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Nutritional Status and the Use of Protease Inhibitors Among Hiv-infected Children in Klang Valley, Malaysia

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ABSTRACT

This study determined the association between nutritional status and the use of protease inhibitors (PI) containing regimen among HIV-infected children receiving treatment at the referral centres in Klang Valley. A total of 95 children currently on antiretroviral (ARV) therapy, aged one to eighteen years, were recruited using purposive sampling. Demographic data, anthropometric measurements, medical history, were collected using a structured questionnaire. Serum micronutrients levels and lipid profile were also examined using blood samples. Mean age was 8.8±3.9 years and 44.2% were on PI. Age ($\chi 2 = 10.351$, $p = .006$), weight-for-age ($\chi 2 = 6.567$, $p = .010$), serum selenium ($\chi 2 = 4.225$, $p = .040$) and HDL-C ($\chi 2 = 7.539$, $p = .006$) were significantly associated with the use of PI. Fewer children on PI were deficient in selenium as compared to those not on PI. On the contrary, more children on PI were underweight and had low HDL-C. The use of PI was found to have both positive and negative effects with better selenium level but poorer HDL-C level and weight status.

Keywords: HIV, protease inhibitors, nutritional status, HIV-infected children, Malaysia

INTRODUCTION

Human Immunodeficiency Virus (HIV) remains of the biggest threat to global health and people living with HIV including children vulnerable to various health-related issues.[1] One of the most affected outcomes of HIV would be the nutritional status of these children. HIV-infected children are prone to malnutrition due to inadequate intake of nutrients, nutrient loss due to malabsorption, metabolic alterations and drug-nutrient interactions.[2, 3] A state of malnutrition would render these children more prone to infections and further deterioration of their overall health specifically their nutritional status.[4] Micronutrients such as selenium, zinc, vitamin A and E are found to be most affected among HIV-infected patients.[5, 6, 7]

The advancement of antiretroviral (ARV) therapy has brought about a dramatic increase in life expectancy of people living with HIV and AIDS.[8] However, its use was not without adverse effects in some patients. Nausea, diarrhoea, fatredistribution, pancreatitis, lactic acidosis, lipid abnormalities, and hyperglycaemia were among the common effects associated with the use of ARV therapy.[8, 9] Specifically, the incorporation of protease inhibitors (PI) into the ARV regimen has been implicated as a possible cause of HIV-associated lipodystrophy not only among adults but also in children.[10]

PI are highly potent antiretroviral agents that act by selectively blocking HIV-1 protease, an enzymenecessary for HIV-1 replication in the later stages ofvirus production.[11] It is usually used in combination with other antiretroviral drugs to maximise the reduction in viral load and increase in CD4+ cell count.[12] In Malaysia, recommendations for first line therapy for children and adolescents are adapted from the US Department of Health and Human Services Guidelines for the Use of Antiretroviral Agents.[13] Some of the recommended choices of regimen to be used include PI as part of the first line therapy and thus, it is not surprising to note that most of these children may be exposed to these medications.

Current literatures pointed to the need for more data on the use of PI and its association with the nutritional status of these children. A longitudinal study conducted by Miller *et al.*,[14] among 67 HIV-infected children found that PI therapy has a positive effect on several growth parameters, including weight, weight/height, and muscle mass. On the contrary, another longitudinal study among 25 Italian HIV-infected children noted that PI treatment did not seem to have significantly influenced their body weight. However, the author highlighted that combined therapy including PI may result in an improved height trend among the children.[15]

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Furthermore, Bitnun *et al.,*[10] noted that studies comparing PI and PI-naive group in terms of lipid profiles and other micronutrients were relatively few. A recent study by Chantry *et al.,*[16] found that the use of PI was associated with the worsening of lipid profiles. Its effect was even worse when combined with a non-nucleoside reverse transcriptase.

This study aimed to describe the nutritional status of HIV-infected children as well as to determine the differences in nutritional status between the children who were taking PI as part of the ARV regimen and the children who do not. This would further enhance and extend our understanding on the effect of PI on the nutritional status of the children.

