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High prevalence of impaired glucose metabolism among children and adolescents living with HIV in Ghana

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Abstract

Background: Antiretroviral therapy (ART)-associated metabolic abnormalities, including impairment of glucose metabolism, are prevalent in adults living with HIV. However, the prevalence and pathogenesis of impaired glucose metabolism in children and adolescents living with HIV, particularly in sub-Saharan Africa, are not well characterized. We investigated the prevalence of impaired glucose metabolism among children and adolescents living with perinatally infected HIV in Ghana.

Methods: In this multicentre, cross-sectional study, we recruited participants from 10 paediatric antiretroviral treatment clinics from January to June 2022 in 10 facilities in Greater Accra and Eastern regions of Ghana. We determined impaired glucose metabolism in the study sample by assessing fasting blood sugar (FBS), insulin resistance as defined by the homeostatic model assessment for insulin resistance (HOMA-IR) index and glycated haemoglobin (HbA1c) levels. The prevalence of impaired glucose metabolism using each criterion was stratified by age and sex. The phenotypic correlates of glucose metabolism markers were also assessed among age, sex, body mass index (BMI) and waist-to-hip ratio (WHR).

Results: We analysed data from 393 children and adolescents living with HIV aged 6–18 years. A little over half (205/393 or 52.25%) of the children were female. The mean age of the participants was 11.60 years (SD = 3.50), with 122/393 (31.00%) aged 6–9 years, 207/393 (52.67%) aged 10–15 years, and 62/393 (15.78%) aged 16–18 years. The prevalence rates of glucose impairment in the study population were 15.52% [95% confidence interval (CI): 12.26–19.45], 22.39% (95% CI: 18.54–26.78), and 26.21% (95% CI: 22.10–30.78) using HbA1c, HOMA-IR, and FBS criteria, respectively. Impaired glucose metabolism detected by FBS and HOMA-IR was higher in the older age group, whereas the prevalence of abnormal HbA1c levels was highest among the youngest age group. Age and BMI were positively associated with FBS and HOMA-IR ($p < 0.001$). However, there was negative correlation of WHR with HOMA-IR ($p < 0.01$) and HbA1c ($p = 0.01$).

Conclusion: The high prevalence of impaired glucose metabolism observed among the children and adolescents living with HIV in sub-Saharan Africa is of concern as this could contribute to the development of metabolic syndrome in adulthood.

KEYWORDS
adolescents, children, impaired glucose metabolism, paediatric HIV

INTRODUCTION

Antiretroviral therapy (ART) has significantly improved the life expectancy of people living with HIV (PLWH) [1]. However, long-term use of ART has been associated with increased susceptibility to metabolic-related morbidities [2]. In this population, metabolic-related disorders are linked with persistent defects in the cellular processes, including impaired glucose metabolism. Impaired glucose metabolism is a recognized precursor of various cardiometabolic sequelae and may serve as an predictive marker for the increasing incidence of metabolic disorders among PLWH [3]. Recent studies have observed a higher occurrence of impaired glucose metabolism among PLWH on ART compared with those not on ART or the HIV-uninfected general population [3, 4]. The prevalence of impaired glucose metabolism in PLWH is estimated to be as high as 32%, compared with a prevalence of 11% in the HIV-uninfected general population [4, 5].

While age is considered a risk factor in the general population, the duration of ART usage has been identified as a significant contributor to metabolic abnormalities in PLWH [6]. Therefore, children who acquired HIV mainly through mother-to-child transmission are at a higher risk of developing metabolic disorder due to lifelong exposure to ART from childhood. Studies assessing impaired glucose metabolism in children and adolescents living with HIV (CALWH) have reported varying prevalence rates, ranging from as low as 1.6% to as high as 40%, depending on the population studied [7–9]. However, although impaired glucose metabolism in children, including insulin resistance, could be a risk or predictor of cardiovascular disease in adulthood [10, 11], diagnosing glucose impairment in children is challenging as it often presents asymptomatically [12]. Likewise, differences in glucose metabolism between children and adults, attributed to factors such as developmental variations, ageing, and physical inactivity, contribute to subclinical glucose abnormalities in children, which poses diagnostic challenge [13, 14].

