Published in final edited form as:
Trop Med Int Health. 2007 July ; 12(7): 856–861. doi:10.1111/j.1365-3156.2007.01857.x.

Influence of body mass index on pregnancy outcomes among HIV-infected and HIV-uninfected Zambian women

Yolan Banda[1,2], **Victoria Chapman**[3], **Robert L. Goldenberg**[2,3], **Benjamin H. Chi**[1,2,4], **Sten H. Vermund**[2,5], and **Jeffrey S. A. Stringer**[2,3]

1*School of Medicine, University of Zambia, Lusaka, Zambia*

2*Centre for Infectious Disease Research in Zambia, Lusaka, Zambia*

3*Center for Research in Women's Health, University of Alabama at Birmingham, Birmingham, AL, USA*

4*Schools of Public Health and Medicine, University of Alabama at Birmingham, Birmingham, AL, USA*

5*School of Medicine, Vanderbilt University, Nashville, TN, USA*

Summary

OBJECTIVES—To determine the influence of body mass index (BMI) on pregnancy outcomes of HIV-infected and HIV-uninfected Zambian women and to assess the possible role of BMI on mother-to-child transmission rate of HIV.

METHODS—We analysed data from a clinical trial on nevirapine administration for the prevention of mother-to-child transmission of HIV in Lusaka, Zambia. Demographic characteristics, medical information and pregnancy outcomes were used in this secondary analysis.

RESULTS—A total of 1211 women were included in this analysis and 36% were HIV-infected. Among HIV-infected women, maternal parity and prior stillbirths increased with increasing BMI in univariate analysis. Mean birth weight rose as well at 28.3 g [95% confidence interval (CI) =14.0-42.6] of infant weight per BMI unit. Transmission of HIV from mother to child appeared inversely related to BMI when compared according to BMI quartile (*P* for trend = 0.07). In the HIV-uninfected group, infant birth weight increased with increasing BMI, at 32.7 g(95% CI = 23.5-41.9) of infant weight per BMI unit.

CONCLUSION—Birth weight increased alongside BMI in both HIV-infected and HIV-uninfected women. There is a suggestion that women with lower BMI have a greater risk of perinatal HIV transmission, even after adjustments for HIV viral load and CD4 count.

Keywords

BMI; pregnancy outcomes; HIV; Zambian women; sub-Saharan Africa; mother-to-child HIV transmission

Introduction

Body mass index (BMI) is an anthropometric measurement for defining body composition and nutritional status. Initially, the BMI was used as a measure of obesity in developed countries,

Correspondence to: Yolan Banda.

Corresponding Author Yolan Banda, Department of Community Medicine, University of Zambia, PO Box 50110, Lusaka, Zambia. Tel.: +26 97-504109; Fax: 26-01-293766; E-mail: yolan.banda@cidrz.org.

but it is now applied to define underweight and overweight adults in countries throughout the world (World Health Organization 2000). In developed countries, poor nutritional status of women - as defined by a low BMI - has a negative effect on pregnancy outcomes, particularly low infant birth weight and preterm delivery (Ogunyemi *et al.* 1998; Ehrenberg *et al.* 2003; Neggers & Goldenberg 2003; Helgstrand & Andersen 2005).

The impact of BMI on pregnancy outcome among HIV-infected women has been less well studied. As BMI is linked to poor survival among HIV-infected individuals in many settings (Lindan *et al.* 1992; Malvy *et al.* 2001; Van der Sande *et al.* 2004), we hypothesized that low BMI in HIV-infected pregnant women would lead to higher proportions of negative birth outcomes. We performed this analysis to determine whether pregnancy outcomes differed by maternal BMI among HIV-infected and HIV-uninfected women. As a secondary aim, we studied the possible correlation between BMI and perinatal HIV transmission.

