Maternal HIV is associated with reduced growth in the first year of life among infants in the Eastern region of Ghana: the Research to Improve Infant Nutrition and Growth (RIING) Project

Anna Lartey*, Grace S. Marquis†‡, Robert Mazur§, Rafael Perez-Escamilla¶, Lucy Brakohiapa**, William Ampofo** and Seth Adu-Afarwuah*

*Department of Nutrition and Food Science, University of Ghana, Legon, Ghana, †School of Dietetics and Human Nutrition, McGill University, Montreal, Canada, ‡Department of Food Science and Human Nutrition, Iowa State University, Ames, Iowa, USA, §Department of Sociology, Iowa State University, Ames, Iowa, USA, ¶School of Public Health, Yale University, New Haven, Connecticut, USA, **Nutrition Department, Noguchi Memorial Institute for Medical Research, Legon, Ghana, and ††Department of Anthropology, University of Toronto, Ontario, Canada

Abstract

Children of HIV-infected mothers experience poor growth, but not much is understood about the extent to which such children are affected. The Research to Improve Infant Nutrition and Growth (RIING) Project used a longitudinal study design to investigate the association between maternal HIV status and growth among Ghanaian infants in the first year of life. Pregnant women in their third trimester were enrolled into three groups: HIV-negative (HIV-N, n = 185), HIV-positive (HIV-P, n = 190) and HIV-unknown (HIV-U, n = 177). Socioeconomic data were collected. Infant weight and length were measured at birth and every month until 12 months of age. Weight-for-age (WAZ), weight-for-length (WLZ) and length-for-age (LAZ) z-scores were compared using analysis of covariance. Infant HIV status was not known as most mothers declined to test their children’s status at 12 months. Adjusted mean WAZ and LAZ at birth were significantly higher for infants of HIV-N compared with infants of HIV-P mothers. The prevalence of underweight at 12 months in the HIV-N, HIV-P and HIV-U were 6.6%, 27.5% and 9.9% (P < 0.05), respectively. By 12 months, the prevalence of stunting was significantly different (HIV-N = 6.0%, HIV-P = 26.5% and HIV-U = 5.0%, P < 0.05). The adjusted mean ± SE LAZ (0.57 ± 0.11 vs. -0.95 ± 0.12; P < 0.005) was significantly greater for infants of HIV-N mothers than infants of HIV-P mothers. Maternal HIV is associated with reduce infant growth in weight and length throughout the first year of life. Children of HIV-P mothers living in socioeconomically deprived communities need special support to mitigate any negative effect on growth performance.

Keywords: HIV-infected mother, birthweight, infant growth, Ghana.

Introduction

The effect of HIV on children is seen very early in life, manifested as intrauterine growth retardation, low birthweight and poor growth during the early months of life (Newell et al. 2004; Fausto et al. 2009; Venkatesh et al. 2010). Stunting and wasting are typical of children affected with HIV. In addition to growth faltering, high rates of morbidity (diarrhoeal and respiratory infections) are common in HIV-infected children (Moye et al. 1996; Fausto et al. 2009; Webb et al. 2009). Diarrhoea, in turn, is associated with decreased growth and increased mortality (Villamor et al. 2004). It is estimated to contribute 19% of deaths among children under 5 years of age in developing countries (Boschi-Pinto et al. 2008).

