances lasting four weeks or more, or (g) death or fetal death.[7]

In managing victims of criminal acts, doctors are bound by regulations that govern their responsibilities toward patients. They are obligated to provide medical care in line with professional standards, standard operating procedures, and the patient's medical needs, as outlined in Article 51, Paragraph (a) of Law No. 29 of 2004 on Medical Practice.[7,10,11]

In this case, the perpetrator of the robbery could face the death penalty as specified in Article 365, Paragraph (4) of the Indonesian Criminal Code. This article pertains to theft accompanied by violence, committed by two or more individuals, which results in severe injury or death.[7]

The cervical spine is a dynamic structure that serves to protect the nervous system and maintain the range of motion for the head and neck. Cervical spine fractures are a leading cause of morbidity and mortality in trauma patients, with fractures accounting for 56% of cervical spine injuries. These fractures are categorized based on the level of involvement, typically divided into three groups: C1, C2, and the sub-axial cervical spine (C3-C7). This study reviews the etiology, presentation, evaluation, and management of cervical spine fractures, as well as the role of the interprofessional team in evaluating, diagnosing, and managing these conditions. Cervical spine fractures typically occur due to abnormal movements or a combination of movements, including hyperflexion, hyperextension, rotation, axial loading, and lateral bending of the spine. Evaluation of a patient with a cervical spine fracture should begin with a thorough trauma assessment of the ABCs (airway, breathing, and circulation). Injuries to the cervical spine may disrupt respiratory and cardiovascular functions, and even after stabilization, these patients must be closely monitored for ongoing respiratory and cardiovascular changes. Early identification of acute spinal cord injury is critical, as early decompression within 24 hours can improve neurological recovery outcomes. Indications for cervical spine imaging include local neck pain, deformity, edema, changes in mental status, head injury, or

neurological deficits. Further evaluation of spinal cord structures using MRI is important for determining spinal stability and planning surgical management. The Spinal Injury Classification System (SLICS), which includes classifications for ligament, bone, and neurological injuries, can be used to help guide surgical or non-surgical management. SLICS scores of 1 to 3 indicate non-surgical treatment, scores of 4 are indeterminate, and scores of 5 or higher indicate the need for surgery.[14,15,16]

Spinal cord injury (SCI) refers to damage to the nerve cells within the spinal cord, which extends from the brain to the lower back. SCI may result from trauma to the spinal cord or its surrounding structures, such as the vertebrae that encase it. This trauma can cause either permanent or temporary impairments in sensation, movement, strength, and function below the injury site. SCI is categorized into two types: incomplete and complete. In incomplete SCI, the spinal cord retains some ability to transmit impulses, enabling the individual to maintain partial control over muscle activity below the injury level. In complete SCI, no impulses are transmitted below the injury site, leading to a total loss of both sensory and motor functions below that point.[11,13]

In a retrospective study involving 98 patients who suffered strangulation, CT scans and MRIs identified trauma in only 8 cases. Specifically, two patients had injuries to the cervical vessels, three had fractures of the thyroid cartilage and hyoid bone, and three presented with vertebral trauma.[5]

In this case, the twisting trauma inflicted by the perpetrator caused a cervical fracture, leading to spinal cord injury and subsequent paralysis. Based on the medical examination findings, the patient is classified as having a severe injury, resulting in permanent disability. As a result, the perpetrator of the robbery faces potential penalties under Article 365, Paragraph (4) of the Criminal Code, which applies to theft with violence, committed by two or more individuals, leading to severe injury or death.[7]

Conclusion

In this case, based on the findings from the examination, it was determined that the victim is a 66-year-old woman. She sustained a cervical fracture at the C5-C6 level, caused by the perpetrator twisting her neck during the robbery. As a result of the injury, the victim experienced paralysis. This case involves theft with violence and/or aggravated assault, as outlined in Article 364 and/or Article 351, Paragraph 3 of the Indonesian Criminal Code (KUHP).

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(Donald Rinaldi Kusumaningrat)

Superficial Spreading Cervical Squamous Cell Carcinoma to Endometrium: A Rare Case Report

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Abstract

Introduction: Squamous cell carcinoma (SCC) was the most common variant of cervical cancer with metastases potential to many organs, commonly parametrium and vagina, but in a rare condition can also spread to endometrium. Further evaluations are needed since superficial spreading of cervical SCC are related to poorer outcomes.