Methods

Data presented in this paper were originally collected during a clinical trial on the administration of nevirapine (NVP) for prevention of maternal to child transmission of HIV (PMTCT). Two strategies were evaluated: (i) ‘targeted’ strategy of HIV testing, with NVP administration only among women who were identified as HIV-infected and (ii) ‘universal’ strategy of NVP administration without prior HIV testing. The primary outcome of the study was maternal adherence to the intrapartum NVP regimen, determined by the presence of NVP in the infant's umbilical cord blood.

This trial was conducted in two Lusaka Health District maternity clinics between September 2000 and May 2001 and has been described in detail elsewhere (Stringer *et al.* 2003, 2004). Our study population consisted of pregnant women receiving obstetric care in the government run, public health system in Lusaka, Zambia. Women were enrolled either: (i) during prenatal care, at approximately 36 weeks' gestation or (ii) on arrival to the labour ward. All participants provided written informed consent.

Maternal HIV status was assessed using a dual rapid test algorithm previously validated in our setting (Determine HIV-1/2, Abbott Laboratories, Abbott Park, IL, USA and Capillus-1/HIV-2, Trinity Biotech, Wicklow Co., Ireland) (Stringer *et al.* 2003, 2004). Umbilical cord blood was collected from the placental specimen following delivery and tested for detectable drug levels of NVP via high performance liquid chromatography (Dailly *et al.* 2001). Those with detectable NVP in their infant's cord blood were considered NVP adherers. Those who did not have NVP detected in the cord blood were considered non-adherers, even if this was inconsistent with their self-report.

Infant HIV status was determined using DNA polymerase chain reaction (PCR) from dried blood spots taken via heelstick at birth and 6 weeks post-partum. Whole blood was collected on filter paper that lysed cells and bound the DNA, eliminating specimen centrifugation and extraction procedures; each specimen was then subjected to two independent amplifications. For the purposes of analysis, we categorized infants with a positive HIV DNA PCR at 6 weeks as HIV-infected. We did not collect additional specimens to confirm the diagnosis of infant HIV infection, nor did we attempt to delineate between intrauterine and intrapartum/early post-partum-HIV infection. Because infant HIV status was not essential to the primary outcome of the study, infant HIV testing was based on maternal choice. This study was conducted before the local availability of long-term paediatric antiretroviral therapy.

To determine our study population, we compared participants who were enrolled during prenatal care to those enrolled during labour. Significant differences in maternal height, BMI, gestational age at delivery and HIV status ($P < 0.001$ for all) were noted between the two

groups. When we controlled for these covariates in a generalized linear model (GLM), however, the effects of maternal BMI on infant birth weight were similar. Among prenatal enrollees, infant weight increased by 29.8 g/BMI unit; among labour ward enrollees, infant weight increased by 31.4 g/BMI unit. Because the relationship between BMI and infant birth weight appeared comparable regardless of time of enrollment, we collapsed the two sub-populations into one to simplify analysis.

Body mass index was computed as weight (kg) divided by height (m) squared. Measurements were taken at the time of enrollment. HIV-infected and HIV-uninfected groups were each subdivided into four separate categories according to maternal BMI quartiles. Because all women were enrolled late in the third trimester of pregnancy, we chose to categorize study participants based on these quartiles rather than internationally accepted thresholds for underweight, overweight and obese individuals (World Health Organization 2000). To have uniform cut points, quartiles were obtained for the combined group before splitting them into HIV-infected and HIV-uninfected women. Quartile one (Q1) was defined as BMI ≤22.7; Q2 as BMI >22.7 and ≤24.5; Q3 as BMI >24.5 and ≤26.8 and Q4 was defined as BMI >26.8.

Both univariate and multivariate analyses were conducted. In univariate analyses, proportional data were compared using Mantel-Haenszel chi-square or the Fisher exact test as appropriate. Analysis of variance (ANOVA) was used to compare the differences in the means in the four BMI quartile groups. For the multivariate analyses, logistic regression and GLM procedures were used. BMI was thus used both as a continuous and categorical (according to quartiles) variable. Data were analysed with SAS, version 8.1 (SAS institute, Cary, NC, USA). Statistical significance was set at $P < 0.05$; all tests were two sided. The study was approved by both the University of Alabama at Birmingham Institutional Review Board and the University of Zambia Research Ethics Committee.