Most studies that have examined the effects of maternal HIV on infant growth have compared infected with uninfected children of HIV-positive (HIV-P) mothers. Evidence from recent studies indi-
icates that uninfected children born to HIV-P mothers are also susceptible to adverse growth effects. The environmental conditions under which the majority of infants of HIV-P women in sub-Saharan Africa live are important factors affecting child growth. Specifically, HIV-affected mothers are more likely to be socially disadvantaged in having lower household incomes (Marinda et al. 2007), and being widowed or separated from their spouse (Koyanagi et al. 2011), and more likely to be living under conditions of food insecurity (FI) (Bentley et al. 2005; Hadley & Patil 2006; Anema et al. 2009). FI is associated with maternal mental health (anxiety and depression) among Tanzanian women (Hadley & Patil 2006). These conditions, together with the effects of HIV infection, influence maternal nutritional status (Nduti et al. 2001). Knowledge of having HIV itself may cause depression and, subsequently, change maternal care practices (Mast et al. 2006). Poor maternal health during pregnancy may also adversely impact the infant’s immune system, resulting in increased frequency of infections and, thereby, poor growth outcomes (Nielson et al. 2001; Chougnet 2003).

Breastfeeding still remains the best option for HIV-infected mothers in regions where environmental conditions predispose infants to high rates of diarrhoeal and infectious diseases. The most recent World Health Organization (WHO) guidelines on HIV and infant feeding recommend breastfeeding and antiretroviral (ARV) therapy for HIV-infected mothers until infants turn 12 months of age (WHO 2010). This recommendation may mitigate growth faltering observed in HIV-infected and HIV-exposed children. Studies in sub-Saharan Africa comparing the growth of children of HIV-P mothers to that of children of HIV-negative (HIV-N) mothers using longitudinal designs are few and inconclusive (Bailey et al. 1999).

The Research to Improve Infant Nutrition and Growth (RIING) Project was designed to identify the pathways by which maternal HIV infection alters households’ ability to provide optimal feeding and caregiving for infants and subsequently influence child growth and development. This paper reports on the analysis to examine the association between maternal HIV status and growth among Ghanaian infants in the first year of life.

Children of HIV-N mothers and those of women of HIV-unknown (HIV-U) status all living in the same communities were used as comparison groups. This design permits the comparison of growth adjusted for known confounders among infants prenatally exposed to HIV (from HIV-P mothers) with those without prenatal exposure (HIV-N mothers). The inclusion of the HIV-U group allowed a comparison with this group of women who represented the majority of the population (who did not know their HIV status) at the time of the study.

Methods

Study site

The study was conducted from 2003 to 2008 in the Yilo Krobo (population 93,586) and Many Krobo (population 165,409) districts located about 80 km north of Accra, in the Eastern region of Ghana. The main adult occupations are trading, fishing, pottery and farming. The districts are served by three hospitals. The Eastern region where the two districts are located had an HIV prevalence of 3.7% compared with the national prevalence of 2.2% at the time of the study (GSS 2004). The prevalence of stunting among children under 5 years in the Eastern region was 27% (GSS 2004). Literacy rates among men and

Key messages

- Maternal HIV status is associated with reduced infant growth in weight and length throughout the first year of life.
- HIV-P mothers are of lower socioeconomic status and are more likely to be food insecure.
- Children of HIV-P mothers living in socioeconomically deprived communities may need special support to mitigate the negative association of HIV with growth.
- Efforts must be intensified to curb the spread of HIV.
women in the region were 81% and 64%, respectively (GSS 2004). Most households in the districts had access to electricity and public pipe-borne water within the community.

**Study design and population**

The study was a prospective cohort involving pregnant women \(n=552\) in their third trimester attending prenatal clinics in three hospitals in the districts. To be eligible, the participant had to be (1) pregnant; (2) at least 18 years of age; (3) undergo voluntary pre-test counselling and if tested agree to have her HIV test results released to the project supervisor; (4) available for the entire duration of the study; and (5) free from clinical and physical conditions that would limit her ability to care for the infant.

The women went through the regular Ghana Health Service (GHS) antenatal clinic procedures, which included voluntary pre-test counselling to offer HIV testing (Okronipa et al. 2012). Women who agreed to be tested were identified as HIV-P or HIV-N those who refused testing were identified as HIV-U. Recruitment into the study was done in partnership with the hospital nursing staff responsible for voluntary counselling and testing (VCT) in the three participating hospitals. After testing (or after pre-test counselling if testing was refused), the GHS nurse informed women about the study. Recruitment of HIV-N and HIV-U (because refusal to be tested) women followed the identification of HIV-P women to assure similar seasonal enrolment in the three groups. All HIV-P women who consented were enrolled. If more HIV-N and HIV-U women were available at the time, participants were randomly chosen from those available that day.

