


The Relationship Between Nutritional Status and Immunological Response in Children with HIV/AIDS at Wangaya Regional General Hospital, Indonesia

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ABSTRACT

Introduction: HIV infection and malnutrition are strongly linked and correlated. Although the exact mechanism is unknown, malnutrition is suspected to disrupt antiretroviral (ART) drug absorption. This research is aimed at determining the relationship between nutritional status and immunological response in children with HIV/AIDS taking ART. **Methods:** A cross-sectional retrospective analytic study was conducted on 30 children with HIV/AIDS in the pediatric clinic at Wangaya Hospital, using medical record data. The sample was taken with purposive sampling. Nutritional status was defined as poor (weight per height [WHZ] < -2 for children <5 years old and BMI for age [BAZ] <-2 for children ≥5 years old) and good nutrition (WHZ ≥-2 and <+1 for <5 years old children and BAZ ≥-2 and <+1 for ≥5 years old). Immunological response was seen by the increase in CD4 level through a certain time span and categorized into poor (did not increase or increase below the average) and good response (increase above the average). The data was analyzed using Chi-Square. **Results:** There is no significant relationship between nutritional status and immunological response in children with HIV/AIDS (p = 0.660). There was an almost equal amount of each immunological response category for both good and poor nutritional status. **Conclusion:** This study showed no difference in immunological response among children with either good or poor nutritional status. Further research on other confounding factors that may affect immunological responses is needed.

Keywords: Children, HIV/AIDS, immunological response, nutritional status.

ABSTRAK

Latar Belakang: Infeksi HIV dan malnutrisi memiliki kaitan erat dan berkorelasi. Walaupun mekanisme yang pasti belum diketahui, malnutrisi diduga dapat mengganggu penyerapan obat antiretroviral (ART). Penelitian ini bertujuan untuk mengetahui hubungan antara status gizi dan respons imunologi pada anak dengan HIV/AIDS pengguna ART. **Metode**: Penelitian analitik retrospektif potong lintang dilakukan terhadap 30 anak dengan HIV/AIDS di klinik anak RSUD Wangaya dengan menggunakan data rekam medis. Sampel diambil dengan metode *purposive sampling*. Status gizi didefinisikan sebagai gizi tidak baik (berat badan menurut tinggi badan [BB/TB] <-2 untuk anak berusia <5 tahun dan BB menurut umur [BB/U] <-2 untuk anak berusia ≥5 tahun) dan gizi baik (BB/TB ≥-2 dan <+1 untuk anak berusia <5 tahun dan BB/U ≥-2 dan <+1 untuk anak berusia ≥5 tahun). Respons imunologi dilihat dari peningkatan jumlah CD4 dalam rentang waktu tertentu, dikategorikan menjadi respons tidak baik (tidak meningkat atau meningkat di bawah rata-rata) dan respons yang baik (meningkat di atas rata-rata). Data dianalisis dengan menggunakan Chi-square. **Hasil**: Hasil penelitian menunjukkan bahwa tidak ada hubungan signifikan antara status gizi dan respons imunologi pada anak dengan HIV/AIDS (p = 0,660). Terdapat jumlah yang hampir sama pada setiap kategori respons imunologi untuk status gizi baik dan buruk. **Simpulan:** Tidak ada perbedaan signifikan antara respons imunologi anak dan status gizi baik ataupun tidak baik. Penelitian lebih lanjut diperlukan untuk mengetahui faktor perancu lain yang dapat memengaruhi respons imunologi. **Runi Arumndari, Asterisa Retno Putri, Claudia Natasha Liman, Made Ratna Dewi, I Wayan Bikin Suryawan. Hubungan Antara Status Gizi dan Respon Imunologi pada Anak dengan HIV/AIDS di Rumah Sakit Umum Daerah Wangaya, Indonesia.**

Kata Kunci: Anak, HIV/AIDS, respons imunologi, status gizi.