METHODS

This study was carried out at the Paediatric Institute of the Kuala Lumpur Hospital and the Paediatric Department of the Universiti Malaya Medical Centre (UMMC) involving children receiving outpatient care for HIV infection. The number of HIV-infected children being treated at the Paediatric Institute totalled 111 and 10 were being treated at the UMMC. The inclusion criteria for the study include: a) HIV-infected children aged 1 to 18 years; and b) HIV-infected children currently treated with ARV medications. The exclusion criteria include: a) HIV-infected children who were yet to start HAART treatment; b) HIV-infected children who were hospitalised due to infections; and c) HIV-infected children who refused to participate or were absent from their appointment. This study utilised a non-probability sampling method whereby both the hospitals were selected as they are the centres of referral for HIV cases among children below the age of 19 years. All children who met the selection criteria were included. Prior consent was obtained from parents/guardians before the child could be included in the study. The response rate of this study was 79.3%.

Ethical approval for the study was obtained from the research ethics committees of the Faculty of Medicine and Health Sciences, Universiti Putra Malaysia; University Malaya Medical Centre; and the Ministry of Health, Malaysia (Research ID: NMRR-08-1233-2501).

All parents/guardians of the children were interviewed using structured questionnaires which include questions on socio-demographic variables (age, sex, ethnicity, and living arrangement), and antiretroviral medications history (duration on treatment, and types of medications prescribed). The medical records of the HIV-infected children were used to validate the information provided by their parents/guardians.

Weight and height were measured using the Tanita digital scale model 314 and SECA wall stadiometer model 206 respectively. Duplicate measurements of each parameter were done and the means of the height and weight were then used for the calculation of Body Mass Index (calculated as weight in kilograms divided by height in meters squared). Body Mass Index-for-age (BMI-for-age), height-for-age (Ht-for-age) and weight-for-age (wt-for-age) were expressed as z-scores to adjust for age and sex. WHO Anthroplus[17]software was used for the calculation of the z-scores. To determine the growth status of the children, the World Health Organization (WHO) Growth Standards 2006[18] and WHO Growth Reference 2007[17] were then used. Weight-for-age computations were only up to the age of 10.0 years due to the limitation of the WHO reference used.

The children were also required to provide non-fasting blood samples for the assessment of serum level of zinc, selenium, vitamin E, vitamin A and lipids. In this study, non-fasting blood samples were used because the children were required to take the prescribed regimen of drugs on time after meals. Therefore, it was deemed unethical to require fasting blood samples from these children.

Fifteen millimetres (ml) of blood samples were drawn by trained nurses from the hospitals. Serum Zn and Se levels were measured using inductively coupled plasma-mass spectrometry (ICP-MS). High-performance liquid chromatography (HPLC) with UV detector was used to measure the serum levels of vitamin A and E. Serum triglycerides, total cholesterol (TC), and high density lipoprotein cholesterol (HDL-C) levels were measured byenzymatic methods. Low-density lipoprotein cholesterol (LDL-C) concentrations were derived by calculation using the Friedewald formula.[19] These analyses were conducted by the Gribbles Pathology (M) Sdn. Bhd. according to laboratory-based protocols.

The cut-off reference values used for vitamins and minerals examined in this study were based on the laboratory values recommended by WHO 2001 report.[20] Cut-offs for lipids are based onthe National Cholesterol Education Program (NCEP)[21] classifications for children and adolescents.

PASW Statistics version 18.0 was used for data management and statistical analysis. The data was analysed descriptively. Chi-square test was used to determine the association between nutritional status and the use of PI. The critical level of $\alpha = 0.05$ was used for statistical significance.

RESULTS

A total of 95 children participated in this study. The age of these children ranged from 15 months to 17 years old with a mean of 8.8 ± 3.9 years. Slightly more respondents were male (56.8%) as compared to female. By ethnicity, majority (53.7%) were Malays, followed by Chinese (32.6%) and other ethnic groups made up the remaining 13.7%. While 64.2% lived with families, 8.4% were adopted and 27.4 % were living in shelter homes around Klang Valley.

