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Maternal mid-upper arm circumference is associated with birth weight among HIV-infected Malawians

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Abstract

We examined the relationship of maternal anthropometry to fetal growth and birth weight among 1005 HIV-infected women in Lilongwe, Malawi, who consented to enrollment in the Breastfeeding, Antiretrovirals, and Nutrition (BAN) Study (www.thebanstudy.org). Anthropometric assessments of mid-upper arm circumference (MUAC), arm muscle area (AMA), and arm fat area (AFA) were collected at the baseline visit between 12 and 30 weeks gestation and in up to 4 follow-up prenatal visits. In longitudinal analysis, fundal height increased monotonically at an estimated rate of 0.92 cm/week and was positively and negatively associated with AMA and AFA, respectively. These latter relationships varied over weeks of follow-up. Baseline MUAC, AMA, and AFA were positively associated with birth weight [MUAC: 31.84 grams per cm increment, 95% CI: 22.18, 41.49 (p<0.01); AMA: 6.88 g/cm², 95% CI: 2.51, 11.26 (p<0.01); AFA: 6.97 g/cm², 95% CI: 3.53, 10.41 (p<0.01)]. In addition, MUAC and AMA were both associated with decreased odds for LBW (<2500 g) [MUAC: OR=0.85, 95% CI: 0.77, 0.94 (p<0.01); AMA: OR=0.95, 95% CI: 0.91, 0.99 (p<0.05)]. These findings support the use of MUAC as an efficient, cost effective screening tool for LBW in HIV-infected women, as in HIV-uninfected women.

INTRODUCTION

In resource-limited settings, low birth weight (LBW) is common. Research comparing data from resource-limited countries to that from resource-rich countries shows that most of the differences in LBW rates may be attributed to an increased prevalence of intrauterine growth restriction (IUGR), rather than preterm birth, with relative risks of 6.6 and 2.0, respectively [1]. It is well established that the short-term consequences of IUGR include increased risk of fetal, neonatal, and infant death and impaired postnatal growth, immune function, and intellectual development [2–4].

Maternal nutritional status, as estimated by anthropometrics, is an important contributor to fetal growth and infant birth weight [5–7]. In pregnant women, weight alone may not be the best indicator of maternal muscle and fat stores, since it is a measure of both the mother and the fetus. Therefore, simple and inexpensive anthropometric measurements, such as mid-upper arm circumference (MUAC) and skinfold thickness measurements, are used in large-scaled epidemiological studies to derive estimates of lean muscle mass and adiposity [8–10].

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

In resource-limited settings, intrauterine growth assessments rely on serial fundal height measurements during antenatal care and determination of intrauterine growth restriction is based on low birth weight for estimated gestational age [11].

The relationship between low MUAC and LBW has been studied extensively in HIV-uninfected populations; therefore, it is commonly used as a screening tool in developing countries [5–7]. However, there is limited data on the utility of maternal anthropometrics as predictors for fetal growth and birth weight among cohorts of pregnant HIV-infected women (8–10). HIV-infected individuals may lose fat mass quicker than HIV-uninfected individuals due to an increased metabolic rate to combat infection and malabsorption of nutrients [12]. In addition, women in sub-Saharan Africa are vulnerable to factors such as high parity and short birth intervals, prevalent infectious disease, and seasonal variations in food insecurity. These combined factors place an added burden on pregnant women and therefore may contribute to poor birth outcomes, such as LBW [2]. We hypothesized that low maternal nutritional stores among HIV positive women, as measured by low arm muscle area (AMA) and low arm fat area (AFA), would relate to slower intrauterine growth and increased risk of LBW.

Subjects and Methods

The current study includes 1005 HIV-infected women who delivered live singleton births between June 2004 and December 2006 and consented to enrollment in the Breastfeeding, Antiretrovirals, and Nutrition (BAN) Study, a postnatal clinical trial (www.thebanstudy.org) [13]. These study participants were recruited from four sites with outreach to all pregnant women in Lilongwe, Malawi who met prenatal screening criteria: 14 years of age, no prior antiretroviral medication use, 30 weeks gestation, and no serious complications of pregnancy, CD4 count ≥ 200 cells/ μ L, hemoglobin ≥ 7 g/dL, and normal liver function tests (≤ 2.5 times the upper limit of normal). At the second antenatal visit approximately one week later, (here to forth referred to as the baseline visit), 1130 eligible women completed a baseline interview, physical exam and provided blood specimens again. Of these, 125 women were excluded from the analysis sample owing to fetal loss, still birth, twins, and late presentation to the clinic following home deliveries or delivery at other clinics (after 48 hours after delivery). Out of 1005 women who had live singleton births, no fundal height was available for 92 women. Of 913 women who had at least one fundal height measurement, 20 women had no baseline measurement of fundal height.