The GHS nurse approached 692 pregnant, of whom 653 expressed interest in the study. HIV status was released only to the project supervisor who personally visited each woman at her home to further explain the study. Informed written consent was obtained from 552 women: HIV-N \((n=185)\), HIV-P \((n=190)\) and HIV-U \((n=177)\). HIV tests were routinely done by the recruiting hospitals using the Rapid Test Abbott Determine HIV-1/2 (Abbott Laboratories, Abbott Park, IL, USA). At the time of the study, the administration of nevirapine to the pregnant woman at labour and to the infant at birth was the national protocol for the prevention of mother-to-child transmission (PMTCT).

**Sample size determination**

Sample size was determined based on estimates of effect sizes and individual-level variability documented for anthropometric, breast milk intake and morbidity data from previous studies in similar low-income communities (Marquis et al. 2002). Calculations used an effect ratio of 1, a one-tailed test, a significance level of 0.05 and a power of 80% (Kelsey et al. 1986). Morbidity rates based on 20% and mean difference of 15% yielded the largest sample size of 151 per group. Assuming a loss to follow-up of 25%, a total sample of 189 per group was considered to be adequate.

**Data collection**

Data were collected on socio-demographic information (age, education, marital status), occupation, household characteristics (size and composition), food production, economic activities, household FI, maternal post-natal depression and maternal stress. These data were collected at baseline, birth, 3, 6, 9 and 12 months after birth. Infant anthropometric measurements (weight and length) were taken within 24 h of birth, and then monthly thereafter until the infant reached 12 months. Infants were weighed naked to the nearest 100 g (Tanita Corporation of America Inc., Arlington Heights, IL, USA), and recumbent length was measured to the nearest 0.1 cm using an infant stadiometer at home (Shorr Productions, Olney, MD, USA). Maternal post-natal depression was measured at birth and at 6 months after birth using the Edinburgh Post-natal Depression Scale as described elsewhere (Okronipa et al. 2012). Maternal stress was measured at baseline, birth, 3, 6, 9 and 12 months using the Perceived Stress Scale as described elsewhere (Okronipa et al. 2012). Other data on infant morbidity and feeding, and maternal anthropometry, morbidity and social capital not reported in this paper were also collected. At 12 months of age, all mothers were given the opportunity through a separate informed consent
process to have their infant tested for HIV. Those who agreed to testing \((n = 81)\) had a finger prick blood taken on to a filter paper to determine the child’s HIV status by DNA polymerase chain reaction (PCR) analysis (Franssen et al. 1994, 1998).

