

# IMMUNOLOGICAL AND VIROLOGICAL CHARACTERISTICS AND PERFORMANCE IN THE VARIABLES FLEXIBILITY AND ABDOMINAL RESISTENCE STRENGTH OF HIV/AIDS ADOLESCENTS UNDER HIGHLY ACTIVE ANTIRRETROVIRAL THERAPY



Fabiana Ferreira dos Santos<sup>1</sup>  
Fernanda Bissigo Pereira<sup>2</sup>  
Carmem Lúcia Oliveira da Silva<sup>3</sup>  
Alexandre Ramos Lazzarotto<sup>4</sup>  
Ricardo Demétrio de Souza Petersen<sup>1</sup>

1. Federal University of Rio Grande do Sul (UFRGS), Porto Alegre Rio Grande do Sul, Brazil.
2. Our Lady of Fátima College of Caxias do Sul, Caxias do Sul Rio Grande do Sul, Brazil.
3. Clinics Hospital of Porto Alegre Porto Alegre, Rio Grande do Sul, Brazil.
4. La Salle University Center, Canoas, Rio Grande do Sul, Brazil.

## Mailing address:

Alexandre Ramos Lazzarotto  
Grupo de Pesquisa Saúde e  
Desenvolvimento Humano, Centro  
Universitário La Salle.  
Av. Victor Barreto, 2.288 CEP 92010-  
000 - Canoas - Rio Grande do Sul,  
Brasil.  
E-mail: alazzar@terra.com.br

## ABSTRACT

**Introduction:** In the context of chronicity of AIDS, few studies have evaluated variables of physical fitness in children and adolescents; however, with adults the importance of adherence to HAART associated with physical exercise to improve these variables has been reported. **Objective:** To identify the immunological and virological characteristics and flexibility (FLEX) and abdominal resistance strength (ARS) variables of children and HIV / AIDS adolescents using HAART. **Methods:** This cross-sectional study took place at the HIV/AIDS Pediatric Clinic of the University Hospital ("Hospital de Clínicas") in the city of Porto Alegre. The sample was obtained consecutively by 63 patients (10 children and 53 adolescents) of both sexes, between ages 07 and 17 years. Data analysis was performed with SPSS, version 18.0 ( $p \leq 0.05$ ). To compare the means, paired Student's t test was used. **Results:** The mean diagnosis time of HIV and HAART was, respectively,  $11 \pm 3.42$  years and  $40 \pm 32.78$  months. The prevalent form of transmission was vertical transmission (98.42%). The undetectable viral load was identified in 73.1%. The count of CD4 + and CD8 + T cells as well as their relationship, presented averages of  $932.25 \pm 445.53$  cells/ml,  $1018 \pm 671.23$  cells/ml and  $0.90 \pm 0.41$ , respectively. Concerning the variables FLEX and ARS, regardless of sex, there was a higher proportion of children and adolescents classified below the cutoff points. Significant difference was observed between AE and their respective cutoff points in the HIV diagnosis ( $p = 0.032$ ); CD4 + ( $p = 0.008$ ) and viral load ( $p = 0.030$ ). There were significant differences between FLEX and its respective cutoffs in variables CD4 + / CD8 + ( $p = 0.022$ ) and in the viral load ( $p = 0.040$ ). **Conclusion:** The results demonstrate that immunological and virological characteristics are stable; however, undesirable levels of fitness are observed in FLEX and ARS variables.

**Keywords:** HIV/AIDS, physical fitness, children, adolescents.

## INTRODUCTION

The acquired immunodeficiency syndrome (SIDA, AIDS) is the advanced clinical manifestation derived from an immunodeficiency scenario caused by the human immunodeficiency virus (VIH, HIV)<sup>1</sup>. The disease is characterized by the continued suppression of the cells of the immune system infected by the HIV, which will make the body prone to the infections known as opportunistic such as tuberculosis, toxoplasmosis and pneumonia (by *pneumocystis jirovecii*)<sup>2</sup>.

In Brazil, the cases of vertical transmission have proportionally increased to the incidence of AIDS, and from 2000 to June, 2011, 61,789 new cases in pregnant women were reported<sup>3</sup>. In children and adolescents younger than 13 years, vertical transmission appears as the predominant exposure category, with percentage above 85% from 2006<sup>4</sup>.

