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High Prevalence of Hypocholesterolaemia among Antiretroviral Therapy-naive HIV-infected Children in Makurdi, Nigeria: A Retrospective Study

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Authors' contributions

This work was carried out in collaboration between the two authors. Author EAA designed the study, wrote the protocol, performed the statistical analysis and its interpretation, performed literature searches, wrote the first draft of the manuscript and critically reviewed the final draft for intellectual content. Author AO also took part in the design and protocol of the study', interpreted the statistical analyses, performed literature searches and critically reviewed it for intellectual content. Both authors read and approved the final manuscript.

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Original Research Article

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ABSTRACT

Aim: To determine the abnormalities in total cholesterol (TC) levels and the potential risk factors in ART–naive, HIV-infected Nigerian children.



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Study Design: A retrospective and cross-sectional study.

Place and Duration of Study: Paediatric antiretroviral therapy (ART) clinic of the Federal Medical Centre, Makurdi, between June 2010 and June 2012.

Methods: Electronic data of 429 HIV-infected ART-naive children, aged 1–15 years, including 223 males and 206 females, were analysed to get the relevant information for the study. Abnormal un-fasted TC levels and the association with potential risk factors were tested in bivariate regression analyses. Abnormal lipid level was defined as hypercholestrolaemia when the TC was>200mg/dL and hypocholesterolaemia when TC was <160mg/dl. Normal TC was value between 160 and 200mg/dl. *P*-value less than 0.05 was significant.

Results: The median age was 5.00 years with an interquartile range of 3.0 to 8.0 years. The TC ranged from 32 to 196 mg/dl with a mean value of 116±34.98mg/dl. Hypocholesterolaemia was the prominent finding in 88.3% (379/429) of the children. Hypercholestrolaemia was not found (0%). In bivariate analyses, no factor was found to significantly impact on hypocholesterolaemia, although a greater proportion of hypocholesterolaemia was seen in children: within 2-15 years age group (92.1%, 349/379); male gender (52.0%): HIV/AIDS stages 1&2 (82.6%); CD4 count>200 cell/mm³(81.5%); viral load>10,000 copies/ml (69.1%); hemoglobin<10g/dl (61.7%); stunting (55.4%, 102/207) and undernourishment with body mass index (BMI)<18.5 (83.7%, 164/222). Multivariate analysis was not done.

Conclusion: A high prevalence of hypocholesterolaemia was found among the ARTnaive, HIV-infected Children, in Makurdi. The study could serve as a stimulus for our centre and other paediatric ART programmes in Nigeria to undertake an elaborate lipid profile of HIV infected children at diagnosis and on follow-up on ART.

Keywords: HIV-infected children; antiretroviral-naive; lipid profile; Makurdi; Nigeria.

1. INTRODUCTION

The advancement in the knowledge of HIV and its treatment has converted HIV infection, a potentially fatal disease to a chronic manageable one [1,2]. Accompanying the successes of highly active antiretroviral therapy (HAART) in promoting longevity is the associated metabolic and chronic disease complications, including coronary artery disease, renal diseases, insulin resistance, lipodystrophy and dyslipidemia [3-6]. The direct relationship between the duration of HAART and the increased risk of cardiovascular disease is particularly noteworthy for HIV-infected infants and children, who likely will have longer cumulative exposure to HAART [5]; though race, gender, host genetics and lifestyle are other notable risk factors [6]. Whereas, lipodystrophy is rare in the general population and in ART naïve HIV infected subjects [7], dyslipidaemia is not [8]. In ART-naïve adults with advanced HIV infection, hypertriglyceridemia, hypocholesterolaemia, low levels of lowdensity lipoprotein cholesterol (LDL-C), and low levels of high-density lipoprotein cholesterol (HDL-C) are common [8]. Hypertriglyceridemia, hypercholestrolaemia and hypo-HDL were prominent findings in 274 ART-naïve HIV-infected Asian children [9]. But, with ARV medicine, mostly protease inhibitors (PIs), elevation in the levels of total cholesterol (TC), triglycerides, and LDL-C are seen [10]. Non-nucleoside reverse-transcriptase inhibitors (NNRTIs) produce increases in levels of TC, LDL-C, and triglycerides; however, increases in HDL-C levels may occur, particularly with nevirapine, which can yield a net reduction in the ratio of TC level to HDL-C level [11]. Similar favorable lipid changes demonstrated by the increase in HDL level and decrease in total cholesterol/HDL ratio are also demonstrated after ART initiation in children [12]. Among the NRTIs, stavudine is associated with increases in levels of TC, LDL-C, and triglycerides [13].