**Statistical analysis**

Analyses were done using SAS v. 9.2 (SAS Institute, Cary, NC, USA). Background characteristics were assessed by using chi-squared tests for categorical variables and analysis of variance (with Ryan–Emot–Gabriel–Weich for post hoc pair-wise comparison) for continuous variables. As a proxy for household socioeconomic status, we created an ‘amenities’ factor from a set of 18 socioeconomic variables (house-building materials, location of household water, toilet, access to electricity, cooking fuel, ownership of appliances) using factor analysis with varimax rotation. Lower values for amenities were assumed to indicate poorer households. Household-level FI at birth, 3, 6, 9 and 12 months after birth was determined using a 14-item scale derived from the US Household Food Security Survey Module. Rasch analyses confirmed the psychometric validity of the scale (R. Perez-Escamilla, ‘unpublished observations’). Based on these analyses, households were classified as food secure if none of the questions were affirmed. The cut-off points for classifying households into different FI levels based on adding the number of questions affirmed were: mild (0), moderate (1–6) and severe (7–14). Questions were asked in reference to the month preceding the survey. Eight questions were asked in reference to adult(s)/household and six in reference to children who were defined as individuals under 16 years of age living in the household. At each time point, household FI was assigned a score of 0 if they were food secure, 1 if they were mildly, 2 if they were moderately or 3 if they were severely food insecure. A mean FI score was calculated across time to obtain the final mean FI level for each household throughout the duration of the study. The mean FI level was considered as a continuous variable, and was used as a covariate in the analysis. Child anthropometric measurements were converted to weight-for-age (WAZ), length-for-age (LAZ) and weight-for-length \(z\)-scores (WLZ) using the WHO Child Growth Standards (WHO Multicenter Growth Reference Study Group 2006). Mean WAZ, LAZ and WLZ for each group at each month from 1 to 12 months were calculated and compared using ANCOVA, adjusting for child sex and birth-weight, and maternal age, education, marital status, household amenities (as a proxy for socioeconomic status) and mean household FI. These variables were selected because they were either different among the three groups at baseline, or were related to growth.

We used a repeated measures analysis (SAS Proc Mixed) to determine whether the growth of children over time differed for children of mothers in the three HIV status categories with Tukey–Kramer post hoc test. A three-way HIV–age–sex interaction term reflecting sex differences in the association between HIV and growth across the first year was tested and found to be not significant and therefore was not included in the final model. In all analyses involving growth, we controlled for the child and maternal characteristics mentioned earlier. The percentage of children with \(z\)-scores \(< -2\) standard deviation at 6 and 12 months was determined.

**Ethics**

Ethical approval for the study was obtained from the Institutional Review Boards of the University of Ghana, Iowa State University, University of Connecticut and McGill University.

**Results**

**Study population**

Of the 552 women who were enrolled in the study, 503 had a live birth (Fig. 1), which included 12 sets of twins (HIV-N = 8; HIV-P = 2 and HIV-U = 2). For twin infants, both sets were in all analyses because randomly selecting and excluding one twin (using SAS ranuni) from the analyses did not change the results. At the end of 12 months of follow-up, there was complete data on 404 mother–infant dyads (80% of live births). The main reasons for maternal postpartum loss to follow-up were refusals (HIV-N = 12, HIV-P = 25 and HIV-U = 11). Moving from the study...
area was more common among HIV-U mothers. There were 22 infant deaths (HIV-N = 6, HIV-P = 13, HIV-U = 3) and 11 maternal deaths (HIV-N = 1, HIV-P = 7, and HIV-U = 3). For seven of the maternal deaths (HIV-N = 1, HIV-P = 4 and HIV-U = 2), their infants continued to be followed and, therefore, these children were not considered to have dropped out of the study. Compare those who completed the study, those who dropped out were younger had lower mean number years of education, had a greater percentage of them being single (not married), but these differences were not significant at 0.05 level of significance.

The baseline characteristics of the mothers at enrolment and for the infants at birth in relation to maternal HIV status are presented in Table 1. HIV-P mothers had less formal education, were less likely to be married, had lower socioeconomic status and were more food insecure compared with HIV-N mothers. Generally, maternal, child, and household characteristics of the HIV-U group did not differ from those of the HIV-N groups.

Infant birthweight was significantly lower ($P = 0.005$) among children of HIV-P mothers than those of HIV-N and HIV-U mothers. Significant differences in birth length were seen only between the HIV-P and HIV-N groups. The prevalence of low birthweight was not significantly different among the three groups.