A majority (61.5%) of the children were diagnosed with HIV or AIDS during the first two years of life and the mean age (in months) of first diagnosis was 28.3 ± 33.6 months. Overall, the mean number of months since diagnosis was 105.5 ± 46.3 months. The average number of months the children had been on ARV was 67.9 ± 38.3 months. Only 4.2% had been on the regimen for less than a year. A total of 42 children (44.2%) were taking PI as part of the regimen. None of the children was on monotherapy. The mean percentage of CD4% was 24.9 ± 8.8 ranging from as low as 2% to as high as 45%. In terms of CD4+ absolute count, the mean was 884.1 ± 510.8 cells/mm3 and ranged between 34 and 2444 cell/mm3.

Table 1: Demographic background and nutritional status of the children and the association with the use of PI containing regimen (n=96 unless otherwise stated)

Characteristics	Intake of Protease Inhibitors (PI)			
	PI	Non-PI	Total	p-value
Demographic background				
Age				0.006*
6.0	8a (23.5b)	26 (76.5)	34 (35.8)	
7.0 to 10.0	19 (61.3)	12 (38.7)	31 (32.6)	
11.0	15 (50.0)	15 (50.0)	30 (31.6)	
Sex				1.000
Male	24 (44.4)	30 (55.6)	54 (56.8)	
Female	18 (43.9)	23 (56.1)	41 (43.2)	
Ethnicity				-
Malay	21 (41.2)	30 (58.8)	51 (53.7)	
Chinese	17 (54.8)	14 (45.2)	31 (32.6)	
Indian	3 (60.0)	2 (40.0)	5 (5.3)	
Sarawak Bumiputera	0 (0.0)	2 (100.0)	2 (2.1)	
Sabah Bumiputera	1 (100.0)	0 (0.0)	1 (1.0)	
Myanmar (Refugees)	0 (0.0)	5 (100.0)	5 (5.3)	
Anthropometric measurements				
BMI-for-age				0.274
Overweight/Obese	11 (33.3)	22 (66.7)	33 (34.7)	
Normal	27 (50.9)	26 (49.1)	53 (55.8)	
Thinness	4 (44.4)	5 (55.6)	9 (9.5)	
Mean Z-score	-0.31 ± 0.15			
Wt-for-age (n=59)				0.010*
Normal/Too heavy	15 (30.6)	34 (69.4)	49 (83.1)	
Underweight	8 (80.0)	2 (20.0)	10 (16.9)	
Mean Z-score	-1.19 ± 0.15			
Ht-for-age				0.135
Normal	23 (37.7)	38 (62.3)	61 (64.2)	
Stunted	19 (55.9)	15 (44.1)	34 (35.8)	
Mean Z-score	-1.54 ± 0.15			

Continuation

Table 1. Demographic background and nutritional status of the children and the association with the use of PI containing regimen (n=96 unless otherwise stated)

Characteristics	Intake of Protease Inhibitors (PI)			
	PI	Non-PI	Total	p-value
Biochemical Indicators				
Selenium (µmol/L)				0.040*
Adequate (0.9)	40(48.2)	43 (51.8)	83 (87.4)	
Deficient (<0.9)	2 (16.7)	10 (83.3)	12 (12.6)	
Zinc (µmol/L)				1.000
Adequate (9.0)	39 (43.8)	50 (56.2)	89 (93.7)	
Deficient (<9.0)	3 (50.0)	3 (50.0)	6 (6.3)	
Vitamin A (µmol/L)				0.148
Adequate (1.05)	19 (36.5)	33 (63.5)	52 (54.7)	
Deficient (<1.05)	23 (53.5)	20 (46.5)	43 (45.3)	
Vitamin E (µmol/L)				0.795
Adequate (25.0)	32 (45.7)	38 (54.3)	70 (73.7)	
Deficient (<25.0)	10 (40.0)	16 (60.0)	25 (26.3)	
Lipid Profile				
Total cholesterol (mg/dL)				0.088
Normal (<170)	10 (29.4)	24 (70.6)	34 (35.8)	
Borderline (170-199)	16 (50.0)	16 (50.0)	32 (33.7)	
High (200)	16 (55.2)	13 (44.8)	29 (30.5)	
HDL-C (mg/dL)				0.006*
Normal (>40)	33 (38.8)	52 (61.3)	85 (83.3)	
Deficient (40)	9 (75.0)	1 (25.0)	10 (16.7)	
LDL-C (mg/dL) (n=93)				0.386
Normal (<110)	24 (43.6)	31 (56.4)	55 (59.2)	
Borderline (110-129)	9 (34.6)	17 (65.4)	26 (27.9)	
High (130)	7 (58.3)	5 (41.7)	12 (12.9)	

* Statistically significant at = 0.05
a = Frequency b = Row %

Table 1 reveals that the intake of PI were associated with age [$\chi 2 = 10.351$, p = .006], weight-for-age [$\chi 2 = 6.567$, p = .010], selenium [$\chi 2 = 4.225$, p = .040], and HDL-C [$\chi 2 = 7.539$, p = .006] classifications.