Case Presentation: A 62 y.o, post-menstrual, P3A0 women came with complaint of vaginal discharged mixed with blood since 6 months ago. Pap smear result suggestive of malignancy so the patient undergo guided biopsy from endocervix that revealed finding similar to carcinoma intraepithelial (CIN) 3. The patient underwent TAH-BSO operation. Microscopic examination from cervix showed tumor cell with round nuclei, prominent nucleoli, pleomorphic, hyperchromatic, increased nuclear-cytoplasm ratio in whole epithelial layer. Microscopic examination from endometrium showed epithelial squamous cell proliferation in almost 98% endometrial tissue and atypical cell nuclei, consistent with tumor founded in cervix. The final diagnosis was superficial endometrial spreading SCC with moderate differentiation. Immunohistochemistry (IHC) assay with p16 showed positive result in endometrium. Patient then consulted to gynecologist – oncology specialist for further treatment and evaluation.

Conclusion: Superficial spreading of cervical SCC to endometrium was a rare finding. Detection of SCC in endocervix can be considered as predictor for proximal spreading of cervical SCC so further examination like endometrial curretage are suggested to assist the early detection. IHC assay with p16 resulted positive in our patient suggesting that endometrial SCC in this patient was correlated with HPV infection that commonly find in cervical cancer.

Introduction

Cervical cancer is 1 of the 4th most common cancer found globally, squamous cell carcinoma (SCC) accounted for most of the type that were recorded.[1] SCC of the cervix can spread to many organs like parametrium and vagina, but in a rare condition this can also spread to upper genital tract like endometrium and also to

intra-abdominal organs.[2] Superficial spreading of SCC to endometrium was a rare founding, therefore the information regarded this condition are poorly known. This case was reported to improve our knowledge related to superficial spreading of SCC from cervix to endometrium.

Case Description

A 62 years old women came with a complain of vaginal discharge mixed with blood since 6 months ago. This patient already menopause at 55 years old. This patient was married at 24 years old and had 3 child birth via vaginal delivery and had a history of using intrauterine device for 5 years. The patient denied similar complaints before, denied history of cervical cancer screening or cervical procedure, nor history of multisexual partner. Pelvic examination revealed purulent discharge mixed with blood and portio erotions. The transvaginal ultrasonography suggested that there was fluid on uterine cavity, left ovarian cyst size 7.1x6.1cm was observed, the right ovarium and cavum douglas, unremarkable. Blood examination showed microcytic hipochromic anemia, the other blood panel within normal range. Conventional pap smear was conducted on the first doctor visit, intermediate squamous epithelial cell and parabasal was founded with large hiperchromatic, pleomorphic nuclear suggested as malignancy so the patient undergo guided biopsy. Guided biopsy from the endocervix showed squamous epithelial cell with rounded nuclei, pleomorphic, hiperchromatic, coarse chromatin, prominent nucleoli, mitosis was also observed in >1/2 upper epithelial area arranged in pile pattern with impression to the squamous epithelial surface. This finding suggest there was squamous epithelial cell with high-grade dysplasia, similar to cervical intraepithelial neoplasm (CIN) 3. CIN 3 finding in the endocervix was suspected to associate with proximal spreading of SCC so this patient was suggested to underwent the *histerectomy and salphingo-oophorectomy bilateral* (TAH-BSO) procedure by the gynecologist. Post-operative specimen was sent to pathology anatomy laboratorium. The gross examination revealed whitish uterus with rubbery consistency, size 6x6x5cm, cervix and both adnexa was also founded but already separated from the uterus, the cervix size 5x4x3cm, parametrium was not observed. Uterus cutting showed whitish area without clear border (**Figure 1**), then conization procedure was done to the cervix.

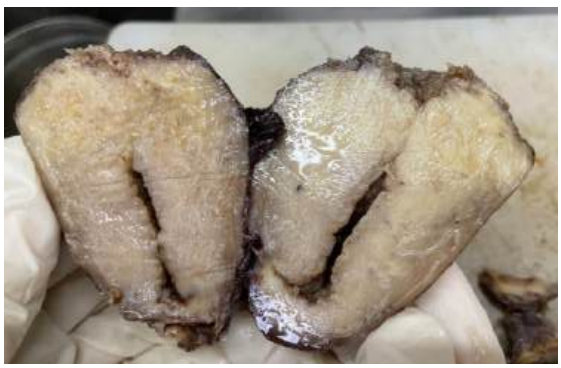

Figure 1. Gross examination of the uterus revealed whitish area without clear border.