Mid-upper arm circumference (MUAC), triceps skinfold thickness, and height were measured by trained BAN nutrition staff. Height was measured once either prenatally or postnatally with a standard height board. At each visit, MUAC was measured at the midpoint between the olecranon and acromion process, to the nearest 0.1 cm using a nonstretchable insertion tape, while the arm hung freely at the side. Triceps skinfold thickness was measured at each visit using Lange Calipers. The mean of three separate determinations was used with MUAC to derive arm fat and muscle areas. Arm muscle area (AMA), an indicator of total muscle mass, was derived from MUAC and triceps skinfold measures as follows: $AMA = [MUAC - (\text{triceps skinfold} \times \pi)]^2 / 4 \pi$. Arm fat area (AFA), an indicator of total fat mass, was derived from MUAC and AMA: $AFA = (MUAC^2 / 4 \pi - AMA)$.

Gestational age at baseline and subsequent prenatal visits were derived from the date of last menstrual period (LMP) or, if LMP was unknown, first available fundal height. Depending upon the estimated gestational age at baseline, women were asked to return for follow-up prenatal care at approximately 28, 32, and 36 weeks gestation and fundal height was used to estimate intrauterine growth. In the BAN Study, fundal height was ascertained by measuring the distance between the upper edge of the pubic symphysis and the top of the uterine

fundus using a tape measure. Beginning in the second trimester, fundal height \pm 1 to 3 cm should estimate gestational age in weeks (i.e., a pregnant woman's uterus at 26 weeks should measure 23 to 29 cm) [14–16]. Birth weight was measured using a Tanita Digital Baby Scale to the nearest 0.1 kilogram immediately after delivery in the hospital or within 48 hours of delivery, upon arrival to the hospital, for home deliveries. LBW was defined according to the WHO definition of less than 2500 g [17].

Basic sociodemographic information was collected during the baseline interview: age, parity, marital status, household characteristics, and the educational level and occupation status of the mother. A wealth index was derived from household characteristics: house construction (type of walls, floors, and roof), number of rooms and residents, electricity, refrigeration, sanitation, and cooking fuel source [18]. CD4 count was measured cross-sectionally during the first screening visit. None of the women took antenatal antiretrovirals during this or prior pregnancies, in accordance with the national guidelines of Malawi's Ministry of Health on initiation of antiretroviral treatment since these women had high CD4 count levels. All participants received iron and folate supplements, malaria prophylaxis and treatment, and mosquito nets. As of December 2005, all pregnant women with CD4 counts below 500 cells/ μ L were administered cotrimoxazole after the first trimester (13). At onset of labor, all participants received the HIVNET 012 regimen and a 7-day postnatal "tail" of zidovudine and lamivudine to prevent perinatal HIV transmission. The BAN Study protocol was approved by the Malawi National Health Sciences Research Committee and the institutional review boards at the University of North Carolina at Chapel Hill and the U.S. Centers for Disease Control and Prevention (ClinicalTrials.gov identifier NCT00164762).

We used STATA version 9.0 for this analysis [19]. First, we evaluated the potential for selection bias by comparing women with anthropometric measurements collected at baseline who were included in our analysis ($n=1005$) to those who were excluded from the analysis sample owing to fetal loss, still birth, home deliveries or late presentation after delivery ($N=125$). Two-sample t-tests and chi-square tests were used to compare means of continuous variables and proportions of categorical variables, respectively, between the samples, and inverse probability weighting was used to evaluate selection bias in our statistical models [20]. The likelihood of being in the analysis sample (with complete data) was estimated from a logistic regression model including baseline socioeconomic and demographic variables, and the inverse predicted probabilities were included as sample weights in regression models for birth outcomes.