The term lipodystrophy was initially limited in its use to the wasting syndrome with selective loss of body fat or lipoatrophy (thinning of the arms, legs and face) central adiposity and accumulation of fat in the breast tissue or the back of the neck (buffalo hump) [14]. But, lipodystrophy now includes dyslipidemia, hyperglycemia, hypercholesterolemia, hepatomegaly, glomerulonephritis and other metabolic syndromes [7].

Few studies described lipid profiles in children. Majority were done for children on ART and among Black, Hispanic, Caucasian and Asian children [15-18]. It is also well known that abnormalities in lipid profile can parallel differences in dietary intakes, race, and lifestyles [6,9] which vary as countries defer.

In Nigeria, studies on the lipid profiles among ART-naïve HIV infected subjects had been predominantly in adults [19,20] with none known to the Authors among the pediatric population.

Thus, the aim of this study is to describe the prevalence and risk factors of dyslipidaemia (with respect to cholesterol) among HIV-infected, ART naïve children in Makurdi, Nigeria.

2. MATERIALS AND METHODS

2.1 Study Area and Setting

This retrospective cross-sectional study was carried out among HIV-infected children receiving care and treatment at the Paediatric ART Clinic of the Federal Medical Centre (FMC), Makurdi between June 2010 and June 2012. The facility is supported by the AIDS Prevention Initiative in Nigeria (APIN) /Harvard PEPFAR (The USA President's Emergency Plan for AIDS Relief) program.

2.2 Inclusion Criteria for the Study

Included in the study were HIV infected children (<15 years of age) who were antiretroviral naïve and whose TC results on enrollment into our ART clinic were available. HIV-infected antiretroviral naïve children with no TC result and or incomplete records of clinical variables of interest were excluded. HIV-infected treatment experienced children were also excluded.

2.3 Recruitment of Subjects and Data Collection

FMC, Makurdi provides paediatric HIV care and treatment in accordance with the Nigerian Guidelines on Paediatric HIV/AIDS Treatment and Care [21,22]. Children were recruited into care and treatment upon confirmation of HIV infection. All subjects ≥18 months had an initial double rapid HIV antibody test using DetermineTM HIV 1/2 (by ABBOTT JAPAN CO., LTD. Minto-Ku, Tokyo, Japan) first and then HIV 1/2STAT-PAKTM (by CHEMBIO DIAGNOSTICS SYSTEMS, INC. Medford, New York 11763 USA) in serial algorithm. HIV infection was confirmed in those with a reactive rapid test by the Western Blot test. Two HIV DNA PCR positivity tests for those <18 months confirmed HIV infection in this age group.

A study proforma was developed to capture the following information that had been recorded on the subjects' Initial Clinical Evaluation Form (ICEF) at enrollment into our programme: socio-demographic factors; previous ARV prophylaxis exposure; presenting complaints; details of symptoms; WHO HIV/AIDS paediatric stage; anthropometric measurements; of the systems physical examination findings and other diagnosed comorbidities/opportunistic infections. These co-morbidities/opportunistic infections include tuberculosis, oro-pharyngeal and oesophageal candidiasis, diarrheal disease, presumed sepsis, malaria fever, pneumonia and undernutrition.

2.4 Operational Definitions

For the purpose of the study, the following terms were defined:

HIV infected ART-naive children were HIV infected children who had received no prior antiretroviral drugs, except for prevention of mother-to-child transmission (PMTCT).

Since there was no study that had documented the normal lipid profile in Nigerian children (1-15 years), we were restricted to define hypocholesterolaemia (TC value below 160mg/dL) and hypercholestrolaemia (TC value above 200mg/dl) according to the Lipid Research Clinics (LRC) Prevalence Study that involved Canadian and US children which was similar with results for African American children [23].

To define under-nutrition in children less than 5 years, anthropometric computations and comparisons were conducted for the weight for age z-score (WAZ-score) and height for age z-score (HAZ-score) using the WHO Anthro software which is based on WHO child growth standards of 2006 [24]. Underweight was defined as a weight for age z-score (WAZ-score) less than-2 standard deviations (SD) from the WHO reference median values [24]. Stunting was defined as height for age z-score (HAZ-score) less than -2SD from the reference values.