Microscopic examination of the cervix showed cell with rounded nuclei, prominent nucleoli, pleomorphic, hiperchromatic, coarse chromatin, mitosis, increased nucleus-to-cytoplasm rasio in almost epithelial layer, part of the tumor cell showed infiltration to fibrous stroma around 3cm of the cervical stromal depth and horizontal spreading >7cm, without penetrating to the serous layer (**Figure 2A)**. Microscopic examination form the endometrium showed minimal surface that still layered by the collumnar epithelial cell, most of the endometrium (± >98%) showed squamous cell proliferation that subtitutes the endometrium stroma, cell with atypic nuclei that similar to the cervical preparation also observed **(Figure 2B)**. The miometrium examination showed tumor cell with infiltration to >1/2 miometrium depth around the smooth muscle cells, but no infiltration to the outer serous layer was founded. Final conclusion from the histopathology examination revealed keratinized squamous cell carcinoma, moderate differentiation with superficial spreading to the endometrium and infiltration to >1/2 miometrium depth (pT1B2). Possible spreading to the vagina or parametrium in this patien cannot be excluded. Immunohistochemisty (IHC) assay found positive p16 marker in the endometrium specimen (**Figure 2C)**. The patient then referred to the gynecologist sub-specialist onkologist for further evaluation and determinaton of the next plan.

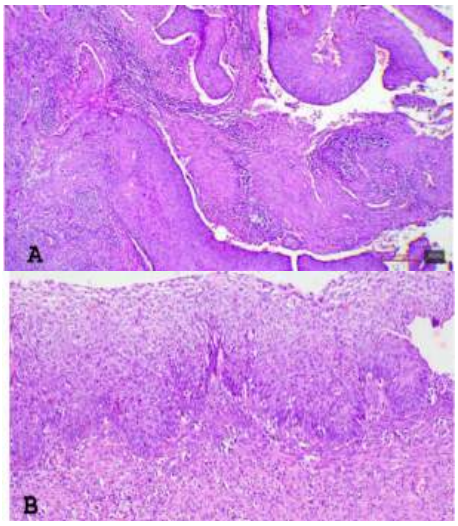

Figure 2A. Microscopic examination from the cervix (HE, 40x). **Fig 2B.** Microscopic examination from the endometrium.
Both suggestive of squamous cell carcinoma (HE, 100x).

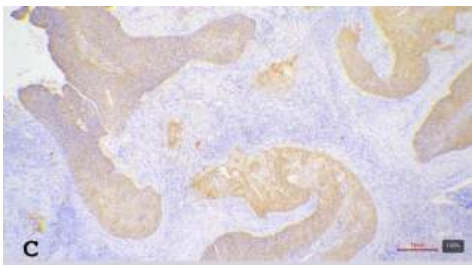

Fig 2C. IHC with p16 showed positive result in endometrium

Discussion

Cervical cancer was malignancy that arise from the cervical cell, including in 1 out of the 4th most common cancer found globally. In Indonesia, cervical cancer occupied the 2nd position as the most common cancer founded in women with estimation of 36,000 new cases each year. Almost 70% of the cases that reported in Indonesia was detected in late stage so the mortality rate related to this case increases.

In 2020, there was 21,000 women died because of cervical cancer, this count was predicted to reach 1.7 million in 2070 and will further increased into 4 million death in 2120 if early intervention was not conducted[1]. Approximately, 70-80% of cervical cancer was squamous cell carcinoma (SCC) variants. SCC of cervix can spread to other organs via direct invasion or lymphatic invasion,[8] most common to the parametrium and vagina, but in a very rare condition this can spread to upper genital tract like endometrium, fallopian tube, ovarium, and can also spread to intraabdominal organs.[\2] Superficial spreading of SCC cervix to the endometrium was a rare condition, marked by cervical SCC spreading superficially to the inner uterus surface followed by replacement of the normal endometrium cells.[3] This rare case was 1st reported in 1900, since that moment few similar cases already reported with prevalence rate around 0.7%.[2] Factor that considered play a role in this SCC spreading to the proximal organ of the cervix was long-term estrogen exposure, vitamin A deficiency, HPV infection, endometrial changes in geriatric, pyometra, radiotherapy, history of cervical procedure, early marriage, and multipara.[2,4] Superficial spreading from cervix to endometrium was thought to happen because of the similar progenitor cell so when both get the same stimulator exposure there will be a cell transformation to malignancy. Genetic factor also thought to have role in this processes, especially the loss of heterozigonity of 6p, 6q, 11p, and 11q chromosomes.[2]