A frequently observed impairment in glucose metabolism is hyperglycaemia, yet it remains a challenge for the paediatric population living with HIV, particularly among adolescents, where it is highly prevalent [15]. Hyperglycaemia in children living with HIV may impact the prevalence of insulin resistance and the risk of developing diabetes in adulthood. Therefore, in populations with high HIV infections, the prevalence of impaired glucose metabolism in children could be high [16]. Although only a few studies have monitored glucose tolerance or sensitivity in children living with HIV in sub-Saharan Africa, where 90% of the paediatric HIV population resides, the reported prevalence of impaired glucose is high compared with the paediatric population without HIV [4, 7, 17–19]. Interestingly, the majority of these individuals with impaired glucose levels are non-obese and primarily exhibit subclinical manifestations [20].

Recent reports have indicated that the prevalence of impaired glucose metabolism in children living with HIV is on the increase [7, 21]. To effectively manage these disorders, it is crucial to identify impaired glucose metabolism in children and adolescents and develop appropriate management strategies. However, there is limited information and lack of harmonized criteria to assess the burden of impaired glucose metabolism in this population, especially in sub-Saharan Africa. This limitation may result in underreported prevalence of impaired glucose metabolism in this population, including those living in Ghana. Currently, Ghana lacks a comprehensive programme to monitor or assess the burden of impaired glucose in children, and few studies have examined impaired glucose levels using multiple assessment parameters in the same cohort of CALWH. Therefore, the aim of this study was to estimate the prevalence of impaired glucose metabolism using different criteria and investigate potential differences in glucose levels based on age and sex. Additionally, this study sought to describe the phenotypic correlates of glucose metabolism markers in CALWH in Ghana.

METHODS

Study population

This cross-sectional, multi-centre study was conducted from January to June 2022 among children and

adolescents living with perinatally acquired HIV, aged 6–18 years. The participants were recruited from 10 paediatric ART treatment clinics at 10 health facilities in Greater Accra and the eastern region of Ghana – Ashiaman Polyclinic, Greater Accra Regional Hospital, Amasaman Government Hospital, Weija-Gbawe Municipal Hospital, LEKMA Hospital, Princess Marie Louise Children Hospital, Tema General Hospital, Tema Polyclinic, and Maamobi Hospital, and Atua Government Hospital in the eastern region of Ghana. All the study sites are known to have similar socioeconomic indices [22]. The study's inclusion criteria were children and adolescents aged 6–18 years who had perinatal HIV and were currently on ART. During the sampling period, national ART treatment for children and adolescents prioritized nucleoside reverse transcriptase inhibitor (NRTIs) and non-NRTIs (NNRTIs) for first-line regimens, NRTIs, NNRTIs and protease inhibitors (PIs) for second-line regimens, and NRTIs, NNRTIs, and integrase strand transfer inhibitors (INSTIs) for third-line regimens. Additionally, individuals with viral hepatitis and tuberculosis followed distinct regimens involving other antivirals or antibiotics [23]. Exclusion criteria included CALWH with coinfections of tuberculosis and viral hepatitis, as these infections and their treatment could introduce potential metabolic cofounding factors such as therapies other than ART. Additionally, individuals who were clinically unstable or unwilling to participate were also excluded. Individuals who met the study's criteria and were willing to participate were recruited. Participants were given a clear explanation of the study's objectives and procedures before consenting. Those who agreed to participate selected a suitable time for the required sampling procedures at the clinic.

Study ethical approvals

The study received approval from the Institutional Review Boards of Ghana Health Service (protocol no. GHS-ERC: 025/09/21) and Noguchi Memorial Institute for Medical Research, University of Ghana (protocol no. CPN 015/21–22). Written parental informed consent for children aged 6–12 years, parental informed consent and assent for those aged 12–17 years, and consent for 18-year-old participants were obtained before their enrolment. Study participants were given a guarantee of anonymity and data protection.

Data collection

Questionnaires were administered to each participant or parent/guardian to extract information regarding demographics, educational background and socioeconomic background of their parents/guardian by trained research assistants.

Anthropometric parameters

Anthropometric measurements were taken by a trained study team member or health staff to record the following: upper arm circumference, waist circumference, hip circumference and neck circumference taken with the children in light clothing using an inelastic tape measure. Weight and height were measured with a vertical stadiometer. Body mass index **(**BMI) was calculated from weight (kg) and height (cm), and obesity was defined as a BMI $\geq$ 28 kg/m^2. Waist-to-hip ratio (WHR) was calculated from waist and hip circumferences (cm). Measurements were recorded to the nearest 1.0 mm, 0.5 cm, and 0.1 kg from an average of two readings.