The Highly Active Antiretroviral Therapy (HAART), from the introduction of the protease inhibitors (PI) in 1996, have provided the sustained suppression of viral load and, consequently, the immunological reconstitution, decreasing the incidence of opportunistic

infections and increasing life expectancy of patients, characterizing hence AIDS as a chronic disease<sup>5</sup>.

In that chronicity context, few studies have evaluated variables of physical fitness in children and adolescents; however, the research with adults has recorded the importance of engagement in physical exercises associated with HAART in order to improve physical fitness and consequently, functional independence<sup>6-8</sup>. From these premises, the need for parameters for the variables which compose physical fitness related to health of children and adolescents with HIV/AIDS becomes evident, and, provides hence qualification in prescription and monitoring of physical training. Thus, a study was designed with the aim to identify the immunological and virological characteristics as well as flexibility (FLEX) and abdominal resistance strength (ARS) variables of children and adolescents with HIV/AIDS undergoing ART.

## METHOD

It is a cross-sectional study held in the HIV/AIDS Unit in Pediatrics of the Clinics Hospital of Porto Alegre - Brazil. The sample was

consecutively obtained by 63 children and adolescents with HIV/AIDS undergoing ART, of both sexes, aged between seven and 17 years and clinically, qualified for practice of physical exercises. The patients who were practicing regular physical exercises in the three months previous to the study were not included in it. The project was approved by the Ethics in Research Committee of the Clinics Hospital of Porto Alegre (CEP/HCPA). Data from the medical record of the patients concerning their clinical profile were collected (sex, age, transmission manner, HIV diagnosis period and current time of HAART use), immunological parameters (T CD4+ – auxiliary lymphocytes, T CD8+ – cytotoxic lymphocytes and T CD4+/T CD8+ ratio) and virological parameters (viral load and log- scientific note which uses the 10 potency to describe number alterations in the viral load). The current HAART time was considered, the most recent therapeutic scheme prescribed by the doctor responsible for the patient.

The T lymphocytes are cells responsible for the cellular immunity of the individuals and are classified in three large groups T CD4+, T CD8+ the *natural killer* lymphocytes, natural killers (NK). The T CD4+ or auxiliary lymphocytes (also known as *helper*) are the first lymphocytes to enter in contact with the HIV for expressing on their surface a phenotype marker named CD4, which presents high affinity with the virus. The T CD8+ are cytotoxic lymphocytes which act in the immunological surveillance, being responsible for the release of cells infected by the HIV. The NK lymphocytes are associated with the surveillance skill in certain tumors and viral infections; however, they did not participate in the HIV replication process<sup>9</sup>.

The FLEX variable was evaluated through the “sit and reach” test and the ARS through the abdominal test in one minute, whose reference protocols compose the Test Battery of the Brazil Sports Project (PROESP-BR)<sup>10</sup>.

FLEX is defined as the maximum skill to move an articulation in a range of motion, while ARS is the ability of a muscular group to perform repeated contractions for a period of time sufficient to cause muscle fatigue or keep specific percentage of an isometric voluntary contraction for a prolonged period of time through tension<sup>11</sup>.

The tests and reference values of the PROESP-BR are valid, reliable, of low cost and easy application, accessible to physical education teachers in order to establish the follow-up of children and adolescents aged between seven and 17 years. Among its aims, we can mention the performance of interventions in the promotion of health markers field through the proposition of a measurement system which enable the evaluation of the health indicators associated with sex, chronological age concerning body growth, nutritional status and physical fitness (figure 1).

Regarding FLEX, the values above the cutoff points are considered with expected levels of physical fitness related to health, while for ARS, the values equal and above the cutoff points suggest expected levels for this aptitude<sup>10</sup>.

Data analysis was performed in the statistical *software Package for the Social Sciences* (SPSS), version 18.0, ( $p \leq 0.05$ ). The descriptive variables were analyzed through measures of central tendency (mean) and dispersion (standard deviation) and the categories were described by the frequency. The means were compared using the paired *Student's t test*.

**Figure 1.** Defines the cut-off points used for the FLEX and ARS variables according to sex and age of the children and adolescents<sup>10</sup>.

| Age | FLEX* (cm) |        | ARS (number of flexions) |        |
|-----|------------|--------|--------------------------|--------|
|     | Male       | Female | Male                     | Female |
| 7   | 29.3       | 21.4   | 20                       | 20     |
| 8   | 29.3       | 21.4   | 20                       | 20     |
| 9   | 29.3       | 21.4   | 22                       | 20     |
| 10  | 29.4       | 23.5   | 22                       | 20     |
| 11  | 27.8       | 23.5   | 25                       | 20     |
| 12  | 24.7       | 23.5   | 30                       | 20     |
| 13  | 23.1       | 23.5   | 35                       | 23     |
| 14  | 22.9       | 24.3   | 35                       | 23     |
| 15  | 24.3       | 24.3   | 35                       | 23     |
| 16  | 25.7       | 24.3   | 40                       | 23     |
| 17  | 25.7       | 24.3   | 45                       | 23     |

\*Without Wells bench.  
Source: Brazil Sport Project Manual (2009)<sup>10</sup>.