A case reported 65 year-old, P3A0 post-menopausal women, with complain of vaginal discharge and post menopausal bleeding, the patient was known to have *loop electrosurigcal excision procedure* (LEETS) 33 years ago, the biopsy result suggested that there was SCC cervix with keratinization, moderate differentiated. The patient underwent TAH-BSO procedure. Histopatological examinaton reveals SCC cervix in situ with metastasis to endometrial withoud lymph node involvement, the IHC result showed positive p53 and CK 5/6 in the tumor corpus, strongly positive p16 in tumor in situ and tumor which already infiltrating the endometrium, other markers like Ca125, CK7, vimentin, p53, GATA binding protein 3, TTF1, CDX2, ER, PR showed negative result. Patient continued to have adjuvant chemotherapy post-operation and was founded to free of tumor reccurency in 8 months follow-up.[6] Another case reported 66 years-old, post-menopausal multipara women without any clinical symptoms but have atypical squamous cell result suggested malignancy in pap smear examination. The patient underwent hysterectomy. The macroscopic findings show yellowish glandular growth in the ectocervix and superficial surface of the endometrium, this was further examined microscopically with a result that confirmed both lesions as SCC with spreading to the

endometrium. The patient undergo IHC examination with strongly positive result in p16, CK5/6, p63 and high Ki67 index in squamous cell at the endometrium. This case did not mention additional data related to patient follow-up.[7] There's also another case report other than this 2, the reports shows variation in clinical characteristic but usually the superficial SCC spreading to endometrium was associated with women aged >50th years-old with clinical symptoms range from post-menopausal bleeding, vaginal discharge, pyometra, abdominal mass, low abdominal pain,[5,8] or sometimes can be found incidential post-operation.[10] Most patient with superficial spreading had a history of cervical lesions few years before and mostly underwent LEEP procedure, this finding associated with cervical stenosis which predispose to pus accumulation in uterine cavity and help the superficial spreading of SCC to endometrium.[10]

Our case report support the previous studies which state that most cases was found in women aged >55 years-old. Beside structural changes in older patient, multiparity also consider to have role in SCC with superficial spreading. Pap smear was firstly conducted to our patient but the result came with a suggestion to malignancy so our patient underwent guided biopsy from endocervix. The guided biopsy showed CIN3 in the endocervix specimen that suggested the possibility of proximal spreading of cervical SCC to the structure above. Proximal spreading of cervical SCC was a rare case so the patient underwent TAH-BSO procedure as recommended by the gynecologist. Post-operative specimen thent sent to the pathology laboratorium, further examination revealed cervical SCC with superficial spreading to endometrium as suspected by the gynecologist, this result was strengthened by positive p16 marker in IHC assay of the endometrium. p16 marker was commonly associated with cancer related to HPV infection[9] but this marker role in determine SCC origin cells in genital tract malignancy was not clearly explained[4] so we suggest to further evaluate the patient with another IHC panel. Beside supporting examination, SCC in endometrium should underwent evaluation with Fluhmann cirteria to exclude the possibility of primary SCC in endometrium which should fullfil this 3 criteria: 1) No evidence of coexisting endometrium adenocarcinoma or primary SCC of the cervix, 2) There are no associaton between endometrial tumor and squamous epithelial from cervix, 3) There are no association between cervical carcinoma in situ and independent endometrial neoplasm.[9] Our patient cannot be classified as PESSC because all the criteria was founded. Patient was consulted post-operation to the gynecologist sub-specialist onkologist for further evaluation, in 1st month post operation there are no sign of metastasis nor recurrence of the disease. Prognosis and additional therapy consideration for patient with superficial SCC cervix are still barely known due to the

minimal reported case and information about the disease, few studies reported different outcomes due to the minimal follow-up period to this cases, further studies are still needed to improve our knowledge. Minimal information available related to the disease directed us to take more detailed evaluation related to SCC cervix and the possible metastasis to further areas like endometrium, this may help us to early diagnosed and accordially will select the best available therapy to improved patient quality of life.

Conclusion

Superficial spreading of cervical SCC to the endometrium was a rare finding that commonly associate with poor outcomes. SCC founded in the endocervix might raise the possibility for superficial spreading to the endometrium and need further assessment to confirm this suspicion. Due to the rarity of primary SCC in endometrium, we should suspect for possible primary SCC lesion and assess the cancer more thoroughly with possible tools like the Fluhman criteria, in order to give the best therapeutic option for the patient.

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