For children \geq 5 years, the Body Mass Index (BMI) was calculated as the weight in kilograms divided by the square of the height in metres (kg/m²). Values<18.5 defined Undernutrition, >25 was overweight and > 30 was obesity [25]. Anaemia was defined as a haemoglobin value less than 10g/dl. Pyrexia was an axillary temperature of >37.5°C. Fast breathing (tachypnoea) a respiratory rate of >40 per minute in children between 1 and 3 years, >35 for 4-10 years and >30 per minute for children >10 years. Diarrhea was defined as the passage of three or more loose or watery stools during a 24h period. Chronic diarrhoea defined as persistent diarrhoea 14 days or more.

Definition of clinical sepsis at enrollment was limited to the presence of two or more of the following: abnormal temperature (<36.0°C or>38.3°C) or age specific tachycardia (>140beat/min for 0-2 years, >120 for 2-6 years and >110 for >6 years) or acute altered mental status; with a clinical suspicion of new infection including cough/chest pain and or abdominal pain/distension/diarrhoea and or dysuria and or headache with neck stiffness and or presence of cellulitis/wound infection/joint infection [26].

Acute respiratory infection (pneumonia) was made if the child presented with cough (less than 72 hours), fever, tachypnea, and focal pulmonary findings on physical examination.

Presumptive tuberculosis (TB) diagnosis was based on radiographic evidence indicative of TB in a child presenting with a persistent cough for more than 2 weeks and/or fever for more than 1 week and/or recent failure to thrive, together with or without a documented TB contact.

Oro-pharyngeal candidiasis is the presence of candidiasis on the tongue, buccal mucosa and the pharynx. Esophageal candidiasis is the presence of extensive oro-pharyngeal candidiasis extending down to the esophagus with accompanying difficulty in swallowing and or painful swallowing. Hepatotoxicity was elevated values of alanine transaminases (ALT) of 1.25-fold over the upper limit of normal (ULN was 37 IU/L) [27].

Hepatomegaly was defined as an enlargement of the liver which was palpable by more than 2cm below the right costal margin and with a span larger than 8cm [28]. Splenomegaly was defined as an enlargement of the spleen which was palpable by more than 2cm below the left costal margin [29]. Hepatosplenomegaly was defined as the presence of both hepatomegaly and splenomegaly simultaneously in the same child and at the same time of performing the physical examination.

2.5 Laboratory Measurements at Enrollment into Our ART Program

The total cholesterol was determined enzymatically by cholesterol esterase and cholesterol oxidase and using the Cobas Mira chemistry analyzer and it did not require fasting [30]. In addition to determining the CD4 count and the viral load, venous blood samples were also collected for: haemoglobin concentration; malaria parasites (Giemsa stain); a full blood count (Coulter Micro Diff II, UK); Hepatitis B surface antigen and Hepatitis C virus antibody (using the third generation ELISA technique, ElAgen HBsAg Kit, ElAgen HCV Ab Kit); catalytic activity of ALT (determined in serum using a Cobas Mira chemistry analyzer); and blood glucose estimation analysed by the glucose oxidase method (GM6 Analox instruments, UK). All tests were done at the APIN/PEPFAR laboratory of FMC, Makurdi.

2.6 Statistical Analysis

Descriptive statistics were tabulated as means and medians for continuous variables and numbers and percentages for categorical variables. Medians were compared using the Mann-Whitney u test. Age was stratified at 2 years (because the concentration of serum lipids and lipoproteins increases during early childhood and reaches concentrations similar to those seen in young adults by this age) [23]. The main outcome variable in the analysis was dyslipidaemia (hypocholestrolemia/hypercholestrolaemia) versus normal cholesterol level. The prevalence of hypocholestrolemia and hypercholestrolaemia were calculated. Potential predictors of dyslipidaemia were tested for significance in a bivariate logistic regression. These predictive variables include a priori factors that determined cholesterol levels (i.e. age, gender, anemia, HBsAg, HCV, undernutrition, hepatotoxicity, WHO clinical staging, CD4 count, viral load [17,18,23,31-34]) and other potential predictors such as the on physical presenting symptoms. signs examinations and diagnosed COmorbidities/opportunistic infections as previously enumerated. Predictive factors that achieved a significance level of 0.1 were considered eligible for multivariate logistic regression analysis. For all analyses, P-values less than 0.05 were considered statistically significant. Statistical analysis was done using SPSS version 16.

