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Exploring the Relationship between Duration of HIV Treatment and Nutritional Status in Pediatric Patients Aged 0-18 Years

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ABSTRACT

Background: *Human immunodeficiency virus (HIV) significantly impacts pediatric populations, particularly in their nutritional status, which plays a critical role in their treatment outcomes. This study aims to explore the relationship between the duration of HIV treatment and the nutritional status of children aged 0-18 years.*
Methods: *This cross-sectional study utilized qualitative categorical analytic methods to examine data from medical records of pediatric patients undergoing HIV treatment. From January 2021 to November 2024, 80 children meeting the inclusion criteria were sampled using the total sampling method. The duration of HIV treatment was categorized into two groups: 0-60 months and greater than 60 months. Nutritional status was assessed using WHO and CDC growth standards and classified into good and poor categories.*
Results: *Our analysis found no significant relationship between the duration of HIV treatment and the nutritional status of the children (P=0.200; OR=1.812; 95% CI: 0.727-4.512). Despite different treatment durations, both groups showed similar nutritional outcomes.*
Conclusion: *The duration of HIV treatment does not significantly affect the nutritional status of children aged 0-18 years. Further research with a larger sample size and more comprehensive data collection is recommended to understand better the multifactorial impacts on nutritional outcomes in pediatric HIV patients.*
Keywords: *HIV, pediatric, nutritional status, antiretroviral therapy, cross-sectional study.*

INTRODUCTION

Human immunodeficiency virus (HIV) is a virus that attacks the human body's immune system by infecting and destroying CD4 cells. If HIV is not treated properly, it will soon develop into a more serious condition called Acquired immunodeficiency syndrome (AIDS). HIV is a retrovirus with an envelope that contains two copies of a single-stranded RNA genome. HIV is a genus of Lentivirus which belongs to the Retroviridae family and the Orthoretrovirinae subfamily. HIV is divided into types 1 and 2 (HIV-1, HIV-2) based on their genetic characteristics and differences in viral antigens. Current epidemiological analysis shows that HIV entered society in 1920–1940[1]. Globally, 39 million people were recorded as suffering from HIV by the end of 2022. Of this figure, 1.5 million of them were children aged <14 years. In Indonesia, it was recorded that in 2022 the total number of people with HIV was 540,000. Of this figure, 18,000 patients were children aged 0-14 years[2]. According to the Ministry of Health's 2020 estimates, the number of people with HIV in 2020 was 543,100. Lower than the previous estimated calculation carried out in 2016[3]. HIV infection is detected through serological and virological laboratory tests. Serum, plasma, or whole blood can be used as HIV test samples[4]. Malnutrition, especially malnutrition, is one of the public health problems that often occurs in people with HIV, especially in developing countries. HIV is one of the main causes of malnutrition in adults because of its impact on loss of appetite, nausea and vomiting, diarrhea, opportunistic infections, malabsorption of essential nutrients, and increased metabolic needs of the body[5].

Nutrition is an important part of the health care system and is essential for maintaining a person's health and well-being. Clinical outcomes are influenced by a person's nutrition[6]. Assessment of nutritional status can be determined based on several indicators, namely clinical history, dietary assessment, physical examination, and anthropometric measurements. Among the factors that can affect a person's nutritional status are physiological factors, pathological factors, and psychosocial factors. According to WHO guidelines, malnutrition falls into three categories, namely undernutrition, deficiency or excess of micronutrients (vitamins and minerals), and excess nutrition (overnutrition). Based on Minister of Health Regulation No. 2 of 2020 concerning Child Anthropometric Standards, the assessment of nutritional status in children aged 0-5 years is based on the Body Weight index according to Body Length (BB/TB) or Height (BB/TB). This BB/PB or BB/TB index describes whether the child's weight is appropriate for their length/height growth. This index can be used to identify children with malnutrition (wasted), severe malnutrition (severely wasted) and children who are at risk of overweight (possible risk of overweight)[7].