## RESULTS

The general characteristics of the participants are presented in table 1. Considering the 63 patients, 10 were children (seven to nine years old) and 53 were adolescents (ten to 17 years old), with 58.7% of the individuals being female. The mean HIV diagnosis time was of  $11 \pm 3.42$  years, and the mean current time of HAART use was of  $40 \pm 32.78$  months. The most prevalent transmission manner was vertical transmission (98.42%). Undetectable viral load ( $< 50$  copies/ml) was identified in 73.1%, and the logarithm mean was of  $0.90 \pm 1.53$ . The T CD4+ and T CD8+ count, as well as their ratio, presented, respectively mean of  $932.25 \pm 445.53$  cells/ml,  $1,018 \pm 671.23$  cells/ml and  $0.90 \pm 0.41$ .

**Table 1.** Clinical characteristics of the participants in the study.

| Variables                        | Total (n = 63)      |
|----------------------------------|---------------------|
| <b>Age (years) n (%)</b>         |                     |
| 7 to 9                           | 10 (15.9)           |
| 10 to 17                         | 53 (84.1)           |
| <b>Sex</b>                       |                     |
| Male                             | 26 (41.3)           |
| Female                           | 37 (58.7)           |
| Diagnosis period (years)         | $11 \pm 3.42$       |
| Time of ART use (months)         | $40 \pm 32.78$      |
| <b>Transmission manner n (%)</b> |                     |
| Vertical transmission            | 62 (98.52)          |
| Others                           | 1 (1.58)            |
| <b>Viral load</b>                |                     |
| $< 50$ copies/ml                 | 46 (73.1)           |
| $\geq 50$ copies/ml              | 17 (26.9)           |
| <b>Log</b>                       | $0.90 \pm 1.53$     |
| T CD4+*                          | $932.25 \pm 445.53$ |
| T CD8+*                          | $1018 \pm 671.23$   |
| Relação T CD4+ / T CD8+          | $0.90 \pm 0.41$     |

cART = combined antiretroviral therapy; \*values expressed in cells/ml.

**Table 2.** Results of the FLEX and ARS of the participants in the study.

| Variables | Male                    | n (%)       | Female       | n (%)       |
|-----------|-------------------------|-------------|--------------|-------------|
| FLEX      | Below c.o.p.            | 15 (57.69%) | Below c.o.p. | 19 (51.35%) |
|           | Above c.o.p./Acima p.c. | 11 (42.31%) | Above c.o.p. | 18 (48.65%) |
| ARS       | Below c.o.p.            | 21 (80.76%) | Below c.o.p. | 27 (72.97%) |
|           | Above c.o.p.            | 5 (19.24%)  | Above c.o.p. | 10 (27.03%) |

FLEX = flexibility; ARS = abdominal resistance strength; c.o.p.= cutoff point; FLEX: from seven to nine years male = 29.3cm; ten years male = 29.4cm; 11 years male = 27.8cm; 12 years male = 24.7cm; 13 years male = 23.1cm; 14 years male = 22.9cm; 15 years male = 24.3cm; 16 and 17 years male = 25.7cm; seven to nine years female = 21.4cm; ten to 13 years female = 23.5cm; 14 to 17 years female = 24.3cm. Cutoff point ARS: seven to eight years male = 20 flexions; nine to ten years male = 22 flexions; 11 years male = 25 flexions; 12 years male = 30 flexions; 13 to 15 years male = 35 flexions; 16 years male = 40 flexions; 17 years male = 45 flexions; seven to 12 years female = 20 flexions; 13 to 17 years female = 23 flexions. Source: Brazil Sport Project Manual (2009)<sup>20</sup>.

The FLEX and ARS variables are described in table 2. Higher proportion of children and adolescents classified below the cutoff point was observed, regardless of sex.