Biochemical parameters

All participants underwent overnight fasting (≥10 h) before the early morning blood draw. Beverages and snacks were provided immediately after specimen collection prior to anthropometric readings and administering of the questionnaire. We collected 2.5 mL of venous blood by sterile techniques from each participant. Whole blood samples were aliquoted in a gel tube (2 mL) for the serum and micro-EDTA (0.5 mL) tube. Fasting blood sugar (FBS) was assessed instantly with a blood drop using a glucometer strip (True Metrix, Trividia Health Inc., Fort Lauderdale, FL, USA). Serum Insulin levels were measured using sandwich ELISA (R&D Systems, USA) following the manufacturer's instructions. In brief, we coated the primary antibody (2 μg/mL) onto a 96-well plate and incubated overnight at 4°C (Nunc MaxiSorp; Fisher Scientific, Leicestershire, UK). 1% bovine serum albumin in phosphate-buffered saline (PBS) was used for blocking and 0.05% Tween 20 in PBS was used for the washing steps. Standard solutions and serum samples were added to the wells and incubated for 2 h. Detection was performed with a secondary antibody (200 ng/mL) and streptavidin-horseradish peroxidase B. Substrate solution was added to bind antibodies, and colour development was stopped with 0.2 M H_2SO4. The absorbance was measured at 450 nm using a microplate reader (Multiskan FC; Thermo Scientific, USA), and the optical density (OD) values were converted into concentration from the mean value of duplicate measurements. Glycated haemoglobin (HbA1c) level was determined using an immunofluorescence assay (Med Source, Haryana, India) at an absorbance of 450 nm on a plate reader

(Varioskan Lux; ThermoFisher Scientific, Waltham, MA). We also assessed individuals with insulin resistance using the Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) index derived from the formula: fasting insulin (μIU/ml) × fasting glucose (mg/dL)/405 formula [24].

Impaired glucose metabolism characterization

Primary outcome of impaired glucose metabolism in the study population was evaluated using three assessment criteria: FBS to determine blood sugar levels after fasting, HbA1c to estimate blood sugar levels within 2–3 months, and HOMA-IR, a surrogate parameter to assess insulin-mediated response to glucose levels. The following cut-off values to classify individuals with impaired glucose metabolism were used for each type of assessment: (1) FBS level ≥ 100 mg/dL, (2) HbA1c ≥6.5%, or (3) HOMA-IR ≥3.0 [25–28].

Statistical analysis

Categorical data were expressed as count (n) and percentage (%), and numeric variables were expressed as means and standard deviation (SD). Analysis were not stratified by site as the sites had similar demographic and social indices, patients frequently sought care outside their catchment area due to HIV-related stigma, and the sample size was not large enough for stratification. Unadjusted prevalence of the primary outcome using each assessment type was summarized as a proportion with 95% confidence intervals (95% CIs). The difference by sex (biological male vs. biological female) and age group (6–9 years, 10–15 years, and 16–18 years) was assessed using the χ^2 test. Means of FBS, HOMA-IR and HbA1c were compared by sex and age using the analysis of variance (ANOVA), followed by pairwise comparisons between groups using Student's t-test. Separate unadjusted and adjusted linear regression models were created for FBS, HOMA-IR and HbA1c, with BMI, WHR, age and sex as predictors. Findings were summarized as estimated regression parameters (slopes) with 95% CIs, with the unadjusted slopes presented within the scatterplot figures and the adjusted slopes. Hypothesis tests were conducted at the two-sided alpha level of 0.05. As these were independent individual hypotheses of interest (three glucose metabolism criteria, sex and age groups) we did not adjust the alpha level (type 1 error rate) [29]. Statistical analyses were performed with Prism version 9.01 (GraphPad Software) and R version 4.3.2 (R Statistical Software).

