CHAPTER 6 - ANTHROPOMETRIC MEASUREMENTS AMONG HIV-INFECTED WOMEN OVER A 24 MONTH PERIOD

6.1. OBJECTIVES

1. To establish the longitudinal changes in body composition, as measured by select anthropometric measurements, amongst a cohort of HIV-infected women from six weeks until 24 months after delivery.
2. To determine the factors that impact on maternal anthropometric measurements over a 24-month period of postnatal follow-up.

6.2. SUBJECTS AND METHODS

HIV-infected women were consecutively recruited from four clinics offering antenatal care (ANC) and PMTCT services in Tshwane between 2003 and 2005 and were followed-up for a period of 24 months after delivery. The four clinics from which the women were recruited are in the peri-urban Mamelodi and Atteridgeville townships. Details on the methodology are described in Chapter 4.

A sample of 53 HIV-negative women was recruited as a comparison group at six weeks postpartum and they were assessed on nutritional status, biomarkers and infant feeding practices at this time only.

6.2.1. Anthropometric measurements

Anthropometric measurements were taken of mothers during the six-week visit as proxy indicators of body composition. These included mid-upper arm circumference measurements (MUAC) and determination of body mass index.

Body mass index (BMI) was calculated as weight in kg divided by height in metres squared. MUAC is the circumference of the left upper arm, measured at the mid-point between the tip of the shoulder and the tip of the elbow (olecranon process and the acromium). Mid-upper arm circumference was measured using a non-stretchable tape.

Height was taken without shoes and measured to the nearest 0.1 cm using a stadiometer (Scales 2000, Durban, SA) and weight was measured in light clothing to the nearest 100g using an electronic digital scale (Scales 2000, Durban, SA). The control mothers were only measured at six weeks postnatally whilst the HIV-infected mothers were measured at intervals between six weeks postnatally and 104 weeks (equivalent to 24 months).

6.3. STATISTICAL ANALYSES

Distributions of anthropometric measurements and indices by HIV status were determined. Anthropometric measurements among HIV-negative women were only taken at six weeks after delivery and not continued thereafter. All the anthropometric measurements that were not normally distributed were logarithmically transformed. Adjusted differences by HIV status were obtained from ANOVA models for repeated measures, in which CD4 count and ferritin were covariates. The same analysis was repeated by infant feeding practice of the mothers. Differences were considered to be statistically significant between the groups at $p \leq 0.05$. All analyses were carried out using the STATA statistical software package version 9.

To compare differences in anthropometric measurements and body composition between the HIV-infected and non-infected women, the t-test was used. The

next phase was to compare groups controlling for ferritin and CD4 cell count, both of which are measures of the inflammatory response.

6.4. RESULTS

6.4.1. Comparison between the baseline anthropometric measurements of HIV-infected and un-infected women at six weeks post-delivery

Table 6.1 indicates that at six weeks postpartum, the HIV-negative women weighed on average less and had lower BMI than HIV-infected women. The differences between the groups was significant only for MUAC ($p<0.05$). The differences between the two groups of women remained significant only for BMI ($p=0.037$), with HIV-infected women having a greater BMI than their HIV-negative counterparts. The differences were not significant for MUAC and weight after controlling for baseline CD4 count. Using ferritin concentration as a marker of the inflammatory response and controlling for it, there was no significant difference between the groups for weight ($p=0.6549$) and for BMI ($p=0.148$), however for MUAC the difference remained significant ($p=0.0466$). Both groups of mothers had a mean BMI falling into the overweight category of BMI$\geq$25 and none of the mothers at six weeks postpartum had a MUAC $\leq$ 23 cm, which is the cut-off for underweight. Both comparison and study subjects were well nourished.

Table 6.1: Comparison of Anthropometric measurements at six weeks postpartum between HIV-infected and HIV-uninfected mothers

Anthropometic Indicator	HIV-infected	N	HIV-un-infected	N	p-value
Mean Wt (SD) Kg	66.4 (12.7)	191	64.7 (12.8)	49	0.4048
Mean BMI (SD) kg/m²	26.3 (5.67)	187	25.0 (4.85)	49	0.1236
Mean MUAC(SD) Cm	29.9 (3.79)	157	28.5(3.69)	47	**0.0250**

6.4.2. Anthropometric measurements and infant feeding practices

In order to determine if there was any effect of infant feeding practice on anthropometric measurements, we assessed anthropometric data at six weeks and also at six months between HIV-infected formula- and breastfeeding women (see Table 6.2). The sample sizes differ between the two tables as measurements because of missing data.

As depicted in Table 6.2, at six weeks and at six months after delivery the most significant differences in anthropometric measurements between formula-feeding mothers and their breastfeeding counterparts were for BMI and MUAC ($p<0.05$). At both visits, the BMI and MUAC of the breastfeeding mothers were lower. At this same time there was no significant difference in CD4 cell count by feeding group.

Table 6.2: Anthropometric measurements and CD4 counts by feeding mode at six weeks and at six months postpartum

At 6 weeks:

Anthropometric Indicator	Formula feeding	N	Breastfeeding	N	P-value
Mean Wt (SD) Kg	67.68 (13.17)	124	64.28 (11.63)	56	0.0994
Mean BMI (SD) kg/m²	26.82 (5.55)	121	24.83 (4.57)	56	**0.0203**
Mean MUAC (SD) Cm	30.41 (3.74)	103	28.96 (3.69)	45	**0.0225**
Mean CD4 cell count (SD)	457 (247)	125	458 (251)	56	0.9793

At 6 months:

Anthropometric Indicator	Formula feeding	N	Breastfeeding	N	P-value
Mean Wt (SD) Kg	67.78 (14.53)	120	63.28(13.43)	41	0.0831
Mean BMI (SD) kg/m²	27.1 (6.29)	117	24.81 (5.51)	41	**0.0392**
Mean MUAC (SD)	30.6 (3.96)	96	28.92 (4.18)	34	**0.0345**

Cm					
Mean CD4 cell count (SD)	390 (210)	134	399(226)	56	0.7733

Between the six week and six month visit the HIV-infected breastfeeding women lost almost 1kg of weight from an average of 64.27kg to 63.28kg, whilst the formula-feeding women gained 0.10kg between six weeks and six months.

6.4.3. Comparison between anthropometric measurements of HIV-infected women from six weeks to 24 months after delivery

Table 6.3 indicates that over a 24-month period the HIV-infected women in this study significantly gained weight and had higher BMI levels as compared to the baseline measurement ($p<0.05$). The MUAC levels tended to remain almost constant with an increment of only 0.3cm between the first and last visits.

Table 6.3: Trends in anthropometric measurements among HIV-infected women between the first (baseline) visit and the last visit (24 months postnatally)

Indicator	**First visit Mean (SD)**	**Last visit Mean (SD)**	**Change**	**p-value**
Weight (kg)	66.4 (12.7) Range: Min: 41 Max: 109 N = 191	68.2 (15.4) Range: Min: 38 Max: 139 N = 162	+1.8	0.0028
BMI (Kg/m²)	26.37 (5.67) Range: Min: 17.9 Max: 57.2 N=187	26.94 (6.13) Range: Min: 16.5 Max: 55.3 N=147	+0.57	0.0038
MUAC (cm)	29.8 (3.79) Range: Min:16 Max:41 N=157	30.1 (4.45) Range: Min:20.5 Max:49 N=137	+ 0.3cm	0.4439

Given that BMI differences between the baseline and the last visit 24 months after delivery remained significant, there was also interest to asses the BMI levels in relation to the reference categories.

6.4.4. Comparing the BMI between the first visit and the last visit by the reference categories

As depicted in Figure 6.1, very few of the study women fell within the underweight category at baseline and the final visit. However, there was a slight decline (10.2%) over 24 months in the percentage of women falling into the normal BMI range and also in the overweight range (6.8%). However, there was notable increase in the percentage of women from baseline to the final visit who were categorised as obese (16.7%).

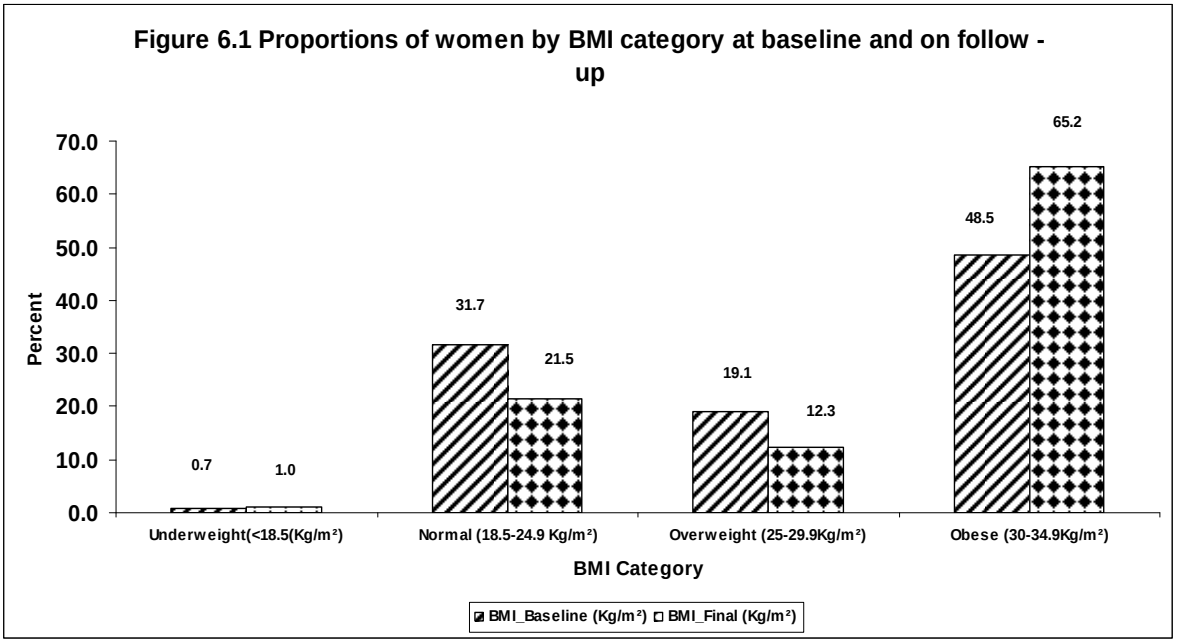

Figure 6.1: Proportions of women by BMI category at baseline and on follow-up

6.4.5. Health status of HIV-infected women over a 24 month period

In order to determine the current state of health of the mothers we asked about the existence of any illnesses since the previous visit date. The types of reported illnesses that the mothers stated included the following: 28 (29.79%) mentioned influenza, 17 (18.09%) diarrhoea, ten (10.64%) each mentioned STI's, headache and rash and five (5.32%) mentioned oral thrush. Only one mentioned having tuberculosis. None of this data was verified by a review of medical records of the mothers.