**Maternal HIV status and infant growth**

Using repeated measures analysis, over the 12 month period, the WAZ of infants of HIV-P mothers was significantly lower than that of children of HIV-N mothers (overall HIV-P vs. HIV-N group difference was $-0.35 \pm 0.12$, $P = 0.009$). A significant difference
in WAZ between HIV-P and HIV-N was consistently seen each month in the ANCOVA analysis, except for ages 2, 8, 9 and 10 months (Fig. 2). Similar differences were not noted between the other HIV group comparisons. Significant growth differences associated with HIV were observed in the adjusted LAZ. Overall, the HIV-P vs. HIV-N group difference was \(-0.38 \pm 0.10, P = 0.0004\). A significant difference was consistently seen each month except for month 9 (Fig. 3). The HIV-P vs. HIV-U group difference approached significance \((-0.23 \pm 0.10, P = 0.0517)\), but these differences were only noted in the monthly analysis in months 3, 6 and 8. There was no overall difference nor monthly difference between the HIV-N and the HIV-U groups in LAZ. The patterns for WLZ was unique. Although analysis of the individual months showed no group differences, the overall HIV estimate for WLZ varied across age (age \times HIV interaction, \(P = 0.49\)) (Fig. 4). Consistently, the WAZ and LAZ of children of HIV-U mothers were between the two growth curves for children of HIV-N and HIV-P mothers. We determined stunting prevalence at 6 and 12 months; at both time points, stunting was significantly greater in children of

| Table 1. Maternal, child and household characteristics by maternal HIV status* |
|-----------------|-----------------|-----------------|-----------------|-----------------|
|                 | HIV-N           | HIV-P           | HIV-U           | \(P\) value†   |
|                 | \(n = 167\)     | \(n = 147\)     | \(n = 160\)     |                 |
| Maternal age (years) | 28.9 \(\pm\) 6.0 | 28.2 \(\pm\) 5.8 | 27.9 \(\pm\) 5.5 | 0.26 |
| Maternal education (years) | 8.3 \(\pm\) 3.4| 6.5 \(\pm\) 3.9| 7.7 \(\pm\) 3.3| <0.0001 |
| Maternal status (n, % married) | 145 (86.8)| 106 (72.1)| 132 (82.5)| 0.0002 |
| Amenities\(^1\) | 0.15 \(\pm\) 0.89| –0.31 \(\pm\) 0.81| 0.15 \(\pm\) 0.91| <0.0001 |
| Food insecurity score\(^3\)| 0.41 \(\pm\) 0.62| 0.63 \(\pm\) 0.91| 0.57 \(\pm\) 0.72| 0.02 |
| Child sex (n, %male) | 89 (51.5) | 76 (51.7) | 80 (49.4) | 0.90 |
| Birthweight (kg) | 3.14 \(\pm\) 0.50| 2.97 \(\pm\) 0.52| 3.13 \(\pm\) 0.44| 0.005 |
| Birth length (cm) | 49.3 \(\pm\) 2.80| 48.5 \(\pm\) 2.71| 49.2 \(\pm\) 2.3| 0.017 |
| Low birthweight (n, %) | 12 (7.32) | 18 (12.31) | 10 (6.12) | 0.15 |

HIV-N, HIV-negative; HIV-P, HIV-positive; HIV-U, HIV-unknown.

*Values are show as mean ± standard deviation or (%). †Analysis was analysis of variance with Ryan–Einot–Gabriel–Weich multiple range post hoc test or chi-squared test. \(^1\)Amenities factor was created from a set of 18 socioeconomic variables (household building material, access to water, electricity and ownership of appliances) using factor analysis with varimax rotation. Amenities is a continuous variable in which lower values reflect poorer status. \(^3\)Food insecurity score was determined based on mean food insecurity rating of the household (0 = no, 1 = mild, 2 = moderate and 3 = severe food insecurity). Food insecurity score at is a continuous variable; lower values reflect better food security.
HIV-P mothers than in children of HIV-N or HIV-U mothers (Table 2).

**Discussion**

The results of this study show that infants born to HIV-infected mothers had compromised growth after controlling for variation associated with maternal age, education and household characteristics. Maternal HIV infection was associated with growth faltering; this was seen in utero as exhibited by significantly low birthweight and birth length. This is consistent with other studies reported in sub-Saharan Africa (Makasa et al. 2007; Ezeaka et al. 2009). However, we did not detect a significant difference in the prevalence of low birthweight among groups because of lack of power (power is 0.43 for one-tailed test).