Introduction

Globally, 38.4 million people were living with HIV by the end of 2021;[1] an estimated 1.8 million are children under the age of 15.[2] In Indonesia, there were 36,902 HIV positive cases and 5,750 new AIDS cases. Of these cases, 0.7% and 3.1% were HIV positive cases in children aged 5-14 years and 15-19 years, respectively. Meanwhile, for new cases of AIDS, 1.1% and 1.7% were children aged 5-14 years and 15-19 years, respectively.[3] In Bali, 3.6% of children aged 0–19 years were infected with HIV, and 5.44% experienced AIDS.[4]

Nutrition and HIV infection are strongly

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linked and influence each other. Globally, 40%–64% of children with HIV/AIDS are malnourished.[5] HIV causes immune decline, leading to malnutrition. HIV causes damage to intestinal cells by causing the villi to flatten and decreasing the absorption of D-xylose, resulting in malabsorption of carbohydrates and fats as well as fat-soluble vitamins such as vitamins A and E.[6] The interaction between malnutrition and HIV infection is complex, but malnutrition is considered a marker of poor prognosis in HIV-infected children.[6] It will increase the higher energy demands on the patient's body and immune system and can lead to further immune deficiencies, contribute to the rapid progression of HIV infection to AIDS, and may affect recovery from infection. Opportunistic infections such as diarrhea, tuberculosis, and pneumonia can also affect nutrient absorption and worsen nutritional status.[6,7] Administration of antiretroviral therapy (ART) can help improve the nutritional status and immunological response in patients with HIV/AIDS. On the other hand, malnutrition can also interfere with treatment by affecting the gut's ability to absorb ART.[7]

The following study aims to determine the relationship between the nutritional status of children with HIV/AIDS at Wangaya Hospital and the immunological response after receiving ART therapy.

Methods

A cross-sectional retrospective analytic study was conducted on children with HIV/AIDS in the pediatric clinic at Wangaya Hospital, Denpasar, Bali, Indonesia. This study was conducted from June 1 to July 31, 2023. The researcher took the sample with the purposive sampling method from a medical record. The population was children with HIV/AIDS who were taking ART and had CD4 level data in two check-ups. The CD4 level and nutritional status data were collected retrospectively from medical records from 2013–2023; incomplete medical record data were excluded. Sample size was calculated with an unpaired categorical analytic research formula.[8] Based on the previous similar research by Omoni, *et al*,[9] samples needed in this study are 30 samples, using the formula for unpaired categorical analytic research:

$$n = \left(\frac{Z\alpha\sqrt{2PQ} + Z\beta\sqrt{P1Q1+P2Q2}}{P1-P2} \right)^2$$

n: total sample
Za: alpha standard deviation; 1.96
Zb: beta standard deviation; 0.84

From a total of 51 HIV/AIDS patients in Wangaya Regional Hospital, 18 were lost to follow up or did not have complete medical record data, and 3 were already over the age of 18.

Data on baseline nutritional status, baseline, and follow-up CD4 level were collected. Nutritional status was defined as poor nutrition (weight per height [WHZ] <-2 for children <5 years old and BMI for age [BAZ] <-2 for children ≥5 years old) or good nutrition (WHZ ≥-2 and <+1 for <5 years old children and BAZ ≥-2 and <+1 for ≥5 years-old).[10-12] Baseline CD4 levels were used to categorize into four immunodeficiency status according to the WHO staging: no immunodeficiency (CD4 level >35%, >30%, >25%, and >500 cells/mm^3 for children aged <11 months, 12-35 months, 36-59 months, and >5 years, respectively), mild (30%-35%, 25%-30%, 20%-25%, and 350-499 cells/mm^3), moderate (25%-30%, 20%-25%, 15%-20%, and 300-349 cells/mm^3), and severe immunodeficiency (<25%, <20%, <15%, and <200 cells/mm^3).[13] Those four categories were then simplified into two categories: no/mild immunodeficiency and moderate/severe immunodeficiency. Immunological response was seen by an increase in CD4 level within 6 months, categorized into poor response (did not increase or increase below average increase of all samples) and good response (increase above average). Data regarding age, sex, and presence of opportunistic infection (OI) such as diarrhea, tuberculosis, and pneumonia were also collected. The operational definition of variables used in this research is shown in **Table 2**. All data were analyzed using Chi-Square with SPSS 29 for Mac; P values <0.05 were considered to be statistically significant. Ethical clearance was obtained from the Medical and Health Research Ethics Committee of Wangaya Hospital.

Results

A total of 30 samples of children with HIV/AIDS were collected; 17 children had good nutritional status and 13 children had poor nutrition. Characteristics of subjects are shown in **Table 3**. Of the 30 respondents, 18 (60%) were <5 years old, with the same amount for each nutritional status category. There were 12 (40%) who were ≥5 years old, with 4 (33.3%) having poor nutritional status and 8 (66.7%) having good nutritional status. Based on the immunodeficiency stage, 13 (43.3%) were in the no immunodeficiency/mild stage, and 17 (56.7%) were in the moderate/severe stage. The proportion of respondents with poor nutrition was more in the opportunistic infections group, 10 (58.8%), while children with good nutrition mostly did not experience opportunistic infections (10%-76.9%).