RESULTS

Characteristics of study participants

We enrolled 400 perinatally acquired HIV-infected children and adolescents into the study, and the analysis included data from 393 participants who had complete results for all three glucose assessment parameters. Seven excluded participants were not systematically different from the analytical sample with respect to demographic and anthropometric variables. About 52.25% of study participants were females. The mean age of the participants was 11.60 years (SD = 3.50), with 31.00% aged 6–9 years, 52.67% aged 10–15 years, and 15.78% aged 16–18 years (Table 1). The age distribution was comparable between females (mean age 11.43, SD = 3.5) and males (mean age 11.72, SD = 3.45) ($p = 0.28$) (Tables 1, S1). Almost all the participants attended school (99.25%), and over three-quarters (76.59%) lived with a biological parent. As expected, there was an increasing trend in mean age, BMI and educational levels from the younger to the older age group. By contrast, a decreasing trend was observed for mean WHR from the younger to the older age group ($p < 0.001$) (Table 1). There were no differences in the mean values for BMI ($p = 0.19$) and WHR ($p = 0.51$) between females (BMI = 17.23 kg/m^2, SD 3.54; WHR = 0.82, SD = 0.07) and males (BMI = 16.66 kg/m^2, SD 3.29; WHR = 0.83; SD = 0.07) (Table S1).

Impairment of glucose metabolism by age

The assessment of the prevalence of glucose impairment using the three criteria showed that FBS (26.21%, 95% CI: 22.10–30.78) and HOMA-IR (22.39%, 95% CI: 18.54–26.78) yielded a higher prevalence of glucose impairment compared with HbA1c (15.50%, 95% CI: 12.26–19.45) (Table 2). Mean FBS and HOMA-IR increased, while mean HbA1c was comparable across the age groups (Figure 1a–c).We observed an increase in the prevalence of glucose impairment using either FBS ($p < 0.001$) or HOMA-IR ($p < 0.001$) with increasing age, while glucose impairment by HbA1c ($p = 0.02$) was more prevalent in the two younger age groups than in those aged 16 years or older (Table 2).

Impairment of glucose metabolism by sex

Females had on average higher values of HOMA-IR, while mean FBS and HbA1c levels were similar by sex (Figure 1d–f). Prevalence of glucose impairment was similar between females and males when assessed either by FBS or HbA1c, but glucose impairment characterized by higher

TABLE 1 Demographic and anthropometric characteristics of the study participants.

Variable	Age groups			Total ($N = 393$)
	6–9 years ($n = 124$)	10–15 years ($n = 207$)	16–18 years ($n = 62$)	
Age (years) [mean (SD)]	7.44 (1.09)	12.56 (1.71)	16.79 (0.77)	11.60 (3.50)
BMI (kg/m^2) [mean (SD)]	14.34 (2.22)	17.58 (3.48)	20.15 (4.36)	17.00 (3.85)
WHR [mean (SD)]	0.87 (0.07)	0.82 (0.06)	0.80 (0.07)	0.83 (0.08)
Sex [*n* (%)]				
Female	72 (58.10)	103 (49.80)	30 (48.40)	205 (52.25)
Education [*n* (%)]				
Basic	124 (100)	196 (94.69)	32 (51.61)	352 (89.57)
Secondary	0 (0.00)	10 (4.83)	29 (46.77)	39 (9.92)
None	0 (0.00)	1 (0.48)	1 (1.61)	2 (0.51)
Guardian [*n* (%)]				
Parent[a]	104 (83.87)	148 (71.49)	49 (79.03)	301 (76.59)
Sibling	1 (0.81)	9 (4.34)	2 (3.22)	12 (3.05)
Grandparent	9 (7.25)	20 (9.66)	2 (3.22)	31 (7.89)
Other relative	6 (4.84)	15 (7.25)	3 (4.84)	24 (6.11)
Others[b]	4 (3.23)	14 (6.76)	6 (9.67)	24 (6.11)

Abbreviations: BMI, body mass index; WHR, waist-to-hip ratio.
[a]Living with mother or father.
[b]Living alone or with a non-relative (including orphanage).

TABLE 2 Prevalence of impaired glucose metabolism stratified by age groups.

Variable	Age groups			*p*-value*	Total ($N = 393$)
	6–9 years ($n = 124$)	10–15 years ($n = 207$)	16–18 years ($n = 62$)		
FBS					
Impaired [*n* (%)]	17 (13.71)	59 (28.50)	27 (43.55)	<0.001	103 (26.21)
95% CI	8.68–20.98	22.75–35.05	31.80–56.07		22.10–30.78
HOMA-IR					
Impaired [*n* (%)]	10 (8.06)	50 (24.15)	28 (45.16)	<0.0001	88 (22.39)
95% CI	4.39–14.37	18.79–30.47	33.27–57.07		18.54–26.78
HbA1c					
Impaired [*n* (%)]	20 (16.13)	36 (17.39)	5 (8.06)	0.02	61 (15.52)
95% CI	10.63–23.71	12.80–23.19	3.39–18.00		12.26–19.45

Abbreviations: CI, confidence interval; FBS, fasting blood sugar; HbA1c, glycated haemoglobin; HOMA-IR, homeostatic model assessment for insulin resistance.
*χ^2 test or analysis of variance (ANOVA) test.