Due to the poor quality of the dietary intake data it was not possible to assess the trends over time in dietary intake in comparison to the anthropometric data of the mothers enrolled in this study.

6.5. DISCUSSION

Our study findings are important in that, unlike other studies in Africa that have documented anthropometric measurement changes among HIV-infected women in pregnancy[80,83],[192,] or among rural HIV-infected lactating women[8], we investigated anthropometric measurement changes as proxy measures of body composition among peri-urban women over a 24-month period after delivery.

Selection of both MUAC and BMI as measures of body composition among the study participants was primarily based on the simplicity of their collection at the clinics and the fact that they are less invasive techniques and affordable within the public health system. However, some researchers[19,193] state that whilst both BMI and MUAC are useful in predicting fat mass they are not useful for determining fat free mass among HIV-positive women and that bio-impedence spectroscopy (BIS) may be a better alternative for this purpose. Others have used skinfold measurements to assess body composition, however this measurement is considered problematic and unreliable as there is a need for

"fastidious attention to standardisation and significant training and practice in order to obtain accurate results."[63]

In accordance with recommendations made by others[8,79] , we undertook baseline measurements of all the HIV-infected and non-infected women at six weeks postpartum, by which time we had estimated that the anthropometric measurements indices would have returned to pre-pregnancy values.

In comparison to the cut-off points for BMI, very few of the study mothers and the control group were underweight (BMI $\leq$ 18.5). Most of the study mothers had BMI ranges falling into the normal range (18.5 to 24.9 kg/m²) and even the overweight range (25.0 to 29.9 kg/m²).[62] These findings may indicate that the pre-pregnancy body weight measurements of the women in this study were either high or within the expected range for their height. This is similar to findings from Rwanda where none of the HIV-infected and non-infected women suffered from chronic energy deficiency in the pre-pregnancy period.[83]

The finding that BMI levels were high but not significantly different (p = 0.1236) among the HIV-infected women (26.3kg/m²) as compared to the HIV-negative controls (25.0kg/m²) in this study is consistent with findings from the North West Province, where the mean BMI among HIV-infected women was 26.1kg/m² and for the uninfected women 27kg/m². These North West study researchers attributed the high BMI to the fact that most of the infected women were asymptomatic and in the early stages of the disease.[139] This same explanation could be the case for our study participants who were also at the asymptomatic stage of HIV disease for the most part for the first two years.

Our findings of a relatively small (1kg only) weight loss among the breastfeeding HIV-infected mothers between six weeks and six months is highly similar to data in KwaZulu-Natal where weight loss (1.4kg between eight weeks and 24 weeks)

amongst lactating women occurred, even though 95% of the mothers in their study had CD4 cell counts above 200cells/mm^3. The KwaZulu-Natal study established that whilst the breastfeeding women lost weight between the two visits, their BMI levels remained high, BMI > 20kg/m^2.[8] Similarly, we found that the mean CD4 cell count among the breastfeeding mothers at six weeks and six months was greater than 200 cells/mm^3, implying that there was no evidence of severe immuno-suppression at this time. Even at six months the breastfeeding mothers still had mean CD4 cell counts (399 cells/mm^3) that were slightly higher than amongst the formula-feeders at this time. The difference in weight was due to breastfeeding even though there was no effect on the immune status. From a socio-economic perspective, the formula-feeding HIV-infected mothers had an insignificantly higher socio-economic score than their breastfeeding counterparts and this may have had a positive or protective effect on their weight as they could have also had a greater food-purchasing power, though this aspect was not fully investigated in this study.

All lactating women have physiologically increased energy needs post-partum regardless of their HIV status. If these physiological needs for energy are not met, it is possible that the energy cost of lactation that may result in weight loss due to increased energy requirements.[5] It has also been reported elsewhere that the weight and fat loss that is observed among women during lactation is independent of the length of breastfeeding, but rather that it results from a negative energy balance and dietary restriction that is self-imposed by mothers wanting to lose body fat accumulated during pregnancy, or it may be attributable to metabolic or hormonal influences.[78] We did not investigate these factors. Regardless of our findings, wherein we had a minority of mothers chosing to breastfeed and where post-partum weight loss was minimal, it has been recommended by other authors that in particular breastfeeding HIV-infected mothers should be provided with nutritional support to avoid any risks to maternal health such as weight loss due to fat mass loss or fat free mass

reduction.[185] Whilst our findings did not necessarily corroborate these recommendations, on a public health level it may be more appropriate to support a targeted nutritional supplementation approach, prioritising HIV infected women with low anthropometric indices and multiple micronutrient deficiencies.

There is a need for caution in the interpretation of the results in this study, especially when comparing anthropometric measurements between HIV-infected and non-infected breastfeeding women, as there were very few HIV-infected breastfeeding women in the study and this may have had an effect on the results.

Furthermore, this study did not assess trends in anthropometry among the HIV-negative mothers beyond the six weeks after delivery. Perhaps if this had been done it would have provided a better indication as to whether the trends in weight loss among breastfeeding HIV-infected mothers fall within a physiological norm or whether this change is only attributable to the HIV infection itself. Given the fact that our research was conducted in a peri-urban setting, it is possible that there was access to greater variety of foods and possibly more energy-dense sources, which could have resulted in greater weight gain in our study mothers. Our study findings reflect that there was a true difference between HIV-infected breastfeeding women and non-breastfeeding HIV-infected women, with the former losing 1Kg of body weight, whilst the latter remained at the same weight between six weeks and six months. However caution is warranted in the interpretation of this result as this difference may be reflective of a normal physiological occurrence and is to be expected regardless of the HIV status of individual women.

Regardless of infant feeding practice, overall, formula-feeding mothers had no significant change in weight, MUAC and BMI. Similarly, anthropometric trends among the breastfeeding mothers also did not change significantly between six

weeks and six months. As such, it is not possible to attribute the observed 1kg weight loss among breastfeeding mothers to feeding mode only. It is possible that the weight loss was in line with the expected levels postpartum or that the mothers were returning to their pre-pregnancy weight levels.

Our research did not use more sophisticated and accurate measurements of body composition which have been used in other studies of this nature and thus could not determine if the weight loss was attributable to greater lean or fat mass loss. Others have documented, using bioelectrical impedence analysis, that HIV-infected underweight women in the USA tended to preferentially lose fat mass whilst conserving their body cell mass.[85]

Interestingly there was a significant difference between the first and the last mean BMI measurements in the study group, reflecting an overall increase of 0.57kg/m². This could, in part, be attributable to a better disease profile, increased access to a varied diet or fewer reported opportunistic infections. However, considering that several of the mothers in this study were also accessing micronutrients and other dietary supplements (see Chapter 7), this may have also resulted in the changes observed. The study findings are similar to those from the Free State Province, which did not find significant reductions in anthropometric measurements among HIV-infected patients and HIV-negative patients, primarily because the former were asymptomatic and in the early stages of disease progression.[139]

The South African Demographic and Health Survey (SADHS) of 2003[57] indicated that in the age group 15–24 years, 11.2% of South African women were classified as obese; this age group being the one closest to the ages of our study participants. Furthermore, the SADHS indicated that 23% of all women were obese with a BMI > 30kg/m² and 29% of these women were classified overweight with a BMI between 25kg/m² and 29.9kg/m². It would appear that

being overweight is particularly prevalent among black women, of whom 28.4% were obese and 27.8% were overweight. It is important to note, however, that the HIV sero-status of these women in the SADHS was unknown and it was assumed that most were healthy persons. In our study, 48.5% of women were considered obese by six weeks postpartum. It is possible that HIV infected women in our study were over-compensating for their HIV status by consuming a higher energy dense diet or that based on local health messaging they too had come to believe that HIV infected persons required increased intake of energy sources. Given that the prevalence of obesity increased to 65% at the end of the follow-up period, there is a need to promote consumption of a prudent diet for all persons in the South African society regardless of HIV status. The notable increase in mean BMI levels among our study group was surprising considering that the claimed median per capita monthly income in the households in which the study mothers resided was R320.00 and the Inter-quartile Range (IQR) was R345.97. There were 185 (63%) participants whose per capita income was below R431.00, the national poverty line in 2006. Given the poverty data we found, it is probable that mothers were able to consume foods or lead sedentary lifestyles which could have resulted in the higher BMI levels we observed. It is of concern that some researchers have found very few overweight or obese African women in South Africa who view themselves as being overweight and instead associate thinness with HIV and AIDS. [194]

The assessment of body composition among HIV-infected persons needs to take into consideration any other co-infections that may be present.[65] Whilst we did not systematically verify the illnesses that the mothers in our study had, at every visit they were asked to state any illnesses they had experienced since the last visit. Unlike other findings among HIV-infected men and women, it would appear that there was minimal co-infection in our study mothers.