The interval between the first and subsequent CD4 counts was varied, ranging from 6 months to 2 years. To reduce bias in the final analysis, based on the recommended timing of CD4 testing from the Guidelines for the Implementation of HIV Therapy in Children,[13] researchers established a 6-month interval by calculating the estimated CD4 increase over 6 months for all respondents using the following formula:

$$\text{CD4 level increase over 6 months} = \frac{\text{CD4 count increase}}{\text{Inspection time interval (months)} \times 6 \text{ (months)}}$$

In this study, 13 children (43.3%) had poor nutritional status and 17 children (56.7%) had good nutritional status. Of the total 30 respondents, 23 children (76.7%) had poor immunological responses, 10 of them (43.5%) had poor nutritional status, and 13 (56.5%) had good nutritional status. Meanwhile, 7 out of 30 respondents (23.3%) had a good immunological response, 3 (42.9%) had poor nutrition, and 4 (57.1%) had good nutrition status. There was an almost equal amount of each immunological response category in both good and poor nutritional status.

The result of the analysis was shown in **Table 4**. There was no significant relationship

Table 1. Sample calculation based on previous research.

Omoni, *et al.*: Immunologic Outcomes of Antiretroviral Therapy among HIV-Infected Nigerian Children and its Association with Early Infant Feeding and Nutritional Status at Treatment Initiation[9]	P1	P2	N
Nutritional Status	0.5	0.76	30


Table 2. Operational definition of variables.

No	Variable	Operational Definition	Unit	Scale
1	Nutritional status	The health condition of individuals in terms of nutrition, as a result of food consumption and nutrient utilization, in which the physical impact is measured anthropometrically. One of the tools to measure is WHO charts.[9,12]	- Poor nutrition (WHZ <-2 for children <5 years-old and BMI for age BAZ <-2 for children ≥5 years-old) - Good nutrition (WHZ ≥-2 and <+1 for <5 years-old children and BAZ ≥-2 and <+1 for ≥5 years-old)	Categoric
2	Immunological response	Assessed based on CD4 count increase within 6 months according to the Guidelines for the Implementation of HIV Therapy in Children.[6,9,15,16]	- Poor immunological response (did not increase or increase below average increase of all samples) - Good immunological response (increase above average).	Categoric
3	Immunodeficiency status	Immunodeficiency status based on the baseline CD4 level, categorized according to the WHO staging.[13]	- No/mild immunodeficiency; based on the category of no immunodeficiency (CD4 level >35%, >30%, >25%, and >500 cells/mm^3 for children aged <11 months, 12-35 months, 36-59 months, and >5 years respectively) and mild (30%-35%, 25%-30%, 20%-25%, and 350-499 cells/mm^3). - Moderate/severe immunodeficiency; based on the category of moderate (25%-30%, 20%-25%, 15%-20%, and 300-349 cells/mm^3), and severe immunodeficiency (<25%, <20%, <15%, and <200 cells/mm^3).	Categoric
4	Opportunistic infections	A viral, bacterial, parasitic, and/or fungal infection because of the low immune system. An opportunistic infection in children with HIV/AIDS could be diarrhea, tuberculosis, and/or pneumonia. Having one of those infections categorized as having an opportunistic infection.	- Yes - No	Categoric

between nutritional status and immunological response (p = 0.660). The results of the analysis of confounding variables such as immunodeficiency stage and the incidence of opportunistic infections also did not have a significant relationship with immunological response (p = 0.326 and 0.340, respectively).

Discussion

Nutritional status plays an important role in infectious diseases. Malnutrition can predispose to infection, cause severe illness, and can affect recovery from infection.[5,6,7,9,14,15] The interaction between malnutrition and HIV infection is complex but can be a contributing factor to an already weakened immune system and can complicate disease treatment by affecting the ability of the intestinal tract to absorb drugs and the ability to absorb various nutrients, thus worsening the condition of malnutrition itself.[7] Opportunistic infectious events such as diarrhea, tuberculosis, and pneumonia can also affect nutrient absorption and worsen nutritional status.[6,7] Malnutrition will also increase the higher energy demand on the patient's body and immune system, which can lead to further immune deficiency.[6]

Table 3. Demographic characteristics of respondents.