Results

The study population for this secondary analysis comprised three groups. Among women enrolled at 36 weeks' gestation, there were 121 HIV-infected women enrolled at clinics using the ‘targeted’ strategy for NVP administration, and 484 HIV-infected and HIV-uninfected women enrolled at clinics using the ‘universal’ strategy for NVP administration (Stringer *et al.* 2003). Another 634 women were enrolled at time of labour to receive NVP without prior HIV testing (Stringer *et al.* 2004).

Of these 1239 participants, 1211 (98%) were interviewed at the time of enrollment to collect demographic and medical information. These women had a mean age of 24.2 ± 5.5 years and 6.7 ± 2.9 years of education. Mean BMI at enrollment for all women was 24.9 ± 3.3. Thirty-six per cent were HIV positive. HIV-infected women tended to be older (24.8 ± 5.2 *vs*. 23.6 ± 6.0; $P < 0.01$) and were more likely to have been treated recently for a sexually transmitted disease (21.6% *vs*. 9.7%; $P < 0.01$).

Maternal characteristics of each of the four BMI quartile groups for HIV-infected and HIV-uninfected women are reported in Table 1. Among the 430 HIV-infected women, there were no significant differences across the four BMI quartile groups in terms of maternal age, income, education, marital status, breastfeeding, CD4 count and HIV viral load. BMI appeared to be directly related to parity ($P = 0.01$). In univariate analysis, history of stillbirth was also related to BMI, with women with higher BMI having had more prior stillbirths (P 0.02); however, this relationship did not persist when parity was taken into account ($P = 0.12$). Among the 781 women who were HIV-uninfected, those with higher BMI were older, had more income and had greater parity. However, no differences were noted by BMI quartile in maternal education, marital status, breast-feeding or history of stillbirths among these women.

Pregnancy outcomes across the four maternal BMI quartile groups for both HIV-infected and HIV-uninfected mothers are reported in Table 2. Among the infants of HIV-infected women, crown heel length, head circumference and 1- and 5-minute Apgar scores were not significantly different across the four BMI categories. Among the infants of HIV-uninfected group, statistically significant differences were observed in the distribution of 1- and 5-minute Apgar scores ($P = 0.04$ for both).

To better understand the relationship between BMI and infant birth weight, we performed separate multivariable analyses according to maternal HIV status via GLM. In each, adjustments were made for covariates, such as age, parity, income and time of enrollment. In the HIV-infected group, infant birth weight increased by 28.3 g [95% confidence interval (CI) = 14.0- 42.6; $P < 0.0001$] for every unit increase in BMI. Among HIV-uninfected women, infant birth weight increased by 32.7 g (95% CI = 23.5- 41.9; $P < 0.0001$) for every unit increase in BMI. The incremental gains in infant birth weight according to BMI were not statistically different between the two groups ($P = 0.13$). No interactions were seen between BMI and covariates in either model.

Overall, 276 of 430 HIV-infected participants agreed to HIV testing for their newborn. Of these, 30 (10.9%) were diagnosed as HIV-infected based on their 6-week PCR test. In the univariate analysis, proportions of women transmitting HIV to their infants in each BMI quartile were as follows: 10/64 (15.6%) in Q1; 10/76 (13.2%) in Q2; five of 65 (7.7%) in Q3 and five of 71 (7.0%) in Q4. This overall distribution did not demonstrate statistical significance ($P = 0.30$); however, there was a suggestive inverse association between perinatal HIV transmission and BMI (P for trend = 0.07). When women below the median BMI were compared with those above it, thinner women were almost twice as likely to transmit HIV to their infants (12.8% *vs.* 7.3%, $P = 0.11$); in a multivariate analysis controlling for CD4 count, viral load and NVP adherence, the relative risk for infant HIV transmission at 6 weeks was 1.7 (95% CI = 0.7-4.1).