An additional factor that may have influenced the trends we observed in anthropometric measurements among the study mothers could have been that some of the study participants had initiated HAART. In South Africa, HAART was introduced within the public health institutions from 1 April 2004, halfway through this study's follow-up period. By the end of the 24 month follow-up period there were 31 women who were on HAART. It has been documented that amongst persons on HAART disturbed fat compartmentalisation and elevated CRP levels may occur.[195] Others have not found fat mass changes amongst persons on HAART, but rather increased bone mass loss.[90] Considering that none of our patients had been on HAART for longer than two years, it is highly unlikely that during the 24-month period of observation these metabolic changes would have been observed. Our study was also not designed to determine the levels of adherence to ARV therapy among the clients and the impact on anthropometry, so we relied on hospital records and the participants' own recall of taking ARV therapy.

The importance of continued monitoring and assessment of nutritional parameters among HIV-infected persons has been emphasised to enable early intervention as required and to avoid more detrimental consequences of HIV-related immuno-suppression and malnutrition.[196] Others have recommended that in South Africa the prevention and treatment of obesity should focus on, amongst other interventions, high level political support and community mobilisation, and behaviour change communication. Further, there should be emphasis on healthy weight goals, increasing levels of physical activity, and identification of persons at risk of obesity at the primary health care level through routine monitoring.[194] Whilst our follow-up period was limited to 24 months, we observed minimal weight loss in our study cohort and, instead, we observed that the majority of the mothers enrolled fell into the overweight and obese BMI categories, which in itself raises concern and requires further monitoring to prevent the onset of non-communicable diseases of lifestyle.

6.6. SUMMARY

The value of our study is that it provides information on changes in anthropometric measurements over a period of two years among HIV-infected women living in a peri-urban setting of South Africa, whereas other studies conducted among the same women had shorter follow-up periods. Whilst we did not detect under-nutrition and wasting, as documented in other studies among HIV-infected persons, our findings point to the importance of continued monitoring and assessment of nutritional parameters, such as anthropometry, among HIV-infected women from as early a stage as possible and preferably at the community level. The follow-up care for HIV-infected mothers should also aim at preventing obesity and ensure that optimal nutritional status, as close as possible to the normal BMI ranges, is maintained.

Our study points to a high prevalence of obesity even among HIV-infected, though asymptomatic, women in Tshwane. We have not observed a significant decline of nutritional status with time even amongst those women where immune status was compromised.

CHAPTER 7 - MICRONUTRIENT STATUS AMONG HIV-INFECTED MOTHERS IN TSHWANE, 2003-2005

7.1. OBJECTIVES

1. To compare the six-week postnatal levels of micronutrients among HIV-infected and HIV-uninfected women.
2. To describe any changes in micronutrient status over a 24-month period of follow-up.
3. To determine the factors that impact on maternal micronutrient status over a 24-month period of follow-up after delivery.

7.2. SUBJECTS AND METHODS

The enrolled HIV-infected women in the Serithi project provided a venous blood sample at six weeks postpartum and at six, 12, 18 and 24 months after delivery. The blood collected was used to measure selected vitamins and minerals as well as biomarkers of immune status. Any woman who was found to be sick, have very low indices of micronutrient status or was immuno-compromised was immediately referred to the Kalafong Hospital Immunology Clinic for further care.

Blood was also collected and analysed for the same parameters from a sub-set of 53 HIV-negative women at six weeks postpartum, to serve as a control group.

7.2.1. Sampling and measurement parameters

Non-fasting venous blood was collected from the women at any time that they reported to one of the clinics for their scheduled visit. All assays were collected in

accordance with the manufacturers' instructions. Samples were placed into mineral-free gel separator tubes for CRP, vitamins and minerals. EDTA tubes were used to collect blood for analysis of vitamins A and E. C-reactive protein (CRP) was used to measure the inflammatory response. The samples were labelled, protected from light by a foil paper and immediately placed in ice-cooled insulated boxes after collection and delivered to the Ampath Laboratory in Pretoria within four hours. The flow diagram used by Ampath for collection of samples is represented in Figure 2. All the analyses were carried out at the Ampath Laboratory using methodologies described in Table 4.5. The normal reference values for each vitamin and mineral and for CRP are also provided in this table.

7.3. STATISTICAL ANALYSIS

STATA package version 9 was used to analyse all the biomarker data. As the distributions of some of the biomarker variables was non-Gaussian, data were log transformed before comparing variables. Differences in biomarker levels between HIV-infected and non-infected women were tested for significance using the Student's t-test for continuous variables. In addition, the t-test for continuous variables was used to assess trends in micronutrient and biomarker levels over the 24-month period. By using the two sample t-tests it was also possible to compare study participants whose biomarker variables fell below or above the cut-off values according to infant feeding practice at six weeks, six months postpartum and at 24-months. These comparisons were made using the Chi square (X^2) test. Statistical significance was set at a probability level of 0.05 ($p<0.05$). Ferritin concentration levels were used as a marker of the inflammatory response and were controlled for in some of the analyses.

7.4. RESULTS

At each of the scheduled visits, at six weeks, six months, 12 months, 18 months and 24 months there were a varying number of HIV-infected mothers who attended the visits, as reflected in Table 7.1. All micronutrients and biomarker levels are presented as a mean concentration +/- SE. The normal reference ranges are also provided in this table.

7.4.1. Comparison of indicators of HIV-infected and un-infected women at six weeks postpartum

As shown in Table 7.1, significant ($p<0.05$) differences in micronutrient and biomarker levels existed between HIV-infected and HIV-uninfected women at the baseline visits for CD4 lymphocytes, red-cell folate, transferrin, transferrin saturation, selenium and vitamin A. In comparison to the normal reference ranges, the mean red-cell folate, transferrin and transferrin saturation concentrations were lowered amongst the HIV-infected women. In relation to the HIV un-infected mothers, HIV-infected women had significantly lower concentrations of folate, transferrin, transferrin saturation and CD4 cell count ($p<0.05$), but significantly higher concentrations of selenium and vitamin A. The HIV-negative mothers had insignificantly higher levels of iron, vitamin B12, vitamin E and haemoglobin.

When controlling for ferritin as a marker of the inflammatory response we noted significant differences ($p<0.05$) among HIV-infected and non-infected women for serum transferrin, vitamin B12, red-cell folate, haemoglobin and iron concentrations. When controlling for baseline CD4 cell counts, significant differences between HIV-infected and HIV-negative women were noted for red-cell folate and haemoglobin concentrations. Therefore, the HIV-infected women had marginally less optimal levels of micronutrients than their HIV-negative

counterparts. Vitamin A and selenium concentrations were elevated among the HIV-infected women, compared to the HIV-negative controls, but were still within the normal ranges. It should be noted that while there were differences, all values were within the normal ranges except transferrin and percentage transferrin saturation.

Table 7.1: Comparison of indicators of HIV-infected and un-infected women at 6 weeks postpartum

Micronutrient or biomarkers	**HIV-infected Women Mean (SE)**	**Number**	**Range**	**HIV-uninfected Women Mean (SE)**	**Number**	**Range**	**p-value**	**Reference range**
Vitamin A µg/L	514.63 (154.66)	164	142-1077	469.23 (124.49)	52	263-855	**0.0344**	260-720 µg/L (18-19yrs) 300-800µg/L (≥ 20yrs)
Vitamin E mg/L	8.62 (3.06)	164	2.8-20.8	9.32 (3.40)	52	2.4-17	0.1930	6-10mg/L (18-19yrs) 5-18 mg/L(≥ 20yrs)
Iron µmol/L	10.56 (5.22)	169	3.0-30.4	11.8 (5.82)	53	2.70 - 24.60	0.1705	6.6-26.0 µmol/L
Transferrin g/L	1.52 (1.34)	290	1- 3.1	2.77 (.45)	53	1.90- 4.10	**0.0000**	2.0-3.6 g/L
Transf sat. %	9.80 (11.1)	290	7-51	18.1 (9.99)	53	3-43	**0.0000**	15-50%
Ferritin ng/mL	35.88 (31.55)	167	2- 188.8	33.56 (30.60)	53	4-166	0.6377	13-150 ng/mL
Vitamin B12 pmol/L	336.65 (113.71)	169	156-715	356.07 (163.68)	53	172.00 - 1065.00	0.4235	145-637 pmol/L
Red cell folate nmol/L	588.18 (526.97)	288	511-2405	988.47 (320.41)	53	441.3-1999.2	**0.0000**	597-2334 nmol/L
Selenium µg/L	96.84 (19.8)	167	59.6-164.4	91.45 (15.7)	53	64.60 - 139.20	**0.0442**	70-130 µg/L
Haemoglobin g/dL	12.65 (1.39)	166	8.5-16.9	12.93 (1.47)	53	7.80- 15.50	0.2198	12-16 g/dL
CD4 lymphocytes cells/µL	459.9 (240.4)	134	5 1482	879.51 (283.14)	53	42 - 1289	**0.0000**	500-2010 cells/µL

7.4.2. Comparison of micronutrient and biomarker levels by infant feeding mode at six weeks and six months

At the six-week post-visit it was found that mean vitamin E concentration was significantly higher among HIV-infected mothers who were formula-feeding as compared to those who were breastfeeding ($p<0.05$), even though the mean concentration in both groups was within the normal reference range. Formula-feeders had slightly lower CD4 cell counts (445.9cells/mm^3) than their breastfeeding counterparts (494.9cells/mm^3) as indicated in Table 7.2. Between six weeks and six months there were no significant differences in micronutrient and biomarker levels between the formula-feeding and breastfeeding HIV-infected women, with most mothers' micronutrient concentrations falling within the normal range.