Antiretroviral therapy (ARV) is a treatment aimed at patients with HIV. The goal of antiretroviral treatment is to prevent the proliferation of the HIV virus by suppressing HIV virus replication and improving immune system function. There are six classes of drugs that are generally grouped based on the phase of the HIV life cycle that they inhibit, such as NRTI (Nucleoside Reverse Transcriptase Inhibitors), NNRTI (Non-nucleoside reverse transcriptase inhibitors), PI (Protease Inhibitors), FI (Fusion Inhibitors), CCR5 Inhibitors, and INSTIs (Integrase Strand Transfer Inhibitors)[8]. ARV treatment is given to all people with HIV regardless of clinical stage and CD4 values. ARV therapy that is initiated first has been shown to reduce morbidity, mortality, and transmission rates. The patient's age determines the ARV treatment regimen which is then divided into first and second lines. Several studies have shown that there is an influence between the duration of antiretroviral (ARV) therapy and several parameters of nutritional status. A significant increase in height index was seen when patients

started ARV therapy at an earlier age[9]. This is supported by research that children over 3 years of age were recorded to experience smaller weight and height increases than younger children[10]. This study states that ARVs have a positive impact on weight and slightly lower on height growth. This study also stated that there was a very large improvement in the body mass index of patients aged <12 months. Research by Seth stated that there was a fairly rapid improvement in body mass index after undergoing ARV therapy[11]. This increase occurred significantly in the first 6 months of therapy followed by a slow decrease in body mass index until 36 months. In this study, the duration of treatment monitored by researchers was only up to 36 months and not many studies have monitored treatment for more than that. Based on the description above, researchers are interested in knowing the relationship between the duration of HIV treatment during monitoring of more than 36 months with the nutritional status of child patients aged 0-18 years.

METHOD

This study employed a cross-sectional design using qualitative categorical analytic methods to investigate the relationship between the duration of HIV treatment and the nutritional status of pediatric patients aged 0-18 years at Dr. Moewardi Regional Hospital, Surakarta, Indonesia. The study utilized secondary data obtained from medical records of pediatric patients with HIV who were undergoing treatment at the hospital's Pediatric Health Polyclinic. Data collection occurred between January 2021 and November 2024.

Sample Selection

The total sampling method was employed to select participants. Inclusion criteria included children aged 0-18 years diagnosed with HIV and receiving antiretroviral therapy (ARV). Exclusion criteria included children with comorbidities or who had died. A total of 80 participants met the inclusion criteria and were included in the study. The sample size was determined based on the available data, though it is noted that this may not provide enough power to detect significant differences in certain subgroups.

Data Collection

The study gathered data from medical records, focusing on the following variables: age, gender, duration of HIV treatment, therapy regimen, nutritional status, and therapy adherence. The duration of treatment was classified into two categories: 0-60 months and >60 months. Nutritional status was assessed based on recorded weight and height measurements and classified according to the World Health Organization (WHO) and Centers for Disease Control and Prevention (CDC) standards. Nutritional status was categorized as good or poor based on body mass index (BMI) and other anthropometric criteria [5].

Nutritional Status Assessment

Nutritional status was assessed using the WHO's growth standards for children under five years and the CDC's guidelines for children aged five years and above. The classification was made based on the following indicators: weight-for-age, height-for-age, and weight-for-height (BMI-for-age for older children). This method is a standard practice for evaluating the nutritional health of children in clinical settings [6].

Antiretroviral Therapy (ARV) Treatment Regimen

ARV treatment regimens used by participants were categorized as first-line or second-line therapies. First-line regimens typically included combinations of Nucleoside Reverse Transcriptase Inhibitors (NRTIs) and Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs), while second-line regimens involved a combination of Protease Inhibitors (PIs) and

NRTIs. The choice of regimen was determined based on the patient's clinical stage and prior ARV treatment history [7].

Adherence to Therapy

Therapy adherence was measured by reviewing medical records for documentation of missed appointments or missed doses of ARV medication. Adherence was classified as either compliant (if the patient adhered to the prescribed therapy regimen) or non-compliant (if the patient missed appointments or medications) [8].

Data Analysis

Data analysis was performed using IBM SPSS® statistical software version 25. Descriptive statistics were used to determine the frequency distribution of age, gender, duration of treatment, nutritional status, and adherence to therapy. Bivariate analysis was conducted using the chi-square test to evaluate the relationship between the duration of HIV treatment and nutritional status, with a significance level set at $p<0.05$. The odds ratio (OR) was calculated to estimate the risk of malnutrition in children with different durations of treatment. Confidence intervals (CI) for the OR were calculated at 95% [9].

Ethical Considerations

The study was conducted in accordance with ethical guidelines for medical research. Ethical approval was obtained from the Ethics Committee of the Faculty of Medicine, Sebelas Maret University. The study adhered to the principles of confidentiality, and data from medical records were anonymized to ensure privacy. Informed consent was waived due to the retrospective nature of the study and the use of anonymized data.