Some researchers have reported the negative effect on birthweight from long in utero exposure to ARV drugs, specifically, zidovudine (Briand et al. 2006). However, this would not explain the birthweight differences in our cohort, as none of the mothers at the time of recruitment was on ARV medication; only nevirapine was administered at the time of labour to the mother and at birth to the infant for the PMTCT.

Other studies in Africa reported lower mean birthweight and length (Sombie et al. 1999; Ezeaka et al. 2009) in infants of HIV-P mothers than in infants of HIV-N mothers (Weng et al. 1998; Sombie et al. 1999; Ezeaka et al. 2009). Adverse effect of maternal HIV
The WAZ and LAZ differences among groups were maintained as the children grew older.

In our study, with the exception of nine HIV-P mothers who did not breastfeed from birth, all the mothers practised exclusive breastfeeding (EBF) or predominant breastfeeding for the first 6 months. This high breastfeeding rate benefited the infants, especially those of HIV-P mothers; despite their lower growth trajectory compared with children of HIV-N or HIV-U mothers, they experienced no faltering in length during the first 5 months.

There are multiple mechanisms through which maternal HIV can affect child growth. First, socioeconomic status of the household can affect child growth through its influence on the quantity and quality of the diet as well as access to safe water, sanitation and good health behaviours (Arpadi et al. 2009). In our study, HIV-P mothers were worse off as indicated by less education, more likely not to be married and of lower socioeconomic status. Another study among Ghanaian lactating women reported that low socioeconomic status was negatively associated with EBF (Aidam et al. 2005). In our study, the HIV-P mothers had lower rates of EBF and were less likely to continue EBF from 1 to 2 months compared with HIV-N mothers (81% vs. 92%) (Marquis et al. 2007). In Tanzania and Zambia, infants born to HIV-P mothers with higher schooling showed less growth faltering compared with infants of HIV-P mothers with less education (Arpadi et al. 2009; Webb et al. 2009; McDonald et al. 2011).

Second, HIV-affected households are more likely to be food insecure. An association between household FI and infant growth in rural Bangladesh has been reported (Na et al. 2011). A likely path is that FI affects dietary intake, nutritional status and subsequently health outcomes such as child growth (Wolfe & Frongillo 2001). We examined the relationship between maternal HIV status and FI at 12 months post-partum among our study mothers. HIV-affected households experienced greater FI compared with HIV-N households (Perez-Escamilla et al. 2009). In a separate analysis, we examined the associations between HIV, persistent FI and maternal stress level. Maternal stress levels were measured with a 4-item Cohen scale (Cohen et al. 1983) and women were classified as having low or high stress 12 months after birth. HIV status was associated with high stress [adjusted odds ratio (AOR) = 2.03; 95% confidence interval (CI): 1.09–3.77] after adjusting for key household socioeconomic and demographic confounders. However, the interaction between being HIV positive and experiencing persistent FI was strongly associated with a substantial increase in maternal stress (AOR = 15.35, 95% CI 1.90–124.14) (Garcia et al. 2011). Others have reported an association between

Table 2. Prevalence of infant underweight, wasting and stunting at 6 and 12 months, by maternal HIV status, %