3. RESULTS

A total of 454 subjects were seen between the study periods, but only 429 were included in the study. 15 children were excluded because their TC results were unavailable and another 10 children with incomplete records of interest were also excluded.

The bivariate and multivariate analyses of hypocholesterolaemia and the clinical evaluation findings; the laboratory findings and the co-morbidities/opportunistic infections among the subjects under the study were done together but for clarity purposes, there were presented separately in three Tables (Tables 1, 2 and 3).

Table 1 shows that the children ranged in age from 1 to 15 years including 223 males and 206 females. The median age was 5.00 years with interquartile range (IQR) of (3.0 to 8.0 years). Table 2 shows that the median CD4 count was 490.00cell/mm³ (253.00-870.50) and median viral load (log 10) was 4.73 (3.73-5.36). The median haemoglobin and ALT were 9.6 g/dl (8.6-10.55) and 24.80 (16.85-38.00) respectively. The mean cholesterol value was 116±34.98mg/dl (Range 32 to 196mg/dl). Table 2 also reveals that hypocholesterolaemia was seen in 379 children (88.3%, 379/429). No child was found with hypercholesterolaemia.

In bivariate analyses (Tables 1-3), no factor was found to significantly impact on hypocholesterolaemia, although a greater proportion hypocholesterolaemia occurred: in 2-15 years age group (92.1%, 349/379); male gender (52.0%):WHO HIV/AIDS stages 1&2 (82.6%); CD4 count >200cell/mm³(81.5%); viral load>10,000copies/ml (69.1%); hemoglobin <10g/dl (61.7%); stunting (55.4%, 102/207) and undernourishment with BMI<18.5 (83.7%, 164/222). Also in multivariate analyses, all the variables (including "food refusal", vomiting, anaemia and under-fives underweight) tested were not statistically significant.

4. DISCUSSION

Documenting the burden of dyslipidemia in children infected with HIV is important as prompt interventions or treatments could prevent or delay dyslipidemia and coronary heart disease in adults [5].

In this study, no child was found with hypercholesterolemia. Available paediatric data would also suggest that hypercholesterolemia is uncommon in HIV-infected ART-naïve children: a low prevalence of 2% and 1.9% were reported by Kanjanavanit et al. [9] and Aurpibul et al. [18] respectively among ART-naïve Thai children. On the contrary, the findings in ART-naïve adults revealed a high prevalence of 12.4% as reported by Raghavan et al. [35].

Similarly, the low mean TC of 116mg/dl in this study was lower than the respective 139mg/dl and 133mg/dl reported by Kanjanavanit et al. and Aurpibul et al. and was also lower than 145.7mg/dl reported by Chantry et al in the USA [16]; suggesting that the low TC levels seen in ART-naïve HIV-infected children also vary in severity from one country to another.

Also, this study revealed no significant association between hypocholesterolaemia and a priori risk factors, including age, gender, anemia, HBsAg, HCV, undernutrition, hepatotoxicity, WHO clinical staging, CD4 count and viral load [17,18,23,31-34].