Discussion

Our primary objective for this analysis was to determine the impact of BMI on pregnancy outcome among HIV-infected and HIV-uninfected women in a sub-Saharan African setting. Among HIV-infected individuals, no association was detected between BMI and crown heel length, head circumference and Apgar scores. Among the HIV-uninfected women, only the distributions of 1- and 5-minute Apgar scores were statistically different; however, the clinical significance of this finding is unclear. In both groups, there appeared to be strong linear associations between BMI and infant birth weight.

In our analysis, BMI appeared to have similar effects on birth weight in both HIV-infected and HIV-uninfected women. This relationship is consistent with other previously described populations in the developed and developing world, suggesting that factors that influence pregnancy outcomes in HIV-infected women are similar to those for the general population (Dreyfuss *et al.* 2001). These findings also refute our original hypothesis that HIV infection and low BMI may have a compounded effect on negative pregnancy outcomes.

Although much of the medical literature in developing countries focuses on individuals with low BMI, we recognize that there is greater risk for adverse pregnancy outcomes at the both ends of the spectrum. Obesity in pregnancy has been associated with obstetric complications and poor outcomes in numerous studies (Doherty *et al.* 2006; Smith *et al.* 2007). In our analysis, we did not observe an increased likelihood of poor outcomes among women in the highest BMI quartile. These findings may have been as a result of our categorization of patients based on BMI distribution among study participants (i.e. quartiles), rather than established

international classifications. It may have also resulted from our outcome measures, which described fetal growth and infant status at time of birth but did not describe obstetric complications or maternal co-morbidities.

As a secondary objective, we studied the relationship between BMI and perinatal HIV transmission. There appeared to be a suggestive inverse relationship between BMI and perinatal HIV transmission, with thinner women having higher rates of HIV transmission to their infants. This finding remained consistent even in multivariable models controlling for markers of advanced HIV disease. While the results did not meet our a *priori* definition of statistical significance, this possible association deserves additional investigation. This is particularly interesting given the sparse — but consistent — literature describing the lack of association between BMI and perinatal HIV transmission. For example, Semba *et al.* (1994) found that the BMI did not predict infant HIV acquisition in a cohort in Malawi. Burns *et al.* (1999) demonstrated an association between the two factors in univariate analysis; however, this finding faded under multivariable analysis.

In summary, we demonstrated few differences in pregnancy outcomes between HIV-infected and HIV-uninfected women in Lusaka, Zambia. BMI was associated with a linear increase in infant birth weight regardless of maternal HIV status. Taken together, these results point to the importance of increased caloric intake and increased maternal weight to pregnancy outcome. From a policy perspective, antenatal programmes that monitor and improve nutritional status can also increase birth weight of enrolled infants, regardless of the HIV status of their mothers. Further investigation is needed to better delineate the relationship between low BMI and increased perinatal HIV transmission.

Acknowledgements

The work reported herein was supported a grant from the Elizabeth Glaser Pediatric AIDS Foundation). Additional investigator salary or trainee support is provided by the National Institutes of Health (K23-AI01411; K01-TW06670; P30-AI027767; D43-TW001035) and the Elizabeth Glaser Pediatric AIDS Foundation (EGSA 19-02).

References

Burns DN, Fitzgerald G, Semba R, Hershow R, Zorrilla C, Pitt J, Hammill H, Cooper ER, Fowler MG, Landesman S. Vitamin A deficiency and other nutritional indices during pregnancy in human immunodeficiency virus infection: prevalence, clinical correlates, and outcome. Clinical Infectious Diseases 1999;29:328–334. [PubMed: 10476737]

Dailly E, Thomas L, Kergueris MF, Jolliet P, Bourin M. High-performance liquid chromatographic assay to determine the plasma levels of HIV-protease inhibitors (amprenavir, indinavir, nelfinavir, ritonavir and saquinavir) and the nonnucleoside reverse transcriptase inhibitor (nevirapine) after liquid-liquid extraction. Journal of Chromatography B 2001;758:129–135.