<table>
<thead>
<tr>
<th></th>
<th>HIV-N</th>
<th>HIV-P</th>
<th>HIV-U</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>WAZ &lt; -2 SD (at 6 months)</td>
<td>4.5</td>
<td>16.2</td>
<td>6.3</td>
<td>0.0016</td>
</tr>
<tr>
<td>WAZ &lt; -2 SD (at 12 months)</td>
<td>6.6</td>
<td>27.5</td>
<td>9.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>WLZ &lt; -2 (at 6 months)</td>
<td>2.6</td>
<td>12.6</td>
<td>6.3</td>
<td>0.0049</td>
</tr>
<tr>
<td>WLZ &lt; -2 (at 12 months)</td>
<td>4.6</td>
<td>14.7</td>
<td>5.0</td>
<td>0.0043</td>
</tr>
<tr>
<td>LAZ &lt; -2 (at 6 months)</td>
<td>3.2</td>
<td>14.4</td>
<td>2.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LAZ &lt; -2 (at 12 months)</td>
<td>6.0</td>
<td>26.5</td>
<td>5.0</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

WAZ, weight-for-age z-score; WLZ, weight-for-length z-score; LAZ, length-for-age z-score; HIV-N, HIV-negative; HIV-P, HIV-positive; HIV-U, HIV-unknown. Chi-square analysis.
FI and maternal anxiety and depression in Tanzania (Hadley & Patil 2006); they indicate that the poor quality of diet associated with FI is likely to influence anxiety and depression. FI and increased stress associated with HIV may affect child caregiving practices and ultimately growth (Webb et al. 2009).

Third, knowledge about having HIV may cause depression for the mother and may affect her caregiving practices (Mast et al. 2006), including infant feeding. Among Malawian women, common mental disorders (depression and anxiety) were associated with stunting after controlling for several maternal and child factors, including poverty, maternal nutritional status and early infant prenatal weight (Stewart et al. 2008). A study on the influence of care practices on nutritional status of Ghanaian children showed that caregivers who exhibited better quality care (responsive feeding, diversity of child’s diet, hygienic practices related to feeding) had well-nourished children (Nti & Larney 2008).

Fourth, HIV-infected mothers are likely to have poor nutritional status and low weight gain during pregnancy, both of which may compromise nutrient transfer to the fetus. Among HIV-infected mothers in Nigeria, poor maternal body weight and low body mass index were significantly associated with infant low birthweight (Ezeaka et al. 2009). Although pregnancy weight gain was not measured in our study, maternal body mass index at 6 months post-partum was significantly lower for HIV-P than for HIV-N mothers ($25.9 \pm 4.6$ vs. $23.0 \pm 4.2$; $P < 0.0001$). To our knowledge, no participant received ARV during the study period. Although currently the protocol for the management of HIV among pregnant women has changed in that they are now given ARV prophylactic from 14 weeks of pregnancy until 7 days after they stop breastfeeding (they are encouraged to breastfeed for 1 year), there still remains a substantial number of HIV-P pregnant women who never received ARV prophylactics. Between January and June 2011, of the 8346 pregnant women who tested positive for HIV, only about 39% were given ARV prophylactics (Ghana AIDS Commission 2011). Thus, despite the change in policy, the results of this study are very applicable to the situation for the majority of HIV-P pregnant women.

Fifth, children born to HIV-infected mothers experience higher rates of morbidity, such as diarrhoea and respiratory illness, in part due to compromised caregiving practices (Mast et al. 2006). Morbidity is independently associated with child growth (Villamor et al. 2004; Kuhn et al. 2005; Webb et al. 2009; Koyanagi et al. 2011). Analysis of diarrhoea incidence among our study participants showed no significant difference by maternal HIV status (Okronipa et al. 2012). However, children of HIV-P mothers with reported symptoms of post-natal depression had higher risk of diarrhoea compared with children of HIV-P mothers with no reported post-natal depression (Okronipa et al. 2012). HIV infection is associated with increased risk of depression (Ciesla & Roberts 2001) and depression is associated with increased risk of diarrhoeal illness in their children (Rahman et al. 2007). Thus, the link among maternal HIV status, maternal depression and diarrhoeal morbidity in children could be a possible mechanism through which maternal HIV infection affects child growth.