| Clinical evaluation | Hypo-cholesterolaemia Normal cholesterol (161-200mg/dl) | | | Bivariate ana | lysis | Multivariate analysis | | | |
|-----------------------|---|--------------|-------|----------------------|---------|-----------------------|-------------|---------|--|
| | (<160mg/dl) N (%) | N (%) | OR | 95% CI | P-value | AOR | 95%CI | P-value | |
| Demography | | | | | | | | | |
| Age (Years) | | | | | | | | | |
| Median (IQR) | 5.0(3.0-8.0) | 5.0(2.0-8.0) | - | - | .61 | - | - | - | |
| <2 | 30 (7.9) | 7(14.0) | 0.528 | 0.219-1.280 | .24 | - | - | - | |
| 2-15 (Ref) | 349(92.1) | 43(86.0) | | | | | | | |
| Gender | х <i>ў</i> | | | | | | | | |
| Male | 197(52.0) | 26(52.0) | 0.999 | 0.554-1.800 | .99 | - | - | - | |
| Female (Ref) | 182(48.0) | 24(48.0) | | | | | | | |
| Symptoms | х <i>у</i> | | | | | | | | |
| Irritable | | | | | | | | | |
| Yes | 13(3.4) | 1 (2.0) | 1.740 | 0.223- | .91 | - | - | - | |
| No (Ref) | 366(96.6) | 49 (98.0) | | 13.600 | | | | | |
| Convulsion | х <i>у</i> | | | | | | | | |
| Yes | 11(2.9) | 1(2.0) | 1.470 | 0.185 - | .13 | - | - | - | |
| No (Ref) | 368(97.1) | 49(98.0) | | 11.590 | | | | | |
| Headache | , , , , , , , , , , , , , , , , , , , | | | | | | | | |
| Yes | 40(10.6) | 5(10.0) | 1.060 | 0.398–2.830 | .90 | - | - | - | |
| No (Ref) | 339(89.4) | 45(90.0) | | | | | | | |
| Food refusal | , , , , , , , , , , , , , , , , , , , | | | | | | | | |
| Yes | 65(17.2) | 4(8.0) | 2.380 | 0.828-6.840 | .09 | 0.871 | 0.181–4.180 | .86 | |
| No (Ref) | 314(82.8) | 4ô(92.0) | | | | | | | |
| Vomiting | , , , , , , , , , , , , , , , , , , , | | | | | | | | |
| Yes | 77(20.3) | 5(10.0) | 2.300 | 0.881–5.980 | .08 | 0.182 | 0.023-1.440 | .12 | |
| No (Ref) | 302(79.7) | 45(90.0) | - | | | | | | |
| Signs/physical examin | · · · · · | 、 <i>、</i> | | | | | | | |
| Fever | 5 | | | | | | | | |
| Yes | 64(16.9) | 6(12.0) | 1.490 | 0.609-3.640 | .38 | - | - | - | |
| No (Ref) | 315(83.1) | 44(88.0) | - | - | | | | | |
| Oral thrush | | · · · / | | | | | | | |
| Yes | 45(11.9) | 3(6.0) | 2.110 | 0.631-7.060 | .22 | - | - | - | |
| No (Ref) | 334(88.1) | 47(94.0) | - | | | | | | |

Table 1. Bivariate and multivariate analyses of hypocholesterolaemia and clinical evaluation findings among the subjects

| Hepatomegaly | | | | | | | | |
|-------------------|------------|---------------------------------------|-------|-------------|-----|---|---|---|
| Yes | 35(9.2) | 4(8.0) | 1.170 | 0.398-3.440 | .78 | - | - | - |
| No (Ref) | 344(90.8) | 46(92.0) | | | | | | |
| Hepatosplenome | galy | | | | | | | |
| Yes | 39 (10.3) | 6(12.0) | 0.841 | 0.337-2.100 | .71 | - | - | - |
| No (Ref) | 340 (89.7) | 44(88.0) | | | | | | |
| Splenomegaly | | , , , , , , , , , , , , , , , , , , , | | | | | | |
| Yes | 5 (1.3) | 0(0.0) | 1.130 | 1.100–1.170 | .91 | - | - | - |
| No (Ref) | 374 (98.7) | 50(100.0) | | | | | | |
| WHO clinical stag | | , , , , , , , , , , , , , , , , , , , | | | | | | |
| 3&4 | 66 (17.4) | 7(14.0) | 1.300 | 0.558-3.010 | .37 | | | |
| 1&2 (Ref) | 313(82.6) | 43(86.0) | | | | | | |

IQR=interquartile range; Ref=Referenced group; _ =Not applicable

Table 2. Bivariate and multivariate analyses of hypocholesterolaemia and laboratory findings among the subjects