Significantly higher percentages of children from the younger age groups of below 6 years (76.5% vs. 23.5%) were not on PI as compared to children from the older age groups. However, as the age increases, more children were treated with PI containing regimen as seen in those aged between 7 to 10 years. Half of the children in their teenage years were on PI containing regimen. On the contrary, no significant association was found between the sexes in terms of treatment approach. Weight-for-age classifications were found to be significantly associated with the use of PI. Significantly more underweight children were on PI as compared to the non-PI. No significant association were found between BMI-for-age classifications and PI groups. Similarly, height-for-age was not associated with the intake of PI

although more children in the PI group were found to be stunted.

Selenium deficiency was more common (83.3%) among children not on PI containing regimen as compared to those on PI. No significant association were noted for serum zinc, vitamin A and vitamin E levels with the use of PI containing regimen. In terms of lipid profile, 75.0% of the children on PI were found to have a low level of HDL-C. Total cholesterol and LDL-C levels were found to have no significant association with the use of PI.

DISCUSSION

It was found that there were more underweight children in the PI group as opposed to the non-PI group. It is unsure whether the poor weight status was due to the use of PI or due to changes in regimen to incorporate PI as part of the subsequent treatment approach given the poor weight status. Lack of data on any change of regimen among the children made it impossible to distinguish whether these children were treated with PI containing regimen as a result of a combination of poor weight status as well as poor immunological and virological factors. It is also worth noting that patients who were found to be losing weight were also more likely to be placed on PI as recommended by WHO treatment guidelines in combination with other factors.[9] However, finding from other studies showed sustained weight gain among those who were treated with PI both in adults[22] and children.[15, 23] A prospective longitudinal study which followed a group of children for a median of 2.4 years even found that PI therapy has a positive effect on muscle mass and not just on weight, height and weight-for-height of the children.[14]

Micronutrient deficiencies are common in HIV, both in the early as well as the late stages of the progression of the infection.[5, 24] The biochemical markers examined in this study showed deficiency in several micronutrients. Deficiency in serum level of vitamin A was more commonly seen among HIV-infected children as compared with other micronutrients. Low status of micronutrients seen in early asymptomatic HIV is mainly due to reduced absorption as a result of structural and functional changes in intestinal tract characterized by villous atrophy and crypt hyperplasia,[25] increased utilization and loss of micronutrients when diarrhoea and other co-infections become more frequent.[26] As such, dietary intake becomes increasingly important and its level of requirement may eventually be higher than that of non-infected children.[7] The treatment approach using PI containing regimen was found to have positive effect on serum selenium level with less children experiencing deficiency as compared to those not on PI. Previous studies have found that serum selenium levels were improved on antiretroviral treatment generally.[6, 7] On the contrary, a 3-year observational study by Rousseau *et al.,*[27] among 44 patients found that serum selenium level were not significantly different between those on antiretroviral treatment and those who do not.

The use of PI as part of the ARV treatment has been associated with dyslipidemia which include elevated levels of total cholesterol, triglycerides, LDL-C and decreased level of HDL-C.[15, 28, 29, 30, 31, 32] In this study, only HDL-C levels were associated with the use of PI containing regimen. HDL-C was lower among children who were on PI. Similarly in a study by Rose *et al.*,[33] it was found that those treated with PI containing regimen for 3 to 6 years period were less likely to have high HDL-C level. However, contradicting findings on the effect of PI on HDL-C levels had been shown in another study by Bitnun *et al.*,[10] which found that children who were on PI containing regimen had significantly higher total cholesterol, LDL-C and triglycerides levels but no effect on HDL-C level.