HOMA-IR values was more prevalent in females than in males (Table 3).

Markers associated with impaired glucose metabolism

In the unadjusted analyses, our results showed that age and BMI were positively associated with FBS and HOMA-IR ($p < 0.001$), while WHR was negatively associated with HOMA-IR ($p < 0.006$) and HbA1c ($p < 0.01$) (Figure 2). For every 1-year increase in age, FBS increased by 0.61 (95% CI: 0.36–0.85) and HOMA-IR increased by 0.17 (95% CI: 0.10–0.25). For every incremental unit of BMI, FBS increased by 0.40 (95% CI: 0.18–0.63), and HOMA-IR increased by 0.20 (95% CI: 0.14–0.27). As WHR increased, HOMA-IR decreased by an average of 5.01 (95% CI: −8.56 to −1.48) and HbA1c

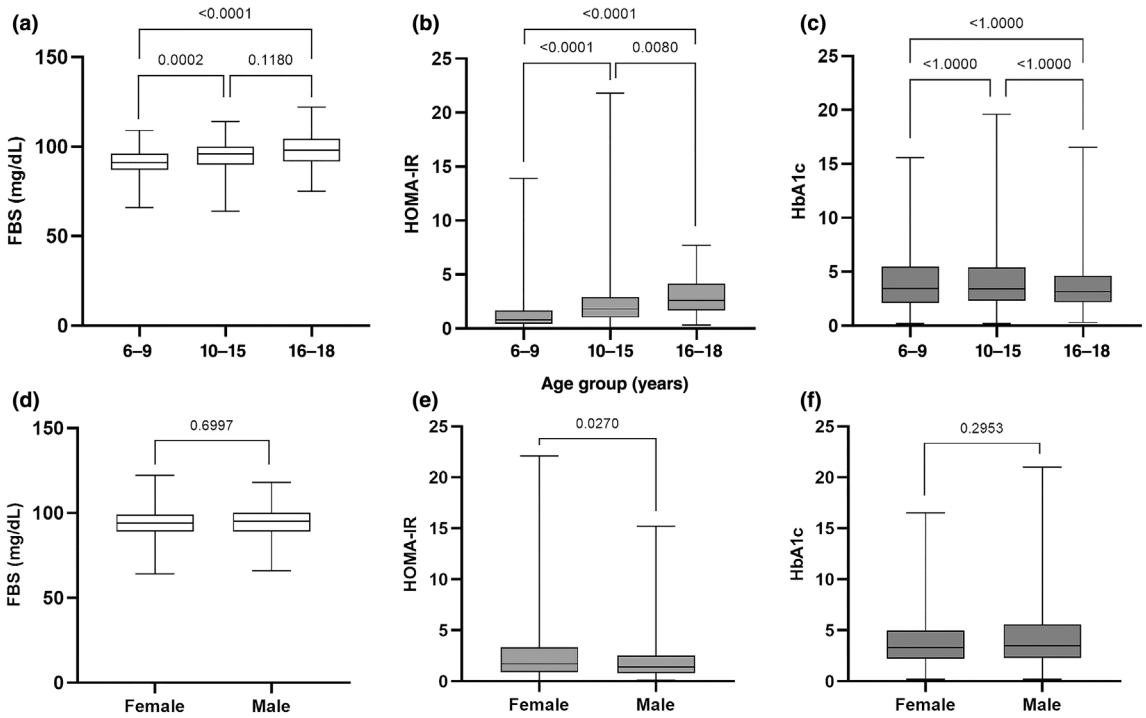

FIGURE 1 Boxplot of age- and sex-stratified glucose parameters ($N = 393$). (a–c) Age-associated fasting blood sugar (FBS) (a), homeostatic model assessment for insulin resistance (HOMA-IR) (b), and glycated haemoglobin (HbA1c) (c). (d–f) Sex-associated FBS (d), HOMA-IR (e), and HbA1c glucose parameters (f).

TABLE 3 Prevalence of impaired glucose metabolism stratified by sex.