Significant difference was observed between ARS and its respective cutoff points in the period of HIV diagnosis ( $p = 0.032$ ), T CD4+ ( $p = 0.008$ ) and viral load ( $p = 0.030$ ). Children and adolescents with ARS above the cutoff point presented higher T CD4+ than those below the cutoff point. Significant difference was observed between FLEX and its respective cutoff points in the T CD4+/T CD8+ ( $p = 0.022$ ) and viral load ( $p = 0.040$ ) variables. Children and adolescents with FLEX above the cutoff point presented higher T CD4+/T CD8+ ratio than those below this point (table 3).

## DISCUSSION

The results of this study demonstrated that there is stability in the immunological and virological characteristics of the participants; however, they presented undesirable levels of physical fitness in the FLEX and ARS variables.

The participants presented mean of 11 years of HIV infection diagnosis and of three years and four months of HAART use. Undetectable viral load was evidenced ( $< 50$  copies/ml) in 73.1% of the participants and T CD4+ count  $> 500$  cells/ml in all of them. T CD4+ count  $> 500$  cells/ml classifies them in the "absent immunological category" concerning the HIV infection<sup>12</sup> and demonstrates positive activity of HAART in its clinical stability, since the natural history of the infection is immunosuppression.

The SRT contribution to the stability of virological and immunological parameters is crucial to hold the progression of morbidity in children and adolescents vertically infected. This premise may be corroborated by other studies, as by Mc Con-

nell *et al.*<sup>13</sup> and Judd *et al.*<sup>14</sup>, in which the use of HAART caused decline (81-93%) in mortality in children and adolescents in the USA and UK between 1994 and 2006. In Brazil, Romanelli *et al.*<sup>15</sup> cite the triple scheme as the most recommended treatment due to its lower viral replication. Matida *et al.*<sup>16</sup> consider the HAART use as the predictor which significantly influences on the survival increase of children exposed to the HIV by vertical transmission ( $p < 0.001$ ). According to Miller<sup>17</sup>, the suppressed viral replication consequent of the HAART engagement characterizes AIDS as a chronic and controllable disease with low mortality rate when compared with other pathologies.

The HIV transmission manner in 98.5% of the participants was vertical, a result which agrees with the Brazilian epidemiological data in which 85.8% (13,540) of the cases of AIDS in individuals younger than 13 years old occur by this transmission manner<sup>3</sup>. Another relevant result is that 58.7% of the patients were female. The sex ratio in Brazil is 1.7 men for each case in women<sup>3</sup>; however, the percentage of this study in the female sex is worrisome, since many of these children and adolescents will reach adulthood, that is to say, sexual and reproductive life; therefore, they will be able to increase the cases of HIV infection if prophylactic strategies to the HIV infection are not implemented.

The FLEX and ARS variables were able to evidence that HIV/AIDS children and adolescents do not present desirable levels of physical fitness, corroborating hence the study by Somarriba *et al.*<sup>18</sup>, which identified that children and adolescents with HIV/AIDS ( $\pm 16.1$  years) presented lower measurements of physical fitness when compared with the non-infected ones in the FLEX (23.71% vs. 46.09%,  $p = 0.0003$ ), VO<sub>2</sub> peak (25.92 vs. 30.90 ml/kg/min,  $p < 0.0001$ ) and strength/weight ratio of lower extremities (0.79 vs. 1.10 kg lifted/kg of body weight,  $p = 0.002$ ) variables. Thus, the physical compromising caused by the HIV associated with the HAART may cause negative alterations in strength, muscular mass and physical endurance<sup>19,20</sup>.

The prospective investigation performed by Mikkelsen *et al.*<sup>21</sup> mentions that low physical fitness in childhood and adolescence negatively reflects in adulthood. The physical fitness components are influenced by sex, maturational status and health conditions of the individuals<sup>22</sup>.

Fortunately, the FLEX and ARS variables may be modified with interventions, as demonstrated by Miller *et al.*<sup>23</sup>, where after 24 physical exercise sessions aimed at HIV/AIDS children, the most