Fundal height at each antenatal visit was modeled using longitudinal random effects regression. Time-varying anthropometric indicators measured concurrently with fundal height (e.g. AMA and AFA) were included in the model, along with time-independent baseline maternal characteristics (age, parity, CD4 count, wealth index) and infant sex and in utero infection. Since food availability, malnutrition, and infectious disease morbidity vary substantially by season due to cycles of rainfall and agricultural production [21], the number of days spent in the famine season (August to March) in the month prior to anthropometric assessment was included as a time-varying cofactor. In addition, due to reported annual variations in the maize production, year at baseline was also included in the models [22]. The time between the baseline visit and each subsequent visit was included in the model for fundal height. To anchor the timing of measurements relative to total gestational duration, the time between the last antenatal visit and delivery was included in the model. Interaction terms between the main predictors (muac, ama, afa) and each of the covariates were considered, estimated and retained in the models if their p-value was <0.15 [23].

Linear regression models were used to estimate the relationship between maternal anthropometry and birth weight and logistic regression models were used to estimate odds ratios for LBW associated with each risk factor after adjustment for covariates. Model specification was guided by studies on nutritional outcomes among pregnant HIV-infected and HIV non-infected women. Two multivariable models were constructed for each outcome. One included AMA and AFA together as the main exposures; a second model included MUAC as the main exposure[24]. Internal sample-based Z-scores were calculated for these anthropometric measures so that the effect sizes of AMA and AFA, and MUAC could be compared. We tested for linear trends between the independent variables and study outcomes, and if non-linear, categorical variables were constructed and included in the models.

Results

The median CD4 count was 439 cells/ μ l (IQR: 319–592), and about a third of women fell into each of three CD4 categories: 200 to 350 cells/ μ l (31%), 350 to 500 (31%), and >500 (38%) (Table 1). Almost two-thirds (62%) of the women were exposed to the famine season in the month prior to their baseline visit. The mean mid-upper arm circumference (MUAC) was 26.5 cm, with a mean arm muscle area of 36.8 cm² and mean arm fat area of 19.7 cm², at baseline. The average birth weight was 2998 g, and the prevalence of low birth weight was 8.7% (Table 1).

Women included in our analysis (n=1005) were significantly younger (p<0.01), commenced prenatal care earlier (p=0.03), and were more likely to be primiparous (p<0.01) than women excluded (n=125); they did not differ significantly on CD4 count, maternal anthropometrics, or fundal height. Weighted and unweighted models were not appreciably different, suggesting that selection bias was not a problem. Thus, we present unweighted results.

Fundal height increased monotonically at a rate of about 0.92 cm/week (Table 2). In the longitudinal analysis, AMA was associated with a subtle, yet significant increase in fundal height over the course of the latter part of pregnancy; in contrast, AFA was associated with a subtle, yet significant decrease in fundal height. MUAC was not significantly related as a predictor ($\beta = 0.01$ (95% CI: -0.06, 0.07; p=0.85). The effects of AMA [$\beta = 0.03$ (95% CI: 0.01, 0.06)] and AFA [$\beta = -0.03$ (95% CI: -0.05, -0.002)] were significantly modified by weeks of follow up [AMA x week: $\beta = -0.003$ (95% CI: -0.006, -0.001); AFA x week: $\beta = 0.003$ (95% CI: 0.001, 0.006)]. The betas of equivalent magnitude but opposite direction for AMA and AFA, as well as their interaction terms with gestational week, are consistent with the lack of an overall effect of MUAC on fundal height. An important predictor of decreased fundal height was infant HIV status [-1.69 cm, 95% CI: -2.61, -0.48 (p < 0.01)]. However, there was no association between fundal height and maternal CD4 count. Furthermore, there was no evidence famine season or year of enrollment impacted fundal height. Although the association between infant sex and fundal height was statistically significant, clinically the difference in association between males and females and fundal height was very subtle. Age, parity and wealth index also had weak associations with fundal height.

Baseline maternal MUAC, AMA, and AFA were strong predictors of infant birth weight, with the greatest effect observed for MUAC based on internal sample z-scores which were calculated. For each 1 cm increase in MUAC, there was a 31.8 g (95% CI: 22.2, 41.5) increase in birth weight (Table 3, **Model 2**). In contrast, each 1 cm² increase in AMA and AFA was associated with a 6.88 g and 6.97 g increase in birth weight, respectively (Table 3, **Model 1**). In models with low birth weight as the outcome, higher baseline maternal MUAC was a strong predictor for decreased odds of low birth weight [OR=0.85, 95% CI: 0.77, 0.94 (p<0.01)] (Table 3, **Model 2**). The odds of having a LBW infant also decreased with

increasing AMA (OR: 0.95, 95% CI: 0.91, 0.99); a similar pattern was observed for the relationship between AFA and LBW, although this was not statistically significant ($p=0.08$) (Table 3, **Model 1**).