Variable	Female ($n = 205$)	Male ($n = 188$)	p-value*
FBS			
Impaired [n (%)]	50 (24.39)	53 (28.19)	0.46
95% CI	19.00–30.72	22.23–35.02	
HOMA-IR			
Impaired [n (%)]	53 (25.85)	35 (18.62)	0.11
95% CI	20.31–32.30	16.00–24.84	
HbA1c			
Impaired [n (%)]	28 (13.66)	33 (17.55)	0.29
95% CI	9.59–19.09	12.74–23.60	

Abbreviations: CI, confidence interval; FBS, fasting blood sugar; HbA1c, glycated haemoglobin; HOMA-IR, homeostatic model assessment for insulin resistance.

*χ^2 test or Student's t-test.

decreased by 4.74 (95% CI: −8.35 to −1.26). In multivariable linear regression, age was significantly associated with FBS (slope = 0.55, 95% CI: 0.23–0.87; $p < 0.001$). In the adjusted model, BMI emerged as the strongest predictor (slope = 0.16, 95% CI: 0.08–0.24; $p < 0.001$) for HOMA-IR, whereas only WHR remained a predictor in the model (slope = −6.38, 95% CI: −10.48 to −2.28; $p = 0.002$) for HbA1c.

DISCUSSION

Perturbation in glucose metabolism in childhood is linked to the onset of cardiovascular diseases in adulthood [30]. In this multicentre cross-sectional study, we assessed impaired glucose metabolism among CALWH. The study explored the prevalence of impaired glucose metabolism among the study population using three different assessment parameters, i.e. HbA1c, FBS, and HOMA-IR. We found a high prevalence of impaired glucose metabolism in 15–26% of study population, depending on the assessment parameter used. Overall, we found that impaired glucose metabolism is prevalent among CALWH in Ghana, suggesting that routine assessment of glucose metabolism could aid in early detection and management of glucose-related conditions in this population.

Using the three assessment parameters, the study observed that HbA1c levels to estimate impaired glucose metabolism yielded the lowest prevalence of 15.5% of the population. However, HbA1c prevalence was slightly higher than the other parameters in 6–9 years age group, possibly because individuals in this group consume higher amounts of carbohydrates such as sugary diets or snacks compared with other age groups [31, 32]. Nonetheless, there are limited available data on HbA1c levels in children and adolescents, posing a challenge in drawing direct comparisons with our study's findings,