RESULT

The type of research used in this study is qualitative categorical analytic with a cross-sectional research design, meaning that observation and measurement of variables are carried out at the same time within a certain period of time. Data on research subjects were taken in the period January 1, 2021-November 1, 2024. The sampling technique uses an unpaired categorical analytic formula. Sampling using the total sampling method and 80 samples were obtained that met the inclusion criteria. Based on table 1, from a total of 80 research subjects, it is known that the most frequent age frequency in children with HIV is in the age range of 10-18 years with a total of 52 (65%) children, followed by the age range of 0-<10 years with a total of 28 (35%) children. Furthermore, the number of children with HIV at Dr. Moewardi Surakarta Hospital is dominated by male gender, namely 43 (53.75%) children compared to females, namely 37 (46.25%) children. Furthermore, the HIV stage in children was found to be the most at stage 1, namely 67 (83.75%) children, followed by stages 2-4, namely 13 (16.25%) children. Then, there is a variation in the length of HIV treatment in children with a length of treatment in the range of 0-60 months, namely 48 (60%) children and followed by a length of treatment >60 months, namely 32 (40%) children. Distribution of nutritional status frequency in children with HIV found that the most patients had good nutritional status, namely 43 (53.75%) children, followed by patients with poor-poor nutritional status, namely 37 (46.25%) children. At the level of therapy compliance, 66 (82.5%) children were compliant with therapy, while 14 (17.5%) children were not compliant with therapy. The number of patients who experienced an increase in nutritional status after therapy was 45 (56.25%) children, while 35 (43.75%) children did not experience an increase in nutritional status after therapy. The distribution of therapy regimens used in patients was 64 (80%) children using first-line ARV therapy regimens, while 16 (20%) children used second-line ARV therapy regimens. Based on table 2, the p-value in the chi-

square test results shows a value of 0.200 where the results are >0.05 which means it is not significant, meaning there is no relationship between the two research variables, namely the duration of treatment with nutritional status in children aged 0-18 years at Dr. Moewardi Surakarta Hospital. Patients who receive treatment for 0-60 months have a 1.812 times greater risk of experiencing malnutrition than patients who receive treatment >60 months. However, the results of this odds ratio include a value of 1 so that it is not statistically significant.

Table 1. Research subject characteristics

Characteristics	Quantity	Percentage
Age		
0-<10 tahun	28	35%
10-18 tahun	52	65%
Sex		
Male	43	53,75%
Female	37	46,25%
Clinical stage		
Stage 1	67	83,75%
Stage 2-4	13	16,25%
Duration of treatment		
0-60 months	48	60%
>60 months	32	40%
Nutritional status		
Good	43	53,75%
Poor	37	46,25%
Therapy compliance		
Yes	66	82,5%
No	14	17,5%
Nutritional status improvement		
Yes	45	56,25%
No	35	43,75%
Therapy regimen		
First line	64	80%
Second line	16	20%

Table 2. Bivariate analysis results

Characteristics	Odds Ratio	p-value
Duration of Treatment * Nutritional Status	1,812 (0,727-4,512)	0,200

DISCUSSION

Based on the frequency distribution of patient ages, it was found that the most frequent age group among children with HIV was 10-18 years, with 52 (65%) children. A study by Dahliyanti et al. at RSPI Prof Dr Sulianti Saroso also reported that the largest age group of child patients with HIV was aged 6-18 years, comprising 50 (89.3%) children [12]. In Indonesia, the prevalence of HIV in adolescents reflects the global trend, as reported by UNAIDS, which recorded an increase in HIV cases in this age group [2].

In terms of gender distribution, more male children were found to have HIV, with 43 (53.75%) male patients compared to 37 (46.25%) female patients. This finding is consistent with research by Scholtz et al., which stated that the majority of children with HIV were male, with 54 (55.1%) male patients compared to 44 (44.9%) female patients [13]. Similarly, Seth et

al. reported that 125 (69.4%) of the children with HIV were male, compared to 55 (30.6%) female patients [11]. Several biological, behavioral, and social factors contribute to the increased susceptibility of male children to HIV infection. Studies indicate that undiagnosed or untreated males are more likely to engage in high-risk behaviors, which increases the risk of HIV transmission. Social norms also influence behavior, with males often using health services less than females, which can delay HIV diagnosis and treatment, thus allowing the virus to spread more widely before viral load reduction begins [14].