Discussion

Birth weight is an important predictor of infant survival and future development. In our study of HIV-infected pregnant women with high CD4 counts, mean baseline MUAC (26.5 cm), fetal growth (0.92 cm/week) and birth weight (2998 g) were similar to other sub-Saharan populations [25, 26]. In addition, maternal MUAC was a strong predictor of birth weight and LBW in this HIV-infected population, as has been reported for HIV-uninfected women.

With repeated measures, we observed similar patterns of increasing fundal height with increasing muscle mass and decreasing fundal height with increasing fat mass during late pregnancy, as seen in comparable HIV-uninfected populations [27]. However, the small increase in fundal height associated with AMA coincided with an equally small decrease associated with AFA, thus explaining why MUAC did not show any relationship to fetal growth [28–30]. Currently, there is no comparative literature that examines maternal factors and their associations with fundal height. The use of fundal height to estimate gestational age has been criticized in resource-limited contexts where intrauterine growth restriction (IUGR) is prevalent because fundal height can misclassify a growth-restricted infant as having an earlier week of gestation [31]. Rather than using fundal height as an indicator of gestation week, we modeled repeated measurements of fundal height as an outcome and examined how it related longitudinally to maternal anthropometry and other maternal characteristics. Serial measurements of fundal height are being increasingly used in resource-limited settings for the prediction of birth weight and diagnosis of IUGR [32–34].

While AMA and AFA minimally affected fetal growth, and MUAC did not affect fetal growth at all, AMA, AFA, and MUAC were directly related to birth weight. MUAC was the strongest predictor for birth weight, both as a continuous measurement and dichotomized to indicate low birth weight. This finding is consistent with reports from European and African women. In pregnant European women, pregravid lean body mass was found to be a significant predictor of birth weight [35]. Among a cohort of 110 Kenyan women, increased odds for low birth weight were reported for mothers with smaller MUAC during the 2nd and 3rd trimesters [6]. Among 1002 HIV-infected women in Tanzania, mothers with the highest quartile of MUAC distribution had higher infant birth weights relative to mothers in the lowest quartile of MUAC [8]. In contrast, the latter study found no association between MUAC and LBW.

While arm muscle area (AMA) was associated with birth weight as a continuous measure and as the dichotomous measure for low birth weight (versus not low birth weight), arm fat area (AFA) was significantly associated only with birth weight as a continuous variable. The positive association between AFA and birth weight may appear contradictory to the inverse association between AFA and fundal height; however, the association between AFA and fundal height was evaluated in a longitudinal model which includes serial measures during pregnancy over which AFA tends to decline while fundal height increases. In contrast the association between AFA and birth weight was evaluated in a cross-sectional model utilizing a baseline AFA measurement, which reflects fat storage earlier in pregnancy. The cross-sectional association between AFA and birth weight is consistent with a study in Zimbabwe among 1669 HIV-infected women that found low AFA (<20 cm²) measured once during late pregnancy was associated with lower birth weight [10]. However, unlike our study, they found no relationship between AMA and LBW.

A major strength of our study is serial anthropometric measurements during pregnancy on a large cohort of HIV-infected women. However, with no HIV-uninfected comparison group in the BAN Study, we could not do a relative comparison to HIV-uninfected pregnant women. Hence, the focus of this analysis was of the effects of nutritional status among HIV-infected pregnant women who received prenatal care on intrauterine growth and birth weight. Our sample comes from those who consent, test positive for HIV/AIDS, and meet the primary eligibility criteria. We do not have follow-up data on women with low CD4 counts or hemoglobin levels below 7 since they were considered ineligible for the BAN Study and referred to care. This is a plausible reason we were not able to derive a cut-off value for MUAC and LBW. However, in an analysis done on 300 women who did not participate, the descriptive characteristics were similar to our sample (unpublished). Higher CD4 counts and low LBW prevalence in our sample may explain why we were unable to detect an association between maternal CD4 count or infant HIV status and LBW, as reported by other studies [36, 37]. Additionally, regular antenatal care and prevention or monitoring and treatment for opportunistic infections may have attenuated any possible effects of HIV status on birth outcomes in this population.

Our study supports the use of MUAC as an efficient, cost-effective screening tool for LBW among HIV-infected women, as currently used among HIV-uninfected women [7], without concern for potential risk factors, such as seasonality, infectious disease and poor SES conditions, often associated with adverse birth outcomes. Wasting among pregnant women regardless of HIV status has been defined as having a MUAC of less than 22 centimeters, according to previous reports that found similar cut-off points to be associated with adverse pregnancy outcomes [38] and increased risk of death, respectively, in African populations [39].