**Table 3.** Comparison of the clinical characteristics with the FLEX and ARS variables

| Clinical variables       | FLEX               |                    | p     | ARS                   |                       | p     |
|--------------------------|--------------------|--------------------|-------|-----------------------|-----------------------|-------|
|                          | Below cutoff point | Above cutoff point |       | Below cutoff point    | Above cutoff point    |       |
| Diagnosis period (years) | 12.0 $\pm$ 3.2     | 10.7 $\pm$ 3.6     | 0.138 | 11.9 $\pm$ 3.5        | 9.8 $\pm$ 2.6         | 0.032 |
| Time of ART use (months) | 42.85 $\pm$ 37.85  | 38.76 $\pm$ 26.10  | 0.989 | 42.02 $\pm$ 35.93     | 37.60 $\pm$ 20.23     | 0.949 |
| T CD4+                   | 912 $\pm$ 445.69   | 955 $\pm$ 452.05   | 0.659 | 858.92 $\pm$ 430.12   | 1166.93 $\pm$ 424.87  | 0.008 |
| T CD8+                   | 1.294 $\pm$ 766.57 | 1.073 $\pm$ 527.04 | 0.190 | 1.200.37 $\pm$ 738.57 | 1.168.60 $\pm$ 404.01 | 0.651 |
| T CD4+/T CD8+            | 0.78 $\pm$ 0.33    | 1.04 $\pm$ 0.46    | 0.022 | 0.84 $\pm$ 0.40       | 1.07 $\pm$ 0.42       | 0.086 |
| Viral load (log)         | 1.27 $\pm$ 1.75    | 0.47 $\pm$ 1.11    | 0.040 | 1.14 $\pm$ 1.66       | 0.15 $\pm$ 0.60       | 0.030 |

FLEX = flexibility; ARS = abdominal resistance strength; Paired Student's *t* test.

remarkable alterations were verified in endurance ( $p = 0.006$ ), flexibility ( $p = 0.001$ ) and cardiorespiratory fitness ( $VO_2$  peak –  $p = 0.001$ ). The authors also mention that interventions with physical exercises in HIV/AIDS children are efficient for lower cardiovascular risk. Continuous administration of HAART is characterized as a risk factor for development of cardiovascular diseases<sup>24</sup>, which can appear in childhood or adolescence, justifying hence the practice of guided physical exercises for prevention or attenuation of the adverse effects of the medication (especially the protease inhibitors), for maintenance of clinical stability and development of physical fitness related to health.

The use of the cutoff points for FLEX and ARS of this study are used in the clinical practice for non-infected children and adolescents, and this limitation may be important, since HIV/AIDS patients present distinct characteristics due to the infection process and use of ART. Specific studies with children and adolescents with HIV/

AIDS are suggested in order to verify the suitability of the cutoff points currently recommended on health-related physical fitness and outlining able to evaluate the physical training efficiency.

## CONCLUSION

As crianças e adolescentes apresentaram estabilidade clínica, porém, necessitam melhorar a aptidão física relacionada à saúde nas variáveis flexibilidade e força de resistência abdominal.

## ACKNOWLEDGEMENTS

To the Graduation Program in Sciences of Human Movement (PPGCMH) of the Federal University of Rio Grande do Sul-UFRGS and the Clinics Hospital of Porto Alegre.

---

All authors have declared there is not any potential conflict of interests concerning this article.