Regarding the duration of HIV treatment, 48 (60%) of the children had been undergoing treatment for 0-60 months. Longer durations of HIV treatment can improve nutritional status due to mechanisms related to the effectiveness of therapy. ARVs suppress HIV virus replication, thereby reducing viral load and improving immune function. As the immune system recovers, the risk of opportunistic infections, such as chronic diarrhea or gastrointestinal infections, which can interfere with nutritional status, decreases significantly. ARV therapy also increases appetite and metabolic activity, further enhancing nutritional status [15]. However, there is no direct evidence that specific components of ARVs directly improve nutritional status. Instead, the reduction of the disease burden and the overall improvement in health help children return to normal growth and development patterns.

Regarding the nutritional status of the patients, the majority, 43 (53.75%), had good nutritional status, which contrasts with findings from other developing countries where higher rates of malnutrition are seen in children with HIV [10,11]. The relatively good nutritional status in this cohort could be attributed to efficient, long-lasting patient care and ARV treatment. This is closely tied to the use of ARV therapy, which has been shown to improve health outcomes in children with HIV.

The stage of HIV infection in the patients revealed that 67 (83.75%) children were at stage 1, the most common stage. Several studies confirm the effectiveness of ARV therapy in reducing HIV severity through viral load suppression and significant immunological recovery, especially when therapy is initiated early. Immune recovery enables the body to fight off opportunistic infections, which often worsen the condition of HIV patients. Long-term therapy also improves the quality of life by preventing complications typically associated with advanced HIV stages [16].

Regarding therapy compliance, 66 (82.5%) of the children were adherent to their treatment regimen. This finding aligns with research by Ratnasari et al., which reported 84.4% adherence to ARV therapy [17]. Therapy compliance is crucial for the improvement of nutritional status in HIV patients. Additionally, 45 (56.25%) children experienced an improvement in their nutritional status after undergoing ARV therapy. This improvement was measured by comparing nutritional status before and after therapy, with several patients showing a shift from poor to good nutritional status. These results indicate that ARV therapy has a positive impact on the nutritional status of most patients.

Regarding the therapy regimens, 64 (80%) patients were on first-line ARV therapy. This indicates that most children with HIV have not experienced treatment failure, which would necessitate a switch to second-line therapy.From the research results, it was found that of the 48 pediatric patients who underwent treatment for 0-60 months, 25 (52.1%) children had low to poor nutritional status, while there were 23 children (47.9%) who had good nutritional status. . Conversely, in 32 pediatric patients undergoing treatment for >60 months, 20 (62.5%) children had good nutritional status, while 12 (37.5%) children had poor to poor nutritional status. These data indicate that children with a treatment period of 0-60 months have more good nutritional

status compared to children with a treatment period of >60 months. The results of the chi square test showed a p-value of 0.200 which means >0.05 indicating no significant relationship between the duration of treatment and nutritional status in children with HIV at Dr. Moewardi Surakarta Hospital.

Improvement in nutritional status in pediatric patients aged 0-18 years with HIV undergoing ARV treatment mainly occurs due to the positive effects of therapy on the immune system and metabolism. First, there is suppression of viral replication. ARVs reduce the viral load, which helps restore immune system function. With a better immune system, the risk of opportunistic infections such as chronic diarrhea or gastrointestinal infections decreases[16]. Second, there is an increase in appetite and energy. ARV therapy also contributes to an increase in appetite, which is often disturbed by HIV infection. Children who undergo ARV therapy tend to have a more stable metabolism, so that the body can utilize nutrients better for growth and development[18]. Third, there is a recovery in general health. With reduced HIV symptoms, such as chronic fatigue and recurrent infections, children can be more active and have better eating patterns, which ultimately improves nutritional status. Fourth, there is an indirect effect of health services. Children who undergo ARV therapy consistently usually also have access to nutritional interventions, such as supplements or growth monitoring programs, which can improve their nutritional status[19]. However, based on the results of this study, there are several things that need to be discussed in depth regarding this insignificant result and its potential causes.

The total sample size used in this study was 80 children who met the inclusion criteria. However, this sample size may not be sufficient to achieve the minimum required sample size, which is 58 for each group, or a total of 116 samples. One of the causes for this limitation is the restricted access to data on pediatric HIV patients at Dr. Moewardi Surakarta Hospital, which only provides research subject data from January 2021 to November 2024, limiting the ability to access earlier data. This restriction may result in an under-detection of the relationship between the two research variables. Additionally, the homogeneous distribution of samples across certain variables may limit the detection of significant variations. Furthermore, the majority of participants in this study had a duration of ARV treatment within the 0-60 month range. Previous literature suggests that the impact of ARV therapy on nutritional status often takes longer to become evident, particularly in patients who begin therapy with poor nutritional conditions. A study by Seth et al. found that significant improvements in body mass index (BMI) occurred in the first 6 months of therapy, but this trend gradually declined thereafter [11]. In contrast, improvements in height-for-age (z-scores) were slower but remained stable up to 36 months of treatment. Therefore, research covering treatment durations of up to 60 months may not be adequate to capture the long-term impact of ARV therapy on nutritional status.