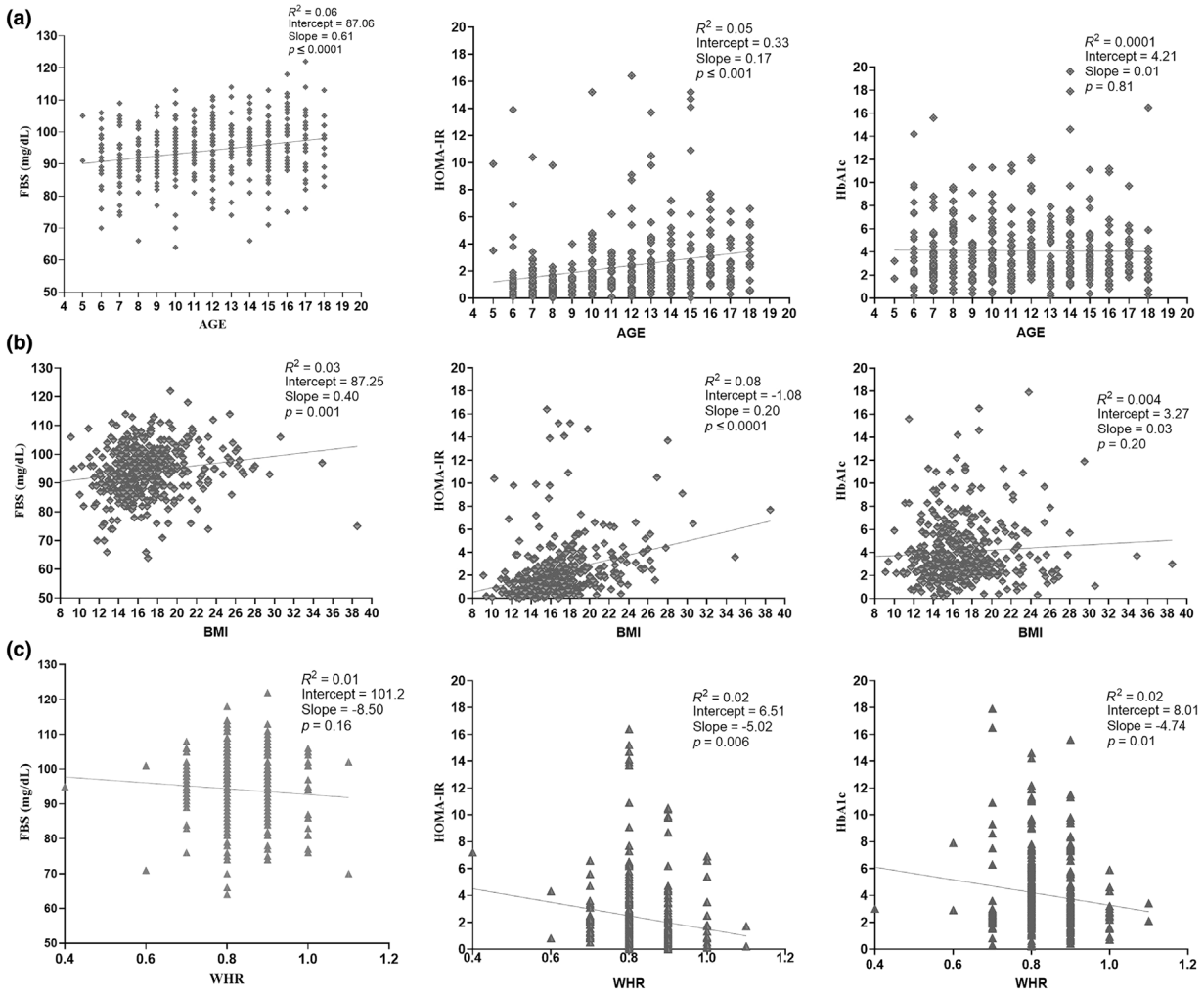

FIGURE 2 Unadjusted associations of age (a), body mass index (BMI) (b), and waist-to-hip ratio (WHR) (c) with glucose metabolism parameters in study population. FBS, fasting blood sugar; HOMA-IR, homeostatic model assessment for insulin resistance; HbA1c, glycated haemoglobin A1c.

particularly among those living with HIV in sub-Saharan Africa. The few studies that have examined HbA1c have reported higher mean values, including non-obese Asian adolescents living with HIV who showed elevated HbA1c with mean values of 5.2% compared with our estimated population's mean value of 4.1% [33]. However, this Asian population was significantly older, with a mean age of 16.7 years [33]. Most studies that have evaluated HbA1c levels in children have focused primarily on monitoring glycaemic levels in diabetics or screening for type 2 diabetes in individuals with obesity [34]. Our study has demonstrated that CALWH in Ghana exhibit elevated HbA1c levels. We observed a prevalence of insulin resistance of 22% based on the HOMA index, which is slightly higher than in previous studies conducted among children in sub-Saharan Africa (20%) [35]. However, a much higher prevalence has been reported in European children (52%) and adults in sub-Saharan Africa (47%) [21, 36]. The prevalence of insulin resistance among children living with HIV varies depending on factors such as age, sex or Tanner stage. Despite being comparable in age, females had higher mean HOMA-IR values than the males in this study. Generally, HOMA-IR levels markedly increase during puberty, the onset of puberty is earlier in females, and females may be more mature than males of the same age. Studies have also reported that the prevalence of insulin resistance tends to be higher among female adolescents than among males of the same age group [37, 38]. We observed the highest prevalence of impaired glucose metabolism using FBS, with 25% of study participants having elevated FBS levels. Wide variability in the prevalence of abnormal glucose levels by FBS have been reported in the literature [28, 39]. Variables such as age, type of ART regimen and BMI have been found to influence the prevalence of abnormal glucose levels assessed by FBS [40]. The prevalence of

elevated FBS levels in our study is lower than in a recent study conducted among adolescents in Tanzania (46%). This could be due to the higher levels of overweight or obese individuals in the Tanzania study [7].