There are several limitations in this study. First, due to the nature of the cross sectional study design, the temporal relation between the variables remained unclear. Thus, it is not possible to distinguish whether poor weight status of the children preceded the use of protease inhibitors. Secondly, lack of data on the use of supplementation limits the interpretation in terms of micronutrients adequacy. Nevertheless, vitamin A deficiency remained one of the most affected micronutrients given the high percentage of inadequate level among the children. It is also worth noting that the lipid profile from this study can only provide an insight for screening purposes and no diagnostic conclusion can be drawn for clinical purposes.

With more children being treated with PI containing regimen, there is a need to ascertain its effect on micronutrient levels. Cohort studies looking at micronutrient levels and the duration of the use of PI containing regimen and other antiretroviral drug groups would be insightful. Furthermore, comprehensive nutritional assessments which include anthropometric, biochemical, clinical and dietary assessment should be an on-going evaluation for these children as the use of PI may have possible effects on the lipid profile and weight status of the children. Intervention trials focusing on the effectiveness of nutrition counselling among children on ARV therapy may be beneficial to help the children and their parents/guardians move towards improvements in nutritional status and overall growth.

CONCLUSION

In conclusion, children receiving PI containing regimen were found to have better selenium levels as compared to the non-PI group. On the contrary, the use of PI therapy among HIV-infected children was found to be associated with poorer HDL-C level and weight status. Our findings suggest that routine monitoring of serum lipids in HIV-infected children particularly those receiving PI containing regimen may be beneficial. Early detection of dyslipidemia and poor growth may warrant for nutritional interventionto be incorporated in an attempt to provide a more holistic approach

in treating HIV-infected children. Dietary counselling and regular exercise may be helpful in the management of dyslipidemia particularly among children receiving PI containing regimen.

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References

[1] UNAIDS. AIDS Epidemic Update: November 2009. Geneva, Switzerland: UNAIDS/WHO;2009.

[2] Khalili H, Soudbakhsh A, Hajiabdolbaghi M, *et al.* Nutritional status and serum zinc and selenium levels in Iranian HIV infected individuals. BMC Infect Dis. 2008;8:165.

[3] Beck MA, Handy J, Levander OA. Host nutritional status: The neglected virulence factor. Trends Microbiol. 2004;12(9):417-423.

[4] Anabwani GM, Navario P. Nutrition and HIV/AIDS in sub-Saharan Africa: An overview. Nutrition. 2005;21(1):96-99.

[5] Bogden JD, Oleske JM. The essential trace minerals, immunity, and progression of HIV-1 infection. Nutr Res. 2007;27(2):69-77.

[6] Baum MK, Campa A. Role of selenium in HIV/AIDS. Selenium. 2nd ed: Springer US; 2006:299-310.

[7] Coyne-Meyers K, Trombley LE. A review of nutrition in human immunodeficiency virus infection in the era of highly active antiretroviral therapy. Nutr Clin Pract. 2004;19(4):340-355.

[8] Esté JA, Cihlar T. Current status and challenges of antiretroviral research and therapy. Antivirl Res. 2010;85(1):25-33.

[9] World Health Organization. Antiretroviral Therapy for HIV infection in Infants and Children: Towards Universal Access. Recommendations for a Public Health Approach. Vienna, Austria: WHO;2010.

[10] Bitnun A, Sochett E, Babyn P, *et al.* Serum lipids, glucose homeostasis and abdominal adipose tissue distribution in protease inhibitor-treated and naive HIV-infected children. AIDS. 2003;17(9):1319-1327.

[11] Kakuda TN, Struble KA, Piscitelli SC. Protease inhibitors for the treatment of human immunodeficiency virus infection. Am J Health-Syst Ph. 1998;55(3):233-254.

[12] Phillips KD. Protease inhibitors: A new weapon and a new strategy against HIV. JANAC. 1996;7(5):57-71.

[13] Ministry of Health Malaysia, Academy of Medicine Malaysia, Malaysian Paediatric Association. Clinical Practice Guidelines: Management of HIV infection in children. Putrajaya, Malaysia: MOH Malaysia;2008.

[14] Miller TL, Mawn BE, Orav EJ, *et al.* The effect of protease inhibitor therapy on growth and body composition in human immunodeficiency virus type 1-infected children. Pediatrics. 2001;107(5):E77-E77.