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Table 1

Characteristics of HIV-infected pregnant women and their infants in Malawi (n=1005)

Characteristic	Value
Maternal characteristics at baseline	
Age (%)	
<20 y	6.76
20–24 y	35.88
25–29 y	34.39
>=30 y	22.96
Education Level (%)	75.83
None	12.46
Primary level	52.74
Secondary level	34.8
Marital Status (%)	
Married or Cohabiting	92.82
Single, divorced, or widowed	7.18
Employment (%)	
No	80.46
Yes	19.54
Exposure to famine season in month prior to baseline visit (%)	
Total	42.83
Partial	19.56
None	37.61
Parity (%)	
0	18.21
1 to 2	58.70
>=3	23.09
Height (cm) (mean ± SD)	155.9± 5.3
Midupper arm circumference (cm) (mean ± SD)	26.5 ± 2.7
Arm muscle area (cm ²) (mean ± SD)	36.8 ± 6.6
Arm fat area (cm ²) (mean ± SD)	19.7 ± 7.8
Fundal Height (cm) *	24.9 ± 4.8
CD4 count (X 10 ⁶ cells/L) **	439 (IQR: 319–592)
Infant characteristics at birth	
Birthweight (g) (mean ± SD)	2998±440
Low birth weight (%)	8.7
Infant sex (% male)	50.8
Infant HIV status (% positive)	3.8

* Sample size reduced to 893; 92 women had no FH and 20 women had FH missing at baseline.

** CD4 count displayed as median and interquartile range (IQR).

Table 2

Longitudinal regression analysis of fundal height as main outcome and maternal arm measurements as main predictors in 913 HIV-infected Malawian women.

Main predictor ¹	Fundal height (cm)			
	β	<i>P</i>	95% CI	
Arm muscle area (cm ²)	0.03	<0.01	0.01	0.06
Arm fat area (cm ²)	-0.03	<0.01	-0.05	-0.002
Weeks ²	0.92	<0.01	0.83	1.02
AMA x weeks	-0.003	<0.01	-0.006	-0.001
AFA x weeks	0.003	<0.01	0.001	0.006
Weeks between last visit and delivery	-0.32	<0.01	-0.39	-0.18
Covariates ⁴				
Age				
<20 y	0.52	0.27	-0.41	1.45
20–24	Reference	-	-	-
25–29	0.78	<0.01	0.22	1.34
30+	0.75	0.01	-0.01	1.51
Parity	0.31	<0.01	0.08	0.54
Wealth index	0.25	0.01	0.07	0.4
Famine ³	-0.19	0.16	-0.46	0.07
Year of enrollment				
2004	-0.59	0.09	-1.27	0.09
2005	-0.15	0.55	-0.63	0.34
2006	Reference	-	-	-
CD4 count				
200–350 cells/uL	-0.36	0.24	-0.95	0.24
350–499 cells/uL	-0.33	0.24	-0.88	0.22
500 cells/uL	Reference	-	-	-
Infant sex (female is referent)	0.48	0.03	0.04	0.93
Infant infected in utero (uninfected is referent)	-1.69	<0.01	-2.91	-0.48

¹Sample size reduced to 913, because 92 had no FH available

²Number of weeks since baseline visit; baseline visit = 0 weeks

³Famine defined as number of days in famine season during preceding month

⁴Maternal height was included in model and was not statistically significant.

Table 3

Multiple variable regression models with birth weight and LBW as main outcomes and baseline maternal arm measurements as main predictors in 1005 HIV-infected Malawian women.

Main predictor	Birth weight ¹ (g)			LBW ² (<2500 g)		
	β	P	95% CI	Odds Ratio	P	95% CI
Model 1:						
Arm muscle area (cm ²)	6.88	<0.01	2.51 11.26	0.95	0.03	0.91 0.99
Arm fat area (cm ²)	6.97	<0.01	3.53 10.41	0.97	0.08	0.94 1
Model 2:						
MUAC (cm)	31.84	<0.01	22.18 41.49	0.85	<0.01	0.77 0.94

¹ Estimated with multiple linear regression; covariates include maternal height, age, parity, education, place of delivery (hospital, home), CD4 cell count, infant sex, infant HIV status at birth.

² Estimated with multivariate logistic regression models with covariates described in footnote 1.