In our study cohort, central obesity, as defined by waist circumference to height ratio > 0.5 [41], was a rare occurrence among our participants and not a risk factor for impaired glucose metabolism. Instead, we observed abnormal waist circumference, as determined by elevated waist-to-hip ratio ≥1 [42], to be more indicative of a potential risk factor for impaired glucose metabolism in our cohort. Participants with abnormal waist circumference were predominately below 10 years old, yet characterized by low BMI, and were referred for nutritional assessment. Consistent with findings from others, the BMI in our study participants was comparable to other CALWH in different regions [18, 43]. BMI tends to increase substantially with age and is more pronounced from early adolescence to adulthood. Despite the cohort's relatively low BMI, a positive trend with glucose values was observed. It is worth noting that most of these children reside in economically disadvantaged households and are more prone to experience nutritional inadequacies with resultant stunted growth [44]. Thus, unsurprisingly, the rate of obesity among CALWH in sub-Saharan Africa is low. Thus, we found that relying solely on central or general obesity as a criterion for monitoring impaired glucose metabolism can underestimate the prevalence of impaired glucose among CALWH or lean children and adolescents in the general population.

Taken together, we observed a wide variability in the proportion of individuals with impaired glucose metabolism in the study population using the three assessment criteria. While the proportion of impaired FBS aligns with insulin resistance, as HOMA-IR is derived from FBS, there is a lower prevalence of individuals with elevated HbA1c. This discrepancy can be attributed to several factors, including wide variations in HbA1c values corresponding to FBS levels, as HbA1c 6.0–7.0% can be equivalent to 100–185 mg/dL mean FBS [45]. Additionally, the presence of hemoglobinopathies, anaemia and nutritional deficiencies within the study population, as highlighted by Wegmüller et al. [46], can affect the haemoglobin glycation gap and index. These factors may lead to clinical inaccuracies in HbA1c values and contribute to the discordance observed between the proportion of individuals with high FBS levels but normal HbA1c. Considering prevailing haemoglobin disorders and nutritional deficiencies in our population, it becomes evident that HbA1c may not be the preferred parameter for assessing impaired glucose metabolism in this specific context. When considering the sensitivity of assessment parameters, FBS provided the highest prevalence, which makes it potentially the most sensitive tool. Previous studies have also reported FBS values as having the best predictive power to identify impaired glucose metabolism in children and adolescents, particularly in healthy or non-obese populations [47]. Although the prevalence of glucose impairment by FBS and HOMA-IR were comparable, factors such as accessibility and robustness of FBS are more practical to a setting in the sub-Sahara African region. Therefore, using FBS as a parameter for assessing impaired glucose metabolism not only offers high sensitivity but is also more practical in resource-constrained settings. Evaluating glucose levels using the FBS parameter may be easier, faster, more affordable and acceptable to individuals due to its less invasive sampling method and lower requirement of blood volume [48].

Our study has several limitations, which need to be considered in the interpretation of the findings. First we relied solely on age as grouping variable instead of also assessing puberty, as age may not fully capture the variations in developmental maturity levels among individuals. Nonetheless, while age may not be a perfect proxy for developmental maturity, it is a solid proxy for cumulative exposure to ART among CALWH with perinatal HIV infection, and we observed associations of age with FBS and HOMA-IR levels. Second, the cross-sectional nature of our study only allowed us to examine the prevalence of glucose impairment at one point in time, which could affect the estimates. The dynamic changes in glucose parameters with respect to age and sex should be further examined in a longitudinal study. However, our findings are consistent with previous research indicating high frequency of impaired glucose metabolism in CALWH, which may serve as a proxy for metabolic diseases in adulthood [17, 49, 50].

CONCLUSION

In summary, this cross-sectional study reveals a high prevalence of impaired glucose metabolism in CALWH. This may pose a potential risk for an increase in cardiometabolic diseases within perinatally infected HIV patients residing in sub-Saharan Africa. Yet, questions remain as to whether the observed impairment in glucose metabolism is transient or permanent. Could it be critical in the causal pathways of metabolic syndrome in early adulthood? Prospective monitoring is crucial to answer these questions, to gain better understanding of the risk predictors for cardiometabolic diseases in individuals living with HIV. Our findings also underscore the importance of the type of assessment used to identify impaired glucose metabolism among children and adolescents. Considering the clinical diagnostic effectiveness,

integrating simple and readily available FBS measurements may aid in predicting early glucose abnormalities, such as hyperglycaemia, and facilitate management.

AUTHOR CONTRIBUTIONS

Conception and design of experiments: EP, RAT, LEA, JKAT. Data collection: RAT, JKAT, AAE, FA, YA-M. Performed experiments: RAT, AAE, EB, JA. Analysed data: RAT, VS. Original draft: RAT, VS.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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