Table 7.2: Micronutrient and biomarker levels by feeding mode at six weeks post-delivery

At 6 weeks:

Micronutrient or biomarkers	**Formula Feeding - mean (SE)**	**Number**	**Breastfeeding - mean (SE)**	**Number**	**P-value**
Vitamin A µg/L	508 (14.9)	91	503 (35.7)	21	0.8956
Vitamin E mg/L	9.13 (0.34)	91	6.97 (0.44)	21	**0.0040**
Iron µmol/L	9.80 (0.52)	92	11.46 (1.06)	21	0.1703
Transferrin g/L	1.83 (0.11)	127	2.11 (0.22)	26	0.2783
% Transf sat.	11.6 (0.97)	127	15.1 (0.22)	26	0.1454
Ferritin ng/mL	36.8 (3.28)	91	35.03 (6.55)	21	0.8140
Vitamin B12 pmol/L	349.6 (12.9)	92	297.8 (19.9)	21	0.0749
Red cell folate nmol/L	732.3 (44.6)	126	799 (87.82)	26	0.5296
Selenium µg/L	97.6 (1.88)	91	95.9 (5.92)	20	0.7282
Haemoglobin g/dL	12.5 (0.153)	90	12.82 (0.306)	19	0.4535
CD4 lymphocytes cells/µL	445.9 (21.7)	106	494.9 (64.4)	23	0.3768

7.4.3. Comparison of micronutrient concentration levels between the 6 weeks baseline visit and the final visit (24 months)

As shown in Table 7.3, significant changes occurred for vitamin A, Vitamin B12, selenium, haemoglobin and CD4 cell counts, over the 24 month period.

Table 7.3: Change in micronutrient and biomarker levels among HIV-infected women over the 24-month period postnatally.

Micronutrient/ Biomarker (N)	Baseline level Mean (SE)	Range	Final level Mean (SE)	Range	Mean Difference	P-value
Vitamin A (µg/L) (106)	514.63 (154.66)	142-1077	372.0 (115.3)	113-851	-146.4	**0.000**
Vitamin E (mg/L) (106)	8.62 (3.06)	2.8-20.8	8.74 (2.57)	3.5-16.8	+0.148	0.6396
Iron (µmol/L) (111)	10.56 (5.22)	3.0-30.4	12.48 (6.50)	3.2-32.9	+1.71	**0.0207**
Transferrin (g/L) (152)	1.52 (1.34)	1- 3.1	2.72 (0.468)	1.8-4.07	+0.84	**0.0000**
Transferrin Saturation (%) (152)	9.80 (11.1)	7-51	40.0 (25.8)	3.0-32	+27.4	0.1945
Ferritin (ng/ml) (110)	35.88 (31.55)	2- 188.8	39.50 (39.3)	4-249	+4.45	0.2659
Vitamin B12 (pmol/L) (113)	336.65 (113.71)	156-715	322.3 (179.8)	122-1476	-5.4	0.6909
Red Cell Folate (nmol/L) (150)	588.18 (526.97)	511-2405	1168.2 (323.8)	233-2646	+430.0	**0.0000**
Selenium (µg/L) (106)	96.84 (19.8)	59.6-164.4	96.9 (28.3)	43.5-199.0	-0.90	0.7949
Haemoglobin (g/dL) (108)	12.65 (1.39)	8.5-16.9	12.30 (1.36)	8.6-15.2	-0.42	**0.0085**
CD4 lymphocytes (cells/µL) (134)	459.9 (240.4)	5 -1482	414.4 (227.9)	42-1289	-45.5	**0.0138**

For those biomarkers or micronutrients for which there was a significant difference between the baseline and final measurement, as depicted in Table 7.3, we undertook further analysis to compare these differences with the cut-off ranges for each. Most mothers fell within the normal cut-off range of 260-800µg/L for vitamin A concentration. However, the mean vitamin A concentration levels dropped significantly but remained within the normal range. At baseline, 1% of mothers had a vitamin A concentration less than 260µg/L and this changed to 8.2% by the last visit. Almost 50% of the mothers also had blood vitamin A concentration above 800µg/L. A similar pattern was observed for iron concentration levels, though more (12.3%) women at baseline than at the final visit (9.9%) were iron deficient (<6.6µmol/L).

Almost 50% of the study participants had low concentrations of transferrin at the baseline visit. However, by the final visit at 24 months this percentage had lowered to less than 1%. Fifty percent of the study participants were within the normal range for transferrin at both baseline and final visits. A similar trend emerged with regard to red cell folate concentrations, with 42% of women at the baseline visit deficient, but by the final visit only 0.7% had levels lower than the normal range of folate concentration, namely <2.0g/L. For both transferrin and red cell folate almost 50% of the study participants had excess concentrations (>3.6g/dL and >2334nmol/L respectively).

As shown in Figure 7.1, at both the baseline and final visits almost 8% of the study population had a CD4 cell count <200cells/mm^3. Sixteen percent (16%) of the women at the baseline visit had a CD4 cell count between 200-350cells/mm^3, but by the last visit this number increased to 19.1%. The proportion of women in the different CD4 categories did not change significantly over time. Almost 60% of the study population fell within the CD4 cell count

category greater than 500cells/mm³, implying that there was not a significant deterioration in CD4 cell counts over time.

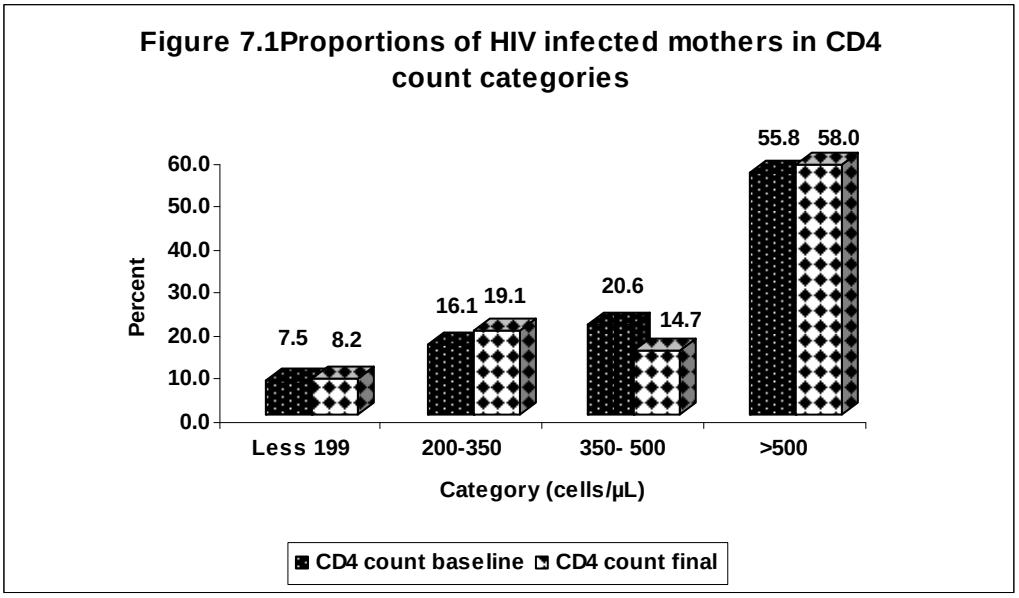

Figure 7.1: Proportions of HIV-infected mothers by CD4 count categories

7.4.4. Assessment of micronutrient supplementation usage amongst HIV-infected women

At the recruitment visit during pregnancy 92.4% of the mothers mentioned that they had received iron and folate supplements during pregnancy, and of these women, 91% stated that they did actually take the tablets. However, this information was not verified. Forty three of the 293 HIV infected women (15%) in our study acknowledged taking immune-boosters and micronutrient supplements, as shown in Table 7.4.

Table 7.4: Micronutrient supplements and traditional "immune boosters" taken by clients.

Category of Immune boosters or vitamin and mineral preparations taken	Number
Vitamin-enriched porridge, "Morvite"	2
"Vuselela" tablets, "Izifo zonke", "Amandla" (traditional preparations/tonics)	4

Spirulina, aloe vera, "Herbal cure", "Stress Active", "Immunadue", (Herb-based remedies)	10
"Centrum", multivitamins, "Moducare", "Bioplus", "Cal-c-vita", Vitamin B6, folic acid, "Viral Guard"	16
Cannot remember the name of the supplement	5
Taking a combination of therapies (Over-the-counter tablets and herbal preparations).	6
Total	43

7.4.5. Sources of information on nutrition and HIV/AIDS

All mothers were asked where they obtained nutritional or health guidance or information to assist them to cope better with their HIV disease. Eighty-five (85) mothers responded to this question. For less than half, 39 (45.9%), the clinic was the primary source of information, for 25 (29.1%) printed matter (magazines and newspapers), for 14 (26.5%) the radio and six (7.1%) relied on the television. One mother mentioned that she obtained information from her community.

A follow-up question to all 293 mothers was "what was the main message" on living better with their HIV. The majority of women did not answer this question correctly. However, of those that did, sixty-five (22%) felt that having a "healthy body of the correct weight" was important, 62 (21%) felt that "improving one's immune system to fight off HIV and to increase CD4 count" was essential, 17 (5.8%) understood the main message to be "eating a variety of fruits and vegetables," 4 (1%) stated that "caring for oneself" was most important and 1 felt that using a condom and leading a healthy lifestyle were the most important messages. Mothers could give more than one response to each of these options.

7.5. DISCUSSION

This study provides information on trends over a 24-month follow-up period among HIV-infected women following delivery in a peri-urban setting. A substantial amount of literature on HIV infection and micronutrient status tends to be focused on pregnancy. [118,119,197,198]

The finding of normal biomarker and micronutrient levels among the study population and the HIV-negative group is similar to the anthropometric trends reported on in Chapter 6. This suggests that our study population was well nourished and not severely immuno-compromised on the whole.

We found few differences in mean serum levels of micronutrients among the HIV-infected and non-infected study participants, unlike several studies in the literature[7,139,199]. At six weeks postpartum most HIV-infected women were replete in micronutrient concentrations with the exception of the mean red cell folate, transferrin and transferrin saturation concentrations. The HIV-infected participants had marginally lower serum levels of vitamin A and El. Vorster et al[139], in their data comparing HIV-infected and non-infected men and women, found only haemoglobin levels among HIV-infected participants to be significantly lower than among non-infected participants. In our study population the levels of haemoglobin of the HIV-infected participants and the controls were almost similar, with significantly higher vitamin A concentration levels, but vitamin E concentrations were lower than amongst the controls.

There were minimal differences in micronutrient concentration levels by feeding mode, unlike others who found that, on average, retinol was significantly lower in HIV-positive lactating mothers, even after controlling for the acute phase response.[129] We found that at the six weeks postnatal visit there was a slightly lower serum retinol concentration amongst breastfeeding women, but this was within the normal range and not significant. The only antioxidant vitamin for which there were significantly lower levels among the breastfeeding mothers was vitamin E, however given the small numbers of mothers with low levels , this

difference is unlikely to be of clinical significance. Others in Tanzania have found higher plasma levels of selenium among HIV-infected women to be marginally associated with higher vitamin A levels and lower vitamin E and haemoglobin levels.[113]

It has been documented that deficiency in selenium as an antioxidant may increase HIV disease progression, increase viral load and increase the risks of infection.[199,200] Similar to findings by others[104] we did not find any of our study participants displaying low levels of selenium. Plasma selenium as an assessment of selenium status is reflective of short term selenium status and tends to respond to changes in intake within a short period, unlike erythrocyte selenium which is more reflective of long term status[100]. During an acute phase response or infections such as HIV, plasma selenium may become a less adequate measure of selenium status as it tends to decline under such situations. The plasma levels of selenium in the HIV-positive mothers at six weeks were higher than among their HIV-uninfected counterparts ($p=0.0442$); this finding is unexplained. Drain[106] found that women with an acute phase response had low levels of selenium but these were women at a more advanced HIV disease stage. In addition Ogunro[201] established that plasma selenium levels were significantly reduced ($p<0.0001$) in HIV-infected patients with a CD4 cell count <200cells/mm³ and that the levels of selenium reduced with advancing HIV disease progression.

Whilst this study was not designed to assess the extent to which the levels of micronutrients suppressed or improved HIV-related immune response, we have noted after the two year follow-up period only 8.2% of mothers in our study could be categorised as severely immuno-compromised (CD4 cell count<200cells/mm³).

Over the 24-month follow-up period specific micronutrient levels declined among the HIV-infected women, with the differences in haemoglobin and vitamin A concentration compared to the baseline becoming significant ($p<0.05$). In a proportion of the women, the vitamin A concentration was indicative of deficiency. This latter finding is consistent with the trends observed in KwaZulu-Natal wherein mean serum retinol concentrations in HIV-infected women were lower by six months after delivery, even after controlling for the acute phase response.[7] Whilst very few of the mothers in our study had a BMI level <18.5kg/m², others have found this lower BMI level to be associated with increased risk of vitamin A and selenium deficiency.[202] In Cape Town the following independent predictors of low levels of serum retinol among untreated HIV-infected included: WHO stage 4 (Odds Ratio: 3.4; 95% CI: 2.1,5.7) and body weight (Odds Ratio: per 5kg decrease 1.15; 95% CI: 1.08,1.25).[203].

Folate deficiency attributable to low dietary intake has been found to be common among women of childbearing age (but unknown HIV status) in South Africa.[206] However, since October 2003, mandatory regulations on flour fortification (including the addition of 25% folic acid to 200g raw maize meal and wheat flour) were promulgated in South Africa. It is also known that since the implementation of this national programme there has been improved folate status (namely a 92.8% reduction in the prevalence of red cell folate deficiency from 26.4% to 1.9%) among women of childbearing age in provinces where folic acid deficiency has been documented.[205] Whilst the dietary intake data in our study was considered unreliable, we noted that most of the women in the study consumed high intakes of bread and maize meal daily. Thus it is possible that the trends observed with regard to red cell folate over a period of 24 months may have been attributable to the increased intake levels through the staple food fortification programme.

Iron deficiency has been documented among women of child-bearing age in South Africa. Our study population had normal serum iron but low serum transferrin and low transferrin saturation at baseline. In the absence of accurate dietary intake data, we are unable to comment on the intake of inhibitors or enhancers of iron absorption in our study population, thus it is possible that the lower iron levels could be attributable to either poor dietary intake or the overall inflammatory response in our study population. Furthermore, as suggested by others[208], the methods we used to determine iron status, namely serum ferritin, haemoglobin and iron concentrations, may not be the most suitable to use in the presence of a possible inflammatory response that manifests itself in the presence of a disease like HIV.

An additional complication is that during inflammation (or acute phase reaction) the levels of serum ferritin are elevated. It is thus difficult to interpret levels of serum ferritin between 12 and 100µg/L as it is not clear whether this reflects a deficiency or is rather a manifestation of inflammation. Serum ferritin levels among our HIV-infected mothers and controls were within the normal range. Given that serum ferritin is also used as a surrogate marker of the inflammatory response, the levels of this biomarker may have been more reflective of disease state than of deficiency. Data collected among HAART-naïve women in the USA indicate that higher serum ferritin concentrations may result in a 1.67 fold increase in the odds of death (95% CI: 0.98;2.86).[207]

This study deliberately did not focus on assessments of maternal biomarkers of nutritional status during pregnancy given that the interpretation of micronutrient status would have been influenced by possible haemo-dilution and thus analysis would have been complex. The US Assembly of Life Sciences[208] indicates that "during pregnancy the concentrations of water-soluble vitamins tend to be lower whereas concentrations of fat-soluble vitamins remain unchanged or are elevated."

Most studies assessing biomarker levels of nutritional status use the serum or plasma level of each nutrient. Semba and Tang[98] state, however, that this methodology has its limitations in small sample sizes or where study participants are acutely ill. Further, for some micronutrients, serum or plasma levels may not be the most sensitive indicators of nutritional status especially in the absence of agreement on cut-off points used to define deficiency levels.

We faced a number of technical challenges in the collection of blood samples. At times there was insufficient blood collected to allow for the analysis of all the variables of micronutrient status. Sometimes samples were haemolysed. At other times mothers were reluctant to have their blood taken or it was deemed inappropriate on medical grounds (for example if the mother appeared clinically lethargic after a medical assessment) to take blood samples from the mothers. This caused the fluctuation in the number of total samples per micronutrient or biomarker collected per visit and thus the analysis of trends could have been flawed to some extent. We also acknowledge that the periodic measurement of CD4 cell counts and the fluctuations in the levels may not have been the ideal method of determining immuno–status or the ideal period for HAART initiation among our participants. Indeed, others have instead recommended that the CD4 percentage could be more reliable than the absolute count.[209]

The Operational Plan for Comprehensive HIV and AIDS Care, Management and Treatment in South Africa[210] includes the provision of a multi-micronutrient supplement and a food supplement to all persons who have a CD4 count below 200cells/mm^3 as the standard of care. On account of this it is possible that the measured levels of micronutrients actually reflected the effect of supplements in these HIV-infected women. In addition, a wide variety of supplements was being consumed by about 15% of our study population, although we have no information on the frequency, dosage and composition of these self–obtained

supplements that the women were taking. The researcher categorised these preparations according to those that had traditional names, those that were based on a herbal substance and the more western registered vitamins and mineral preparations. Some of the study participants reported taking combinations of the various preparations. It is possible that some mothers displayed recall bias in the listing of the types of supplements they were taking or because some were taking traditional herbs, they did not necessarily name them specifically. It is thus not known what the medical and nutritional contributions of all these herbs was in relation to the overall diet and health of the mothers or whether any of these medications and supplements could have had any adverse effects on the mothers. It is concerning to notice that some of the mothers took a combination of the various preparations, a situation that could have resulted in adverse drug-nutrient interactions or nutrient-nutrient interactions.

The consumption of nutritional supplements and immune boosters among HIV-infected persons has also been documented in the USA, where extreme intakes (often above the tolerable levels) were observed. The use of such supplements among both men and women was associated with higher levels of affluence, being white, well educated, being on HAART and having higher CD4 cell counts.[211] We show that this practice is also common in semi-urban people, non-affluent people in this country.

Our follow-up period was much longer than in other studies on micronutrient status of HIV-infected women in South Africa. We observed no significant deficiencies developing over time, possibly because 31 of our study participants had already commenced HAART and reported taking supplements of various forms. We conclude that the micronutrient status of our study population was satisfactory, possibly as a result of supplementation and even because most of the mothers in our study were overweight and not under-nourished.

On an individual patient level, it is possible that antioxidant micronutrients may be an important contribution to the the optimal management of persons living with HIV; however, a prudent approach is required in recommending extent and dosages of micronutrient supplementation among HIV-infected patients, as this will be informed by their current nutritional status. This targeted or more focussed approach to nutritional supplementation of personsl living with HIV will have to be balanced with facilitating a reduction in viral load and enhancement of the immune status. Within resource-constrained environments the improvement of the quality and diversity of dietary intake is the most economically sustainable intervention towards optimal nutritional status among persons living with HIV.

Prior to making population-based recommendations on large scale micronutrient supplementation, full assessments on current intake levels enhancers or inhibitors of absorption are essential. With increasing access to HAART in South Africa there will be a need to continue to research the role of micronutrients in advancing HIV disease and any biochemical changes (such as insulin resistance, lipid abnormalities) that may arise.

We acknowledge that using biochemical markers alone does not provide the true overview of nutritional status. Further, it has been mentioned that low levels of micronutrients may be indicative of HIV disease stage and not necessarily a deficiency of the particular micronutrient in question. Alternatively, the extent of HIV disease may itself compromise micronutrient absorption and utilisation leading to low serum levels of the micronutrient. We did not identify significantly low serum micronutrient levels, and this correlated with the generally good nutritional state of the study subjects as measured by anthropometric indices. Our data corroborates the cautious stance of the leading authors in the field of

HIV and micronutrients that nutritional interventions alone are insufficient in preventing the impact of HIV.[76]

7.6. SUMMARY

We have not observed widespread micronutrient deficiencies among our study participants, even when compared to other data generated within South Africa. This is similar to the findings in Chapter 6, where there were hardly any women who could be categorised as malnourished. Thus, it is possible that in an urban setting, where women have greater access to information, including information on HIV and nutrition, they are in a better position to access a more varied diet which is augmented by micronutrient supplementation. Our findings substantiate the need for continuous monitoring and issuance of cautionary advice against the intake of a wide spectrum of immune boosters. This information would need to be imparted in counselling sessions, upon assessment of current dietary intake patterns and provided to persons who are immuno-suppressed, regardless of whether they had initiated HAART.

CHAPTER 8 - CHILD OUTCOMES IN RELATION TO MATERNAL HEALTH

8.1. OBJECTIVES

1. To determine the HIV transmission rate attributable to infant feeding practices among children born to HIV-infected mothers over a two year period.
2. To describe the outcome of mothers and children over a period of 24 months and link this to maternal health factors and feeding patterns of HIV-infected mothers.

8.2. SUBJECTS AND METHODS

Within a period of three days postpartum the HIV-1 infection status of the children was determined by collecting heel prick blood and using a nested HIV-1 DNA PCR assay performed on dried blood on filter paper (Roche Amplicor version 1.5 HIV DNA PCR; Roche molecular systems, Basel, Switzerland). Tests were repeated at 6 weeks and 3 months of age. Subsequent PCR testing was performed on breastfed infants until three months after cessation of breastfeeding.

Children enrolled in the study had their weight and length measurements taken at various intervals between birth and 24 months of age. Table 8.1 depicts the schedule of each of the five visits. Birth weight of each of the children was obtained from the first visit records or from the "road to health" chart. Weight was measured to the nearest 0.1kg using an electronic scale (Durban Scales, 2000) in 100g increments. To measure the length of the children who could not

yet stand unassisted, supine length measurements (using non-stretchable tapes affixed to the bed) were taken, with the child lying on an examination bed. For those children who could stand unassisted, height was measured in a standing position. The height measurements were taken to the nearest 0.1cm with a tape measure affixed to the wall.

Table 8.1: Schedule of visits for growth assessment

Visit	Approximate age of infant or child
0	Birth or within 3 days of delivery
1	6 weeks after birth
2	6 months
3	12 months
4	18 months
5	24 months

Infant feeding practices of all the children enrolled in the study were also assessed and the methods used have been described in Chapter 5.

A thorough review of the patient records was undertaken so as to establish as accurately as possible the actual administration of and timing of the mother and newborn nevirapine dose and also to verify the feeding practice immediately after birth. For this study it was possible to review 258 of the 293 mother and child records. In 35 cases, no hospital records could be identified in the hospitals serving the local population. The data on HIV transmission will thus be based on 258 cases only. There was no identifiable systematic difference between this group of 35 missing data and the main study group.

8.3. STATISTICAL ANALYSES

Nutritional status was assessed using algorithms developed by the WHO and CDC's anthropometrical programme (Nutristat). The raw anthropometric data were transformed into Z-scores and the data were evaluated using the sex-specific 1978 CDC/WHO normalised version of the 1977 NCHS reference curves. These anthropometric measurements were used to compute weight-for-height (w/ht), weight-for-age (w/a) and height-for-age (ht/a).The interpretation of each of the Z-scores is given in Table 8.2.

Table 8.2: Z-scores and their interpretation

Z- score	**Interpretation**
Low weight for height Z-score (WHZ)	A WHZ score below -2SD is wasting, an indicator of acute weight loss
Low weight for age Z-score (WAZ)	A WAZ below -2SD indicates underweight or poor weight gain
Low height for age Z-score (HAZ)	A HAZ below -2SD indicates stunted growth, and reflects chronic malnutrition

8.4. RESULTS

8.4.1. HIV transmission

Of the 258 children, 39 (15.1%) were HIV-infected, 205 (79.5%) uninfected, and 14 (5.4%) had incomplete data on HIV status at the end of 24 months follow-up. See Figure 8.1

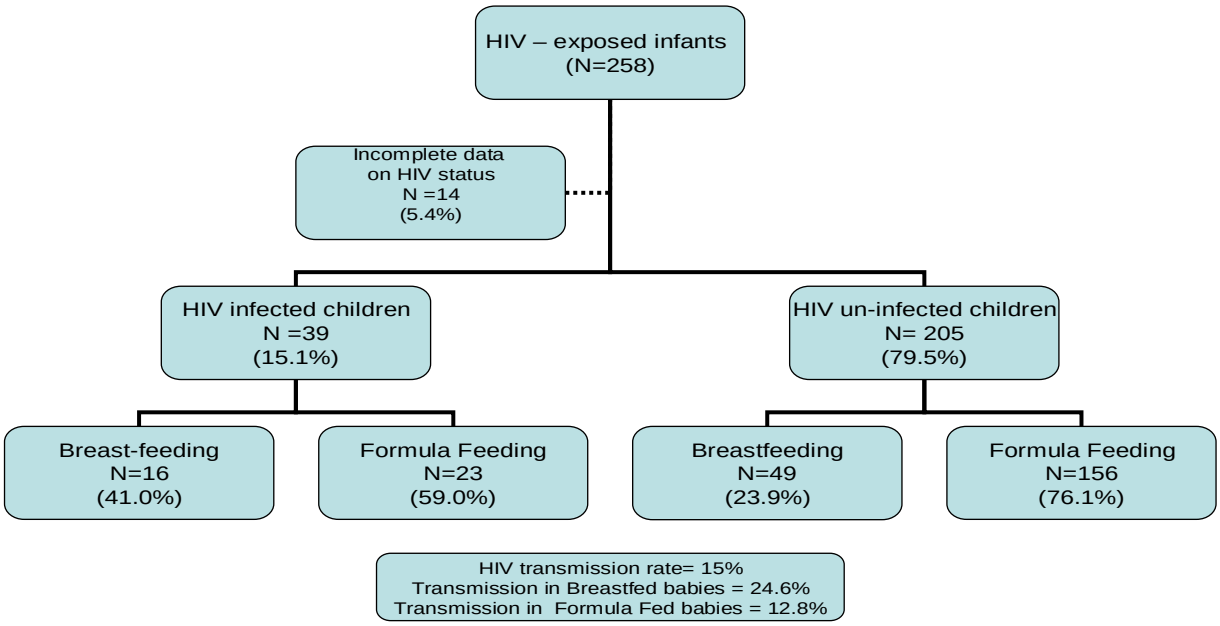

Figure 8.1: Flow Diagram on HIV transmission and infant feeding practices

There were no differences between HIV-infected and uninfected babies with respect to socio-demographic variables, except that mothers of infected babies were more often single (89.5%) than the uninfected mothers (79.5%), although the difference was not statistically significant (p=0.15).

The majority of babies were term infants (77.9%) and about 18.1% were under 2.5 kg at birth, with an overall mean gestational age of 38.2 weeks, with no difference between HIV-infected and uninfected children. There was a larger percentage of HIV-infected infants who were born prematurely (29.4%) than in the HIV-uninfected group of children (16.3%).

Nearly 72% of infants were never breastfed, with a statistically significant difference in the rate of breastfeeding among HIV-infected and uninfected infants (41.0% vs.24% respectively; p=0.03). Of the children who had ever been

breastfed (n= 65), 16 were found to be HIV-infected (24.6%), compared to 23 of 179 children never breastfed (12.8%).

8.4.2 Nevirapine Administration

Of the 252 mother-child pairs on whom either hospital record or Serithi interview data for either the mother, child, or both was available, nevirapine (NVP) was taken by 230 mothers (91.3%), in 2.4% of women (N=6) it was unknown if NVP was taken, and in 16 cases the NVP dose had been missed by the mother. The record-keeping was woefully inadequate in the medical records. For the 230 women reported as having received NVP, 111 (48.3%) were reported by the mother and also documented in the medical records, 101 (nearly 43.9%) were reported by the mother alone (N=101), and 18 (7.8%) were documented in the medical record, but information from the mother was missing.

Similarly, 229 (88.7%) of 258 babies received NVP, and it was unknown if the child received his/her dose of NVP in four (1.7%) cases. Of the 229 children that had received NVP, 56.8% (N=130) had documentation from both sources, 28.8% were reported by the mother alone, and for 14.4% documentation of NVP was only from the medical record review. Five percent of children had no recorded dose of NVP, even though the file was available.

8.4.3 HIV-infected study participants on HAART

At the end of the follow-up period of 24 months there were a total of 31 mothers on ARV therapy in the study. Of these mothers on HAART, 15 claimed that they had experienced side effects from taking the medication, including dizziness, headaches, nausea, loss of appetite, skin rash and swollen feet.

The commonly advised system of "treatment buddies" as support and reminder for people on HAART was found to be only moderately effective. At least 4 mothers claimed they did not have a treatment "buddy". Of those mothers on regular treatment, 12 (38.7%) named a sister as the most common treatment "buddy", followed by 19.4% who relied on partner or husband. Four (12.9%) had a friend or mother as the treatment "buddy" of choice. For 16 (69.6%) of the mothers the most common means of communication with the treatment "buddy" was via cell phone text message reminding them to take their medication. Four mothers (17.4%) stated that the treatment "buddy" cared for them and 28 (70%) stated that the "buddy" provided advice to them on healthy living.

The study highlighted a serious problem with compliance to treatment, with nine mothers (29%) stating that they had missed going to replenish their supply of ARVs. Five of these (56%) stated they had no money for transport to the health facility, two stated that they avoided the long queues, one stated that the administrative fee of R45.00 for the file was too high and one stated that she was unable to get time off from work to collect her treatment.

8.4.4. Child Growth

Data on child growth was available at all the five scheduled visits. However, large gaps in the data occurred because babies were not always available at each of the mother follow-up visits for assessment of growth. Accordingly, the data was presented as a series of cross-sectional measurements at each of the time points, rather than as a longitudinal follow-up. The anthropometric indices of weight-for-age Z-score (WAZ), height-for-age Z-score (HAZ) and weight-for-height Z-score (WHZ) are presented in Figures 8.1 and 8.2. Over the 24-month period, it was possible to compute the WHZ score for 725 contacts, the HAZ score for 718 and the WAZ score for 797 contacts.

At the first three time points (corresponding to the first 12 months of follow-up) the mean WAZ was -2.03, the mean HAZ was -1.60 and the mean WHZ score was -1.22. However, at the next two time points up to 24 months, there was an improvement towards the reference range in all three indices. At 24 months, the mean WAZ score was 0.38, the mean HAZ was 0.76 and the mean WHZ was 0.14. See Figures 8.2 and 8.3.

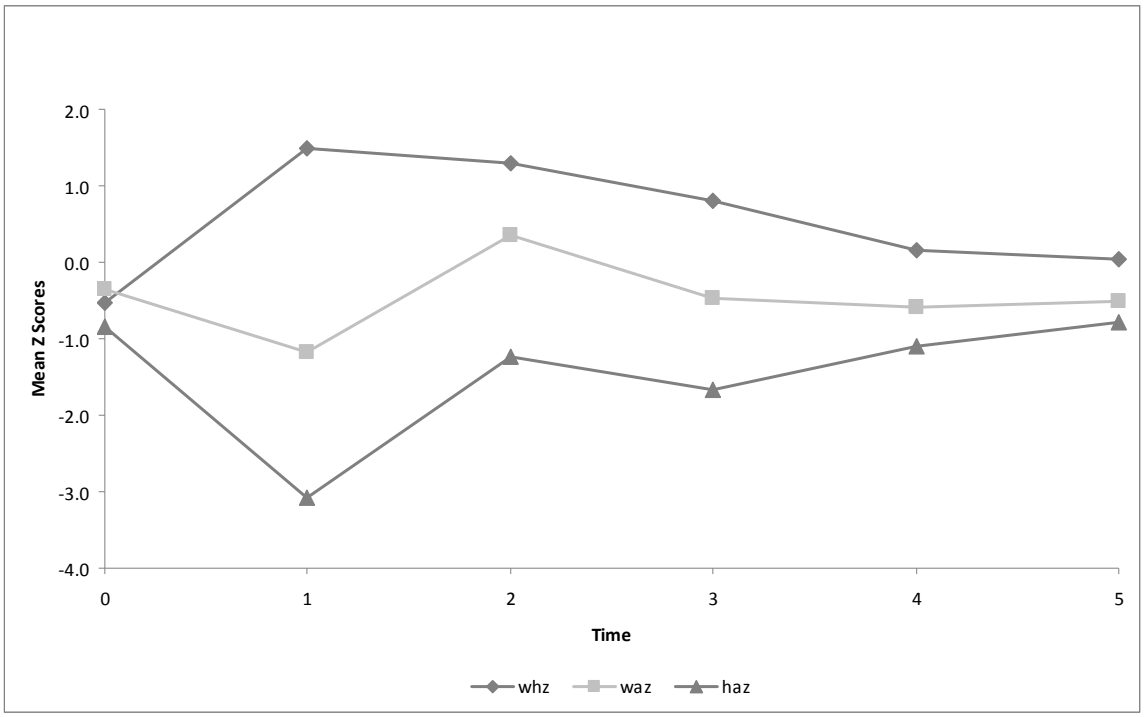

Figure 8.2: Mean Z-scores of HIV-exposed girls over time

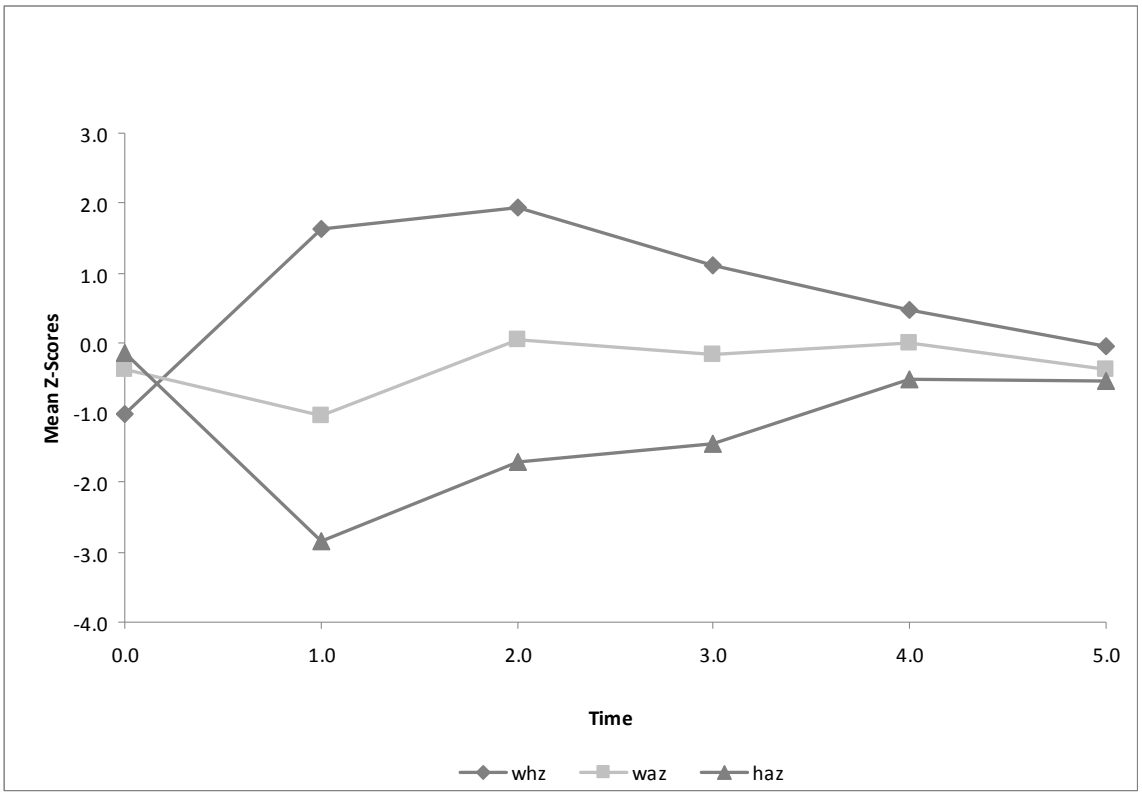

Figure 8.3: Mean Z-scores of HIV-exposed boys over time

Weight for age Z-scores (WAZ)

For both the girls and the boys at around birth the mean WAZ scores were close to the reference population, but by six weeks after birth there was a decreasing trend for both. After six weeks after birth there was evidence of catch-up growth (which was higher for the boys). However, even with the catch-up growth the mean WAZ-score for both sexes remained slightly lower than the reference population for the remainder of the 24-month follow-up period. Overall, however, this group of children had a normal early growth pattern.