	Total	Poor Nutritional Status (n=13)	Good Nutritional Status (n=17)
CD4 Increase			
Poor immunological response	23 (76.7%)	10 (43.5%)	13 (56.5%)
Good immunological response	7 (23.3%)	3 (42.9%)	4 (57.1%)
Age			
<5 years old	18 (60%)	9 (50%)	9 (50%)
≥5 years old	12 (40%)	4 (33.3%)	8 (66.7%)
Sex			
Female	19 (63.3%)	8 (42.1%)	11 (57.9%)
Male	11 (36.7%)	5 (45.5%)	6 (54.5%)
Immunodeficiency Status			
No/mild	13 (43.3%)	6 (46.2%)	7 (53.8%)
Moderate/severe	17 (56.7%)	7 (41.2%)	10 (58.8%)
Opportunistic Infections			
Yes	17 (56.7%)	10 (58.8%)	7 (41.2%)
No	13 (43.3%)	3 (23.1%)	10 (76.9%)

In this study, 76.9% of respondents with poor nutritional status had poor immunological responses. This proportion was almost similar to the proportion of the good nutritional status group, which was 76.5%; there was no significant relationship between nutritional status and immunological response in the form of CD4 increase (p = 0.660). Similarly, the relationship between immunodeficiency state and the incidence of opportunistic infections with immunological responses was also not significant (p = 0.326 and 0.340, respectively).

These results were similar to research by Naidoo, *et al,*[14] and Aaradhana, *et al,*[15] who each found no significant relationship between

Table 4. Chi-square analysis result.

Variable	N	Δ CD4		*P*-value
		Poor Immunological Response	Good Immunological Response	
Nutritional Status				0.660
Poor nutrition	13 (43.3%)	10 (76.9%)	3 (23.1%)	
Good nutrition	17 (56.7%)	13 (76.5%)	4 (23.5%)	
Immunodeficiency State				0.326
Moderate/severe	17 (56.7%)	12 (70.6%)	5 (29.4%)	
No/mild	13 (43.3%)	11 (84.6%)	2(29.4%)	
Opportunistic Infections				0.340
Yes	17 (56.7%)	14 (82.4%)	3 (17.6%)	
No	13 (43.3%)	9 (63.2%)	4 (36.8%)	

initial nutritional status and immunological response. The study by Ebissa, *et al,* which divided nutritional status into 3 groups based on height for age Z score (HAZ), weight for age (WAZ), and WHZ, also showed the same result: there was no significant relationship between nutritional status and immunological response. However, while all categories in HAZ and WAZ had similar immunological responses, children with WHZ ≤-2 did not have as good an immunological response as other children in their category.[16] Meanwhile, research conducted by Omoni, *et al,* showed that although overall there was no significant relationship between nutritional status and immunological response and no significant difference between immunological response in children with stunting and wasting, children with underweight status or WAZ <-3 had significantly lower CD4 values after 12 months of treatment compared to the wasting and stunting groups. This, according to Omoni, *et al,* may be related to the underdosing effect.[9]

Although the exact mechanism of the interaction between malnutrition, HIV infection, and treatment outcome has yet to be elucidated, the absence of a significant association between nutritional status and immunologic response in this study could be due to several reasons. First, all respondents in this study, as well as in the similar studies mentioned above, were already on ART. It is well known that ART improves immunologic, virologic, and nutritional responses.[5,6] This study adds to the growing body of evidence demonstrating the effectiveness of ART in improving pediatric immune status despite severe immune suppression and malnutrition at treatment initiation. Second, the study did not examine drug adherence and had a limited sample size. Other things that may affect the treatment outcome, such as nutritional intake, are also weaknesses of this study. In addition, in this study, pediatric patients with HIV/AIDS at Wangaya Hospital were not routinely checked for CD4 counts for the same period of time, thus the assessment of CD4 count increase was uneven and had to be equalized manually using a formula determined by the researcher.

Conclusion

This study showed no difference in immunological response for children with either good or poor nutritional status. Further research is needed with a larger sample size and longer period on other confounding factors that may affect immunological responses.

Conflict of Interests

None declared.

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Abbreviations

HIV, Human Immunodeficiency Virus; AIDS, Acquired Immunodeficiency Syndrome; ART, Antiretroviral therapy; WHZ, weight per height Z score; WAZ, weight per age Z score; HAZ, height per age Z score; BAZ, BMI for age Z score; OI, opportunistic infection.

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