[15] Fiore P, Donelli E, Boni S, Pontali E, Tramalloni R, Bassetti D. Nutritional status changes in HIV-infected children receiving combined antiretroviral therapy including protease inhibitors. Int J Antimicro Ag. 2000;16(3):365-369.

[16] Chantry CJ, Hughes MD, Alvero C, *et al.* Lipid and glucose alterations in HIV-infected children beginning or changing antiretroviral therapy. Pediatrics. 2008;122(1):e129-138.

[17] World Health Organization. WHO AnthroPlus for personal computers Manual: Software for assessing growth of

the world's children and adolescents. Geneva, Switzerland: WHO;2007.

[18] World Health Organization. Training Course on Child Growth Assessment. Geneva, Swtizerland: WHO;2006.

[19] Friedewald WT, Levy RI, Fredrickson DS. Estimation of the Concentration of Low-Density Lipoprotein Cholesterol in Plasma, Without Use of the Preparative Ultracentrifuge. Clin Chem. June 1, 1972 1972;18(6):499-502.

[20] World Health Organization, Food and Agriculture Organization. Vitamin and Mineral requirements in human nutrition. Bangkok, Thailand: WHO;2001.

[21] National Cholesterol Education Program (NCEP). Highlights of the Report of the Expert Panel on Blood Cholesterol Levels in Children and Adolescents. Pediatrics. 1992;89(3):495.

[22] Mahlungulu SSN. Nutritional interventions for reducing morbidity and mortality in people with HIV. Cochrane Database of Syst Rev. 2008(4).

[23] Verweel G, van Rossum AMC, Hartwig NG, Wolfs TFW, Scherpbier HJ, de Groot R. Treatment with highly active antiretroviral therapy in human immunodeficiency virus type 1-infected children is associated with a sustained effect on growth. Pediatrics. 2002;109(2 part 1):7p.

[24] Patrick L. Nutrients and HIV" Part 2 - Vitamins A and E, zinc, b-vitamins and magnesium. Altern Med Rev. 2000;5(1):38-51.

[25] Ullrich R, Zeitz M, Heise W, L'age M, Höffken G, Riecken EO. Small intestinal structure and function in patients infected with human immunodeficiency virus (HIV): evidence for HIV-induced enteropathy. Ann Intern Med. 1989;111:15-21.

[26] World Health Organization. Nutrition and HIV: Report by the Secretariat. Geneva, Switzerland: WHO;2005.

[27] Rousseau MC, Molines C, Moreau J, Delmont J. Influence of highly active antiretroviral therapy on micronutrient profiles in HIV-infected patients. Ann Nutr Metab. 2000;44(5-6):212-216.

[28] Lainka E, Oezbek S, Falck M, Ndagijimana J, Niehues T. Marked dyslipidemia in HIV-infected children on protease inhibitor-containing antiretroviral therapy. Pediatrics. 2002;110:156.

[29] Carter RJ, Wiener J, Abrams EJ, *et al.* Dyslipidemia among perinatally HIV-infected children enrolled in the PACTS-HOPE cohort, 1999-2004: A longitudinal analysis. J Acq Immun Def Synd. 2006;41(4):453-460.

[30] Lapphra K, Vanprapar N, Phongsamart W, Chearskul P, Chokephaibulkit K. Dyslipidemia and lipodystrophy in HIV-infected Thai children on highly active antiretroviral therapy (HAART). J Med Assoc Thai. 2005;88(7):956-966.

[31] Beraldo Battistini TR, Saccardo Sarni RO, Suano de Souza FI, *et al.* Lipodystrophy, lipid profile changes, and low serum retinol and carotenoid levels in children and adolescents with acquired immunodeficiency syndrome. Nutrition. 2010;26(6):612-616.

[32] Solórzano Santos F, Gochicoa Rangel LG, Palacios Saucedo G, Vázquez Rosales G, Miranda Novales MG. Hypertriglyceridemia and Hypercholesterolemia in Human Immunodeficiency Virus-1-Infected Children Treated with Protease Inhibitors. Arch Med Res. 2006;37(1):129-132.

[33] Rose H, Woolley I, Hoy J, *et al.* HIV infection and high-density lipoprotein: the effect of the disease vs the effect of treatment. Metabolism. 2006;55(1):90-95.