Doherty DA, Magann EF, Francis J, Morrison JC, Nwenham JP. Pre-pregnancy body mass index and pregnancy outcomes. International Journal of Gynaecology Obstetrics 2006;95:242–247. [PubMed: 17007857]

Dreyfuss ML, Msamanga GI, Spiegelman D, et al. Determinants of low birth weight among HIV-infected pregnant women in Tanzania. American Journal of Clinical Nutrition 2001;74:814–826. [PubMed: 11722965]

Ehrenberg HM, Dierker L, Milluzzi C, Mercer BM. Low maternal weight, failure to thrive in pregnancy, and adverse pregnancy outcomes. American Journal of Obstetrics Gynecology 2003;189:1726–1730. [PubMed: 14710105]

Helgstrand S, Andersen AM. Maternal underweight and the risk of spontaneous abortion. Acta Obstetrics Gynecology Scandinavica 2005;84:1197–1201.

Lindan CP, Allen S, Serufilira A, et al. Predictors of mortality among HIV-infected women in Kigali, Rwanda. Annual International Medicine 1992;116:320–328.

Malvy D, Thiébaut R, Marimoutou C, Dabis F. Weight loss and body mass index as predictors of HIV disease progression to AIDS in adults. Aquitaine cohort, France, 1985-1997. Journal of the American College of Nutrition 2001;20:609–615. [PubMed: 11771676]

Neggers Y, Goldenberg RL. Some thoughts on body mass index, micronutrient intakes and pregnancy outcome. Journal of Nutrition 2003;133:1737S–1740S. [PubMed: 12730492]

Ogunyemi D, Hullett S, Leeper J, Risk A. Prepregnancy body mass index, weight gain during pregnancy, and perinatal outcome in a rural black population. Journal of Maternal Fetal Medicine 1998;7:190–193. [PubMed: 9730485]

Semba RD, Miotti PG, Chiphangwi JD, Saah AJ, Canner JK, Dallabetta GA, Hoover DR. Maternal Vitamin A deficiency and mother-to-child transmissions of HIV-1. The Lancet 1994;25:1593–1597.

Smith GC, Shah I, Pell JP, Crossley JA, Dobbie R. Maternal obesity in early pregnancy and risk of spontaneous and elective preterm deliveries: a retrospective cohort study. American Journal of Public Health 2007;97:157–162. [PubMed: 17138924]

Stringer JS, Sinkala M, Stout JP, et al. Comparison of two strategies for administering nevirapine to prevent perinatal HIV transmission in high-prevalence, resource-poor settings. Journal of Acquire Immune Deficiency Syndrome 2003;32:506–513.

Stringer JS, Sinkala M, Goldenberg RL, et al. Universal nevirapine upon presentation in labor to prevent mother-to-child HIV transmission in high prevalence settings. AIDS 2004;18:939–943. [PubMed: 15060442]

Van der Sande MA, Schim van der Loeff MF, Aveika AA, et al. Body mass index at time of HIV diagnosis: a strong and independent predictor of survival. J Acquire Immune Deficiency Syndrome 2004;37:1288–1294.

World Health Organization. Obesity: preventing and managing the global epidemic: report of a WHO consultation. WHO Press; Geneva: 2000. WHO Technical Report Series 894.

Table 1

Maternal Characteristics by BMI quartiles (Q)

	HIV-infected (*n* = 430)					HIV-uninfected (*n* = 781)				
	Q1 (*n* = 101)	**Q2 (*n* = 109)**	**Q3 (*n* = 98)**	**Q4 (*n* = 114)**	***P*-value**	**Q1 (*n* = 192)**	**Q2 (*n* = 186)**	**Q3 (*n* = 195)**	**Q4 (*n* = 186)**	***P*-value**
BMI, mean (SD)	21.2 (1.2)	23.6 (0.5)	25.5 (0.7)	29.3 (2.4)	-	21.2 (1.3)	23.5 (0.5)	25.6 (0.7)	29.4 (2.5)	-
Age, mean (SD)	24.1 (4.5)	24.3 (4.7)	24.9 (5.8)	25.8 (5.8)	0.11	22.9 (5.8)	23.2 (5.4)	23.2 (6.1)	25.1 (6.3)	<0.0001
Weekly income, USD, mean (SD)	4.72 (10.00)	4.41 (5.67)	6.94 (17.74)	4.96 (4.95)	0.39	3.67 (5.79)	4.37 (5.17)	5.91 (9.88)	6.74 (11.30)	<0.0001
Years education, mean (SD)	6.8 (2.9)	6.2 (2.9)	6.7 (2.8)	7.1 (2.6)	0.13	6.4 (3.0)	6.5 (2.9)	7.1 (2.8)	6.8 (2.9)	0.14
Parity, mean (SD)	1.5 (1.3)	1.9 (1.4)	2.0 (1.6)	2.2 (1.8)	0.01	1.4 (1.5)	1.5 (1.6)	1.8 (1.9)	2.1 (2.0)	<0.0001
% married	90.1%	94.5%	91.8%	93.9%	0.45	93.2%	93.0%	93.3%	94.6%	0.57
% breast-feeding	95.2%	97.9%	94.9%	97.8%	0.56	96.0%	97.2%	98.0%	96.9%	0.57
% prior stillbirth	4.0%	8.3%	12.2%	12.3%	0.02	9.3%	7.0%	8.7%	6.4%	0.42
CD4 count	355 (198)	370 (213)	392 (212)	377 (206)	0.66	-	-	-	-	-
% CD4 <200	22.8%	21.1%	14.7%	21.2%	0.57	-	-	-	-	-
Log10 viral load	5.04 (4.87)	4.87 (5.08)	4.91 (5.18)	4.85 (5.27)	0.47	-	-	-	-	-
% adherent to nevirapine	63.4%	69.7%	66.3%	67.3%	0.66	-	-	-	-	-

See text for BMI ranges for Q1 (lowest) to Q4 (highest).
Unless otherwise noted, continuous variables are expressed in mean (SD).
BMI, body mass index; USD, US dollar equivalent.

Trop Med Int Health. Author manuscript; available in PMC 2008 October 20.

Table 2

Pregnancy outcomes by body mass index quartiles

	HIV-infected (*n*= 430)					HIV-uninfected (*n* =781)				
	Q1 (*n* = 101)	**Q2 (*n* = 109)**	**Q3 (*n* = 98)**	**Q4 (*n* = 114)**	***P*-value**	**Q1 (*n* = 192)**	**Q2 (*n* = 186)**	**Q3 (*n* = 195)**	**Q4 (*n* = 186)**	***P*-value**
Birth weight (g), mean (SD)	2924 (366)	2990 (366)	3025 (438)	3193 (392)	<0.0001	2918 (397)	2966 (374)	3093 (417)	3242 (397)	<0.0001
Crown-heel length (cm), mean (SD)	49.8 (10.5)	50.9 (10.2)	50.3 (12.0)	51.4 (8.4)	0.72	51.2 (7.3)	50.9 (8.3)	51.7 (7.0)	52 (6.8)	0.75
Head circumference (cm), mean (SD)	36.9 (7.6)	37.3 (7.1)	36.7 (8.6)	38.3 (6.1)	0.49	38.0 (4.8)	38.0 (6.0)	38.5 (5.0)	38.9 (4.8)	0.40
1-minute Apgar, mean (SD)	8.9 (0.3)	8.7 (1.4)	8.9 (0.4)	8.8 (1.3)	0.30	8.1 (1.1)	9.0 (0.2)	8.7 (1.6)	8.9 (0.7)	0.04
5-minute Apgar, mean (SD)	9.1 (0.4)	8.9 (1.4)	9.1 (0.4)	9.0 (1.3)	0.35	9.0 (1.1)	9.1 (0.3)	8.9 (1.5)	9.2 (0.8)	0.04

See text for BMI ranges for Q1 (lowest) to Q4 (highest).
Unless otherwise noted, continuous variables are expressed in mean (SD).