---

## REFERÊNCIAS

1. CDC. Centers Disease Control and Prevention. Revised Recommendations for HIV Testing of Adults, Adolescents and Pregnant Women in Health-Care Settings In: CDC MMWR Recommendations and reports, 22 de setembro de 2006. Disponível em: [http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5514a1.htm?s\\_cid](http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5514a1.htm?s_cid). Acesso em: 25 out 2011.
2. CDC. Centers for Disease Control and Prevention. HIV/AIDS Surveillance Report. Atlanta, 2006. GA, 2008.
3. BRASIL. Boletim Epidemiológico – Aids – DST. Ano VIII nº 1 – 27ª a 52ª semanas epidemiológicas – julho a dezembro de 2010, 01ª a 26ª semanas epidemiológicas – janeiro a junho de 2011, 2012.
4. BRASIL. Boletim Epidemiológico – Aids – DST. Ano VII nº 1 – 27ª a 52ª semanas epidemiológicas – julho a dezembro de 2009, 01ª a 26ª semanas epidemiológicas – janeiro a junho de 2010, 2010.
5. Sterne JAC, Hernan MA, Ledergerber B, Tilling K, Weber R, Sendi P, et al. Long term effectiveness of potent antiretroviral therapy in preventing AIDS and death: a prospective cohort study. *Lancet*. 2005;366:378-84.
6. Cade WT, Peralta L, Keyser RE. Aerobic exercise dysfunction in human immunodeficiency virus: a potential link to disability. *Phys Ther* 2004; 84 (7):655-64.
7. Lazzarotto AR, Deresz LF, Sprinz E. HIV/AIDS e Treinamento Concorrente: Revisão Sistemática. *Rev Bras Med Esporte* 2010;16 (2):149-54.
8. Palermo PC, Feijó OG. Exercício Físico e infecção pelo HIV: atualização e recomendações. *Rev Bras Fisiol Exercício* 2003; 2 (3): 218-46.
9. Peakman M, Vergani D. *Imunologia Básica e Clínica*. 1ª. ed. Guanabara Koogan: Rio de Janeiro: 1999.
10. Gaya A, Silva G. Manual de Aplicação de medidas e testes, normas e critérios de avaliação PROESP-BR. Porto Alegre julho de 2009. Disponível em: <http://www.proesp.ufrgs.br/institucional/index.php nov/2009>. Acesso em: 18 de abril 2010.
11. Fontoura AS, Formentini CM, Abech EA. Guia prático de avaliação física: uma abordagem didática, abrangente e atualizada. São Paulo: Phorte, 2008.
12. CDC. Centers for Disease Control and Prevention. 1994 revised classification system for Human Immunodeficiency Virus infection in children less than 13 years of age. *MMWR Recomm Rep* 1994;43:1-10.
13. Mc Connell MS, Byers RH, Frederick T, Peters VB, Dominguez KL, Sukalac T, et al. Trends in antiretroviral therapy use and survival rates for a large cohort of HIV-infected children and adolescents in the United States, 1989-2001. *J Acquir Immune Defic Syndr* 2005;38:488-94.
14. Judd A, Doerholt K, Tookey PA, Sharland M, Riordan A, Menson E, et al. Morbidity, mortality, and response to treatment by children in the United Kingdom and Ireland with perinatally acquired HIV infection during 1996-2006: planning for teenage and adult care. *Clin Infect Dis* 2007;45:918-24.
15. Romanelli RM, Pinto JA, Melo LT, Vasconcelos MA, Pereira R de M. Effectiveness of dual and triple antiretroviral therapy in the treatment of HIV-infected children. *J Pediatr* 2006;82:260-5.
16. Matida LH, Junior ANR, Heukelbach J, Saúdo A, Succu RC de M, Marques H H de S, Negra MD, Hearst N. Improving survival in children with AIDS in Brazil: results of the second national study, 1999-2002. *Cad. Saúde Pública* 2011;27(Sup 1):S93-103.
17. Miller TL. The next decade: cardiovascular risks, outcomes, prevention, and treatment in pediatric HIV infection. *J Pediatr* 2010;86:3-5.
18. Somarriba G, Lopez-Mitnik G, Ludwig DA, Neri D, Schaefer N, Lipshultz S, Scott GB, Miller T. Physical Fitness in Children Infected with the Human Immunodeficiency Virus: Associations with Highly Active Antiretroviral Therapy. *AIDS Res Hum Retroviruses* 2012. doi:10.1089/AID.2012.0047.
19. Verweel G, Annemarie MC, Rossum V, Hartwig NC, Wolfs TFW, Scherpier HJ. Treatment with highly active antiretroviral therapy in human immunodeficiency virus type 1- infected children is associated with a sustained effect on growth. *Pediatrics* 2002;109:2-7.
20. Leonard EG, Mc Comsey GA. Metabolic Complication of Antiretroviral Therapy in Children. *Pediatrics Infect Dis J* 2003;22:77-84.
21. Mikkelsson LO, Nupponen H, Kaprio J, Kautiainen H, Mikkelsson M, Kujala UM. Adolescent flexibility, endurance strength, and physical activity as predictors of adult tension neck, low back pain, and knee injury: a 25 year follow up study. *Br J Sports Med* 2006;40:107-13.
22. Nev CM, Rouch F, Rittweger J, Manz F et al. Influence of Puberty on Muscle Development of the forearm. *Am J Physical Endocrinol Metab* 2002;283:E103-7.
23. Miller TL, Somarriba G, Kinnamon DD, Weinberg GA, Friedman LB, Scott GB. The effect of a structured exercise program on nutrition and fitness outcomes in human immunodeficiency virus infected children. *AIDS Res Hum Retroviruses* 2010;26:313-9.
24. Werner ML, Pone MV, Fonseca VM, Chaves CR. Lipodystrophy syndrome and cardiovascular risk factors in children and adolescents infected with HIV/AIDS receiving highly active antiretroviral therapy. *J Pediatr* 2010;86:27-32.