Our study had some limitations. Although we tried to control for several maternal, child and household factors, there may have been other confounders such as maternal HIV viral load and CD4 count, which are known to affect child growth, but were not taken into consideration. The differences because of HIV remained with or without the confounders. However, this should be interpreted with caution as this limited analysis only looks at a few confounders. Further analysis is needed to take into consideration the extended list of factors to give a better understanding of the mechanisms by which these factors influence growth in HIV-affected children. It is possible that there could have been some selection bias because the nature of the study did not permit random assignment of mothers to groups. Also, 80% of the initial number of pregnant women approached gave consent to participate. It is possible that those who agreed to participate are better off than those who did not agree and this could affect external validity. The study was unable to verify this as we could not collect data on unconsented subjects. However, once recruited, we did not find any significant difference in the background characteristics between those who dropped
out and those who completed the study. The study had a category of women whose HIV status was unknown, enabling the inclusion of a broad category of women. An important determinant of birthweight is gestational age, a factor not documented in the study. Previous research in a similar community in Zambia found no difference in the prevalence of prematurity related to HIV (Makasa et al. 2007); although our study cannot confirm this because of the small number of low birthweights in the sample.

We assumed that the HIV status of the women remained unchanged throughout the study. It is possible that women who tested negative at the onset of study may have become infected later. We do not know the HIV status of most of the children. Although an opportunity was provided for women to have their infants tested at 12 months of age, only 81 out of the total cohort accepted for their infants to be tested (HIV-N = 37, HIV-P = 22, HIV-U = 22). Of these, 11 tested HIV-P by PCR (HIV-N = 0, HIV-P = 7, HIV-U = 4). Not knowing the infants’ HIV status, we were unable to control for this in the analysis and thus growth differences are attributed solely to maternal HIV status. The study had a very intensive follow-up schedule. Mothers were visited twice weekly. Frequent home visits may have influenced mothers’ behaviour with respect to care given to the children. The prevalence of underweight and stunting among our study cohort by 12 months were 14.7% and 12.5%, respectively, compared with the average national figures for 9–11 months old infants of 17.8% and 16.7%, respectively (GSS 2004). During the study when mothers had questions regarding feeding or growth of their infants, they were referred to a GHS nurse for advice. These interventions may have reduced the difference in growth between groups but did not eliminate them.

A unique aspect of this study is the inclusion of a category of mothers who refused to know their HIV status (HIV-U) after going through counselling. The reasons for refusal are not clear, but fear of being diagnosed with HIV may have contributed to their decision. Interestingly, the growth of infants in this category of mothers consistently fell between the other two groups (HIV-N and HIV-P), and often was closer to the growth of infants of the HIV-N mothers. These results suggest that some of the women in the HIV-U category were HIV-P.

**Conclusion**

This study used a longitudinal design to determine the association between maternal HIV status and infant growth in the first year of life. The results suggest that maternal HIV adversely influences child growth. Background characteristics indicate that the HIV-P mothers are of lower socioeconomic status and are more likely to be food insecure, which may impact mental health and caregiving (including child feeding). Many health care facilities offer VCT for pregnant women. The HIV test will be of little value to mothers and their infants if it is not followed by comprehensive support, including the provision of ARV therapy and nutrition support for mothers and their infants. Although the PMTCT policy has changed since this study was undertaken, the fact that a majority of HIV-P pregnant women do not receive ARV prophylactics makes the findings of this study quite relevant in Ghana and other countries with similar situations. Special social services targeting such mothers and children living in vulnerable communities are urgently needed to reduce any negative impact maternal HIV is likely to have on child growth. Intensified effort to curb the spread of the disease is paramount.

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Conflicts of interest
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Contributions
AL and GSM drafted the paper; GSM, AL, RM, RPE, DS & LB designed the study and contributed to writing of the paper; WA did the PCR assays; SAA did statistical analysis; all authors contributed to the interpretation of data.

References


according to maternal and infant characteristics. *Tropical Medicine & International Health: TM & IH* **15**, 1364–1374.