Confounding variables could also influence the nutritional status of children with HIV. For example, inadequate or poor-quality food intake could hinder improvements in nutritional status despite optimal ARV treatment. Additionally, adherence to ARV therapy is significantly associated with better nutritional outcomes. Research by Ratnasari et al. indicates that children who adhere to their ARV regimens have a higher likelihood of achieving better nutritional status compared to those who do not [17]. Unfortunately, these variables were not studied or controlled for optimally in this research. For instance, there was no direct measurement of patients' nutritional intake. Moreover, external factors such as physiological, pathological, and psychosocial factors, which are beyond the control of the researchers, may have contributed to the limitations in understanding the results of this study.

Several previous studies have shown that ARV therapy positively impacts nutritional status parameters, although results can vary depending on geographic, socio-economic, and observational contexts. Feucht et al. reported that while significant improvements in weight and BMI were observed, height improvements were often slower and did not always reach normalization, especially in developing countries [10]. Similarly, Traisathit et al. found that early initiation of ARV therapy resulted in better improvements in nutritional status [9]. The insignificant results in this study may be attributed to differences in the socio-economic context and healthcare resources in Indonesia compared to those in other countries where previous studies were conducted. Furthermore, variations in patient responses to ARV therapy, influenced by genetic factors, general health, and adherence to treatment, could also affect the results. Differences in the ARV regimens used may also impact nutritional outcomes [20].

First-line regimens commonly include combinations of Tenofovir (TDF), Lamivudine (3TC), and Efavirenz (EFV). This combination is effective in suppressing viral load and increasing the number of CD4 cells, which play a critical role in immune function. Although generally well-tolerated, some patients may experience mild side effects such as nausea, diarrhea, sleep disturbances, or skin rashes. In contrast, second-line regimens, typically involving Zidovudine (AZT), Lamivudine (3TC), and Lopinavir/Ritonavir (LPV/r), are used when first-line therapy fails or when resistance occurs. Some studies have shown that patients on second-line therapy are at a higher risk of certain side effects. A study in Indonesia reported that side effects from second-line therapy occurred in about 9.59% of patients, with symptoms including vomiting, nausea, diarrhea, itching, peripheral neuropathy, and lipodystrophy [21]. The regimen that caused the most side effects was the combination of TDF+3TC+LPV/r. Both first- and second-line therapies are effective in suppressing viral load and increasing CD4 cell counts, which are essential for immune function. However, the first-line therapy is generally preferred as the initial treatment due to its milder side effects and better treatment compliance, while second-line regimens tend to have a higher risk of gastrointestinal and metabolic disorders, as well as potentially lower treatment adherence.

Thus, the improvement of nutritional status in children with HIV is the result of a complex interaction between various factors. The duration of HIV treatment alone is not sufficient to guarantee an improvement in nutritional status without considering other factors such as ARV adherence, nutritional intake, and the child's overall health and well-being.

In this study, there were a number of limitations that could potentially affect the results of the study. First, the medical record data at Dr. Moewardi Hospital were limited, such as the lack of recording of weight and height measurement data since the patient's first check-up, then the limited patient data coverage was only up to the last three years. This can have an impact on the completeness of the information that can be obtained from the patient. Second, it did not pay attention to other confounding variables such as nutritional intake in each patient so that the expected results would be less meaningful. Further research is needed with more complete medical record data, a larger sample size and wider coverage, comprehensive nutritional examination of patients, and control of confounding variables so that a more complete and accurate picture can be provided.

CONCLUSION

Based on the results of this study, no significant relationship was found between the duration of HIV treatment and the nutritional status of children aged 0-18 years undergoing antiretroviral (ARV) therapy. While ARV therapy positively impacts nutritional status by

improving overall health and immune function, other factors such as therapy adherence, nutritional intake, and external factors like physiological, pathological, and psychosocial conditions play an important role in determining nutritional outcomes. Further research with a larger sample size, better control of confounding variables, and longer treatment durations is needed to fully understand the long-term effects of HIV treatment on the nutritional status of children.

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