| Laboratory findings | Hypo-cholesterolaemia | Normal cholesterol(161-200mg/dl) | Bivaria | ate analysis | | Multivariate analysis | | |
|-----------------------------|-----------------------|----------------------------------|---------|--------------|----------|-----------------------|-------------|---------|
| | (<160mg/dl) N (%) | N (%) | OR | 95% ČI | P -value | AOR | 95%CI | P-value |
| CD4 count Median (IQR) | 490.0(256.0-850.0) | 484.50(187.50-1029.00) | - | - | .60 | - | - | - |
| ≤200 | 70 (18.5) | 13 (26.0) | 0.645 | 0.326 –1.280 | .21 | - | - | - |
| >200(Ref) | 309(81.5) | 37(74.0) | | | | | | |
| Viral load (copies/ml) | | 4.455(3.863-5.211) | - | - | .50 | | | |
| Median Log10(IQR) | 4.743(3.713-5.372) | | | | | | | |
| >10,000 | 117(30.9) | 16(32.0) | 1.054 | 0.560-1.984 | .88 | - | - | - |
| <10,000(Ref) | 262(69.1) | 34(68.0) | | | | | | |
| Haemoglobin (g/dl) | | 10.0(8.95-11.00) | - | - | .15 | - | - | - |
| Median(IQR) | 9.6(8.6-10.5) | | | | | | | |
| <10 | 234 (61.7) | 24(48.0) | 1.780 | 0.967–3.160 | .06 | 1.190 | 0.481-2.960 | .70 |
| ≥10(Ref) | 145 (38.3) | 26(52.0) | | | | | | |
| Hepatitis B surface antigen | | | | | | | | |
| Yes | | | | | | | | |
| No(Ref) | 41(10.8) | 8(16.0) | 0.637 | 0.280-1.450 | .28 | - | - | - |
| | 338 (89.2) | 42(84.0) | | | | | | |

Table 2 continued in next page

| Hepatitis C antibodies | | | | | | | | |
|--------------------------|------------------|-------------------|-------|--------------|-----|---|---|---|
| Yes | 10(2.6) | 1(2.0) | 1.330 | 0.167–10.630 | .79 | - | | - |
| No(Ref) | 369(97.4) | 49(98.0) | | | | | | |
| Alanine aminotransferase | | | | | | | | |
| Median(IQR) | 24.8(17.0-38.10) | 23.8(14.50-37.20) | - | - | .49 | - | - | - |
| Elevated (>46.3) | 66(17.4) | 8(16.0) | 1.110 | 0.497-2.470 | .80 | | | |
| Normal(≤46.3) (Ref) | 313(82.6) | 42(84.0) | | | | | | |

The mean cholesterol value was 116±34.98mg/dl (Range 32 to 196mg/dl). The prevalence of Hypocholesterolaemia was 88.3% (379/429).IQR=Interquartile range; Ref=Referenced group; _ = Not applicable

Table 3. Bivariate and multivariate analyses of hypocholesterolaemia and co-morbidities/opportunistic infections among the subjects

| Co-orbidities/opportunistic | Hypo-cholesterolaemia | Normal cholesterol | Bivaria | ate analysis | | Multiva | ariate analys | is |
|-----------------------------|-----------------------|----------------------|---------|--------------|----------|---------|---------------|---------|
| infections | (<160mg/dl) N (%) | (161-200mg/dl) N (%) | OR | 95% CI | P -value | AOR | 95%CI | P-value |
| Tuberculosis | | | | | | | | |
| Yes | 48(12.7) | 4(8.0) | 1.670 | 0.575 –4.840 | .34 | - | - | - |
| No(Ref) | 331(87.3) | 46(92.0) | | | | | | |
| Esophageal candidiasis | | | | | | | | |
| Yes | 6(1.6) | 2(4.0) | 0.386 | 0.076 -1.960 | .53 | - | - | - |
| No(Ref) | 373(98.4) | 48(96.0) | | | | | | |
| Diarrhoeal disease | | | | | | | | |
| Yes | 11(2.9) | 1(2.0) | 1.470 | 0.185– | .72 | - | - | - |
| No(Ref) | 368(97.1) | 49(98.0) | | 11.590 | | | | |
| Sepsis | | | | | | | | |
| Yes | 11(2.9) | 3(6.0) | 1.340 | 0.126 –1.740 | .46 | - | - | - |
| No(Ref) | 368(97.1) | 47(94.0) | | | | | | |
| Malaria fever | | | | | | | | |
| Yes | 48(12.7) | 9(18.0) | 0.661 | 0.302 –1.450 | .29 | - | - | - |
| No(Ref) | 331(87.3) | 41(82.0) | | | | | | |
| Pneumonia | | | | | | | | |
| Yes | 22(5.8) | 3(6.0) | 0.965 | 0.278 –3.350 | .95 | - | - | - |
| No(Ref) | 357(94.2) | 47(94.0) | | | | | | |