Height for age Z–scores (HAZ)

The HAZ-scores for both girls and boys were very close to the reference population at birth, but showed a decline by six weeks and, similar to WAZ-

scores, there was evidence of catch-up growth thereafter. By 24 months, the mean HAZ-score was approaching the reference population. In view of the recognised variability in the accuracy of length measurements under routine service conditions, some of the length measurements were excluded from the data analysis..

Weight for height Z-scores (WHZ)

The computation of WHZ scores is dependent on the accuracy of the component weight and height measurements. In view of the low early HAZ score obtained in this study, high WHZ scores should be expected and indeed were found. The mean WHZ scores of both the girls and the boys at birth were lower than the reference population. However, from the six weeks visit onwards they remained higher than the reference population, declining slightly by 24 months. These data do not suggest significant wasting to be present in this population.

8.4.4.1 Comparison of Growth of HIV-exposed boys and girls according to feeding mode

The growth of all the boys and girls was assessed according to whether the children had ever been breastfed or not, as depicted in Tables 8.3 and 8.4. Differences in growth according to the three indices (WAZ, HAZ, and WHZ scores) between the six-week and 24-month visit for all the children were also determined. Table 8.3 and 8.4 show the values for WAZ and WHZ scores. They show the same tendencies as demonstrated for the whole group and no significant differences according to feeding mode.

Table 8.3: Growth of HIV-exposed boys according to feeding mode at visit 1 and 5

		Visit 1		Visit 5	
		Breastfed	**Not breastfed**	**Breastfed**	**Not breastfed**
	Mean	**-0.72**	**-1.18**	**0.94**	**-0.31**

WAZ	**SD** **(N)**	**2.26** **(12)**	**2.33** **(53)**	**0.72** **(14)**	**1.16** **(53)**
WHZ	**Mean** **SD** **(N)**	**1.95** **1.40** **(18)**	**1.43** **1.27** **(60)**	**0.12** **0.58** **(12)**	**0.10** **1.37** **(52)**

We also set out to establish whether initial breastfeeding changed the growth patterns of HIV-infected babies between the six-week and 24-month visits. Significant changes in the mean WHZ-score ($p<0.05$) among breastfed boys and girls between the six-week visit and the 24-month visit were observed. The mean WAZ-score was not significantly different among breastfed girls and boys from the six-week visit to the last visit, again showing that both groups of babies seemed to grow equally well on follow-up.

Table 8.4: Growth of HIV-exposed girls according to feeding mode at visit 1 and 5

		Visit 1		Visit 5	
		Breastfed	Not breastfed	Breastfed	Not breastfed
WAZ	Mean	-1.34	-0.87	-0.57	-0.25
	SD	2.33	1.87	1.18	1.09
	(N)	(22)	(34)	(24)	(35)
WHZ	Mean	1.92	1.43	-0.14	0.02
	SD	1.76	1.57	0.92	1.06
	(N)	(28)	(37)	(23)	(34)

8.4.4.2 Comparison of the growth of HIV-infected and non-infected children

A comparison of the growth of HIV-infected babies with those that were uninfected showed no significant differences. Both groups grew normally and there was no significant cross-sectional difference. There was a significant increase in the WAZ-score among PCR-positive and negative children between visit one and visit five ($p<0.05$). From Table 8.5 there appears to be a decline in the mean WHZ for both the PCR-positive and PCR-negative children.

Table 8.5: Comparison of growth among HIV-infected and non-infected children by visits

		Visit 1		Visit 5	
		PCR positive	PCR negative	PCR positive	PCR negative
	Mean	-1.68	-1.21	-0.57	-0.35

WAZ	**SD** **(N)**	**(2.36)** **25**	**(2.31)** **104**	**(1.00)** **34**	**(1.11)** **115**
WHZ	**Mean** **SD** **(N)**	**1.78** **(1.61)** **35**	**1.52** **(1.47)** **123**	**0.05** **(0.71)** **33**	**0.08** **(1.13)** **112**

8.4.4.3. Growth of boys and girls in relation to maternal CD4 count

We assessed the growth of the children of mothers who had severe immuno-suppression, as indicated by a CD4 cell count of less than 200cells/mm³, and compared this with the growth of children whose mothers had a CD4 cell count greater than 200cells/mm³. At around the six-week visit there were only 30 children whose mothers had a CD4 cell count less than 200cells/mm³. There were no significant differences in the anthropometric indices between children born to mothers with a low CD4 cell count (<200cells/mm³) as compared to those born to mothers with a higher CD4 cell count (>200cells/mm³).

We also assessed the rate of decline of CD4 count according to feeding mode. By 24 months we found the mean CD4 cell count amongst mothers who had ever breastfed to be 390cells/mm³ whereas for the mothers who had practiced formula-feeding the mean CD4cell count was 400cells/mm³. Our findings report on observations and given that few mothers practiced breastfeeding there would not be sufficient data to conduct more extensive analysis on the role of , breastfeeding on immunological progression of HIV in this study.

8.4.5. Maternal and child deaths and morbidity

During the 24-month follow-up period, eight HIV-infected mothers died. The cause of death was known only for three mothers, namely neurological AIDS-related disorder, tuberculosis and smoke inhalation. We found equal numbers of deaths amongst mothers who either chose to breastfeed or formula-feed their infants, specifically four in each group. In Chapter 5 we obtained postnatal feeding practices from 222 mothers, of whom 154 practiced formula-feeding whilst 68 breastfed. Thus, while 2.59% (4/154) of the women who had formula-feddied, compared to 5.88% (4/68) of those who had ever breastfed, the data does not allow for Cox regression or further analysis. It is possible though that the mothers who chose to breastfed may have been sicker and at greater risk of death.

All mothers were asked to name the most common illnesses they had experienced during the course of the follow-up. There were a total of 94 mothers who responded to this question. However, this information was not verified by review of hospital records. The main reported illnesses were: influenza - 28 (29.79%); diarrhoea - 17 (18.09); STI's, headache and rash - 10 (10.64%) each; and five (5.32%) mentioned oral thrush. One mother mentioned tuberculosis.

During the 24 months of follow-up, there were a total of 33 (11.2%) neonatal and infant deaths in the total study of 293. Of the 33 children who died, 12 (36%) had at least one positive PCR result. The remaining 21 children who died were PCR-negative. Accordingly, the mortality rate for HIV-infected children in this study was at least 12 of 39 (30.7%), and 21 of 254 (8.3%) of uninfected children died. HIV uninfected children also had unacceptably high mortality. This indicates serious risk to these children, possibly related to poor feeding practices and inadequate care. At the end of the 24 months of follow-up 21 children were on ARV therapy in our study. It was possible to obtain the cause of death of the child from the mother or through the hospital records for 15 of the study participants. The reported causes of death included

pneumonia/bronchitis/respiratory infection (9), foetal distress, stillbirth or congenital malformations (3), diarrhoea (2), and other cause (1).

8.5. DISCUSSION

We have observed that in our study the HIV transmission rate by 24 months was 15%. This finding is not that different from many other studies in Africa. In an operational setting in South Africa the rate of early (3 to 4 weeks) transmission ranged from 8.6% in an urban site to 13.7% in a rural site.[212] In another operational PMTCT setting in Kenya in similar conditions to those under which our study was conducted, the HIVNET 012 regimen was found to yield a perinatal HIV-transmission rate at 14 weeks postnatally of 18.1%, whereas before the introduction of nevirapine it had been 21.7%.[213] The HIV transmission rate by 24 months in our study was slightly higher than the HIV transmission rate in the SAINT trial. That trial included a second dose of nevirapine to the mother between 24 and 48 hours after delivery and resulted in an early 12.3% transmission rate by 8 weeks among children who had received a short course of nevirapine.[214] The PETRA Study found a transmission rate of 11.6% at 6 weeks.[215]

Several trials demonstrating the efficacy of short course ARVs in reducing intrauterine and intrapartum transmission have been conducted among breastfed populations in Burkina Faso, Ivory Coast and Uganda.[216,217,218] However, most of these studies are different from ours as they are predominantly reporting on early HIV transmission rates and not for a period as long as 24 months after delivery. At the time that this study was conducted the PMTCT protocol made reference only to the use of single doses of NVP given to the mother during labour and to the newborn within 72 hours of delivery. Research drawn from a pooled analysis to determine the efficacy of peripartum anti-retroviral regimens

in the reduction of MTCT[219] indicated that combination therapy of ZDV and 3TC from 36 weeks of pregnancy had a greater efficacy in preventing MTCT than the monotherapy that was provided as part of policy when our study was undertaken. It is thus highly likely, given the low breastfeeding rates in our study population, that we would have observed even lower transmission rates if dual therapy was practiced as the policy during the conduct of this study.

There is a need for caution in the comparison of HIV transmission rates between studies as this may be complicated by the location of the study, the type of study (whether an observational study or a clinical trial), usage of different prophylactic ARV drugs, and differences in infant feeding practices and in the length of follow-up to assess long-term transmission rates.

We found that breastfeeding is a risk for transmission, as it approximately doubled the risk for transmission (16 of 65 ever breastfed versus 23 of 179 never breastfed; 24.6% vs 12.8%). This finding is consistent with other studies that show that breastfeeding almost doubles the risk of MTCT[220,221,222]. Of greater concern is our finding that ever breastfeeding doubled the risk of death amongst the mothers in this study. However, this finding may not necessarily have clinical significance given that the breastfeeding mothers in our study did so for a limited period of time. Our findings show less risk of