Table 3 continued in next page

International Journal of TROPICAL DISEASE & Health, 4(11): 1132-1145, 2014

| WAZ | | | | | | | | |
|--------------|----------------------|----------|-------|---------------|-----|-------|-------------|-----|
| Median(IQR) | -1.13(-2.73 -0 .680) | - | - | - | .19 | - | - | - |
| <-2SD | 61(33.2) | 4(17.4) | 2.520 | 0.820 - 1.740 | .09 | 0.377 | 0.121–1.170 | .09 |
| ≥-2SD (Ref) | 123(66.8) | 19(82.6) | | | | | | |
| NA | 222 | | | | | | | |
| HAZ | | | | | | | | |
| Median(IQR) | -2.18(-4.00-0.350) | - | - | - | .26 | - | - | - |
| <-2SD | 102(55.4) | 10(43.5) | 1.460 | 0.607-3.500 | .39 | - | - | - |
| ≥-2SD (Ref) | 82(44.6) | 13(56.5) | | | | | | |
| NA | 222 | | | | | | | |
| BMI | | | | | | | | |
| Median (IQR) | (14.80 –17.60) | - | - | - | .01 | - | - | - |
| ≥18.5 (Ref) | 32(16.3) | 23(88.5) | 0.668 | 0.189 –2.360 | .53 | - | - | - |
| <18.5 | 164(83.7) | 3(11.5) | | | | | | |
| NA | 207 | · · · | | | | | | |

IQR=Interquartile range; WAZ=Weight for age Z -score; HAZ=Height for age Z-score; BMI=Body mass index; Ref=Referenced group; _ = Not applicable

However, the high prevalence of hypocholesterolaemia among the HIV-infected children in our setting may be consequent to the pervasive low dietary cholesterol content of the subjects. The subjects are essentially children of peasant farmers who live on peasant meals containing low cholesterol. Taylor and Akande [36], and Taylor and Agbedana [37], had earlier reported the low serum total cholesterol level in Nigerians of low socio-economic status, thereby giving credence to this assertion.

The mechanism of HIV and hypocholesterolaemia is unclear. Mujawar et al. [38] had reported that HIV viral replication dysregulates intracellular lipid metabolism in HIV-infected macro-phages and that; viral suppression with ART therapy unmasks and stimulates increased cholesterol production [16,17,38].

The knowledge of the high hypocholesterolaemia in this study is important because it serves as baseline information upon which future evolution of lipid abnormalities consequent on HAART would be compared. This has initiated a desire to follow up the full lipid profile (TC, LDL-C, and HDL-C) in some of our subjects who are still retained on HAART.

To the best of the authors' knowledge, this is the first study in Nigeria that described the TC profile in ART-naïve HIV-infected children.

5. LIMITATION OF STUDY

This study could not conclude on other dyslipidemia in HIV-infected ART-naïve Nigerian children as other important products of lipoprotein metabolism, including LDL-C, triglycerides and HDL-C were not studied, as they were not routinely screened for at enrollment in our ART program.

Secondly, being a retrospective study, we could not explore other potentially important predictors of hypocholesterolaemia such as dietary cholesterol content, socioeconomic factors, and hypothyroidism. Also, there was no comparison group of non-HIV infected children living on a similarly low cholesterol diets.

Thirdly, the study took place among Nigerian children who lived mainly in rural agrarian communities in Benue State and as such, caution must be exercised in generalizing these findings as differences also exist in the cholesterol contents of the staple meals in rural and urban settings. [37].

6. CONCLUSION

In conclusion, this study indicates high prevalence of hypocholesterolaemia among the antiretroviral therapy-naïve, HIV-infected Children, in Makurdi. It is expected that the study would serves as a stimulus for our centre and other paediatric ART programmes in Nigeria to undertake a more extensive investigations of the lipid profile of HIV infected children at diagnosis and on follow-up on ART.

CONSENT AND ETHICAL CONSIDERATION

Upon enrollment into care, all parents or caregivers of the HIV-infected children were required to provide written informed consent (and assent from the children if \geq 7 years of age) for the use of their data for research as approved by the Hospital Research and Ethics

Committee of the FMC, Makurdi and the AIDS Prevention Initiative in Nigeria (APIN)/Harvard PEPFAR (The USA President's Emergency Plan for AIDS Relief) program. For this study, permission was sought for and gotten for the use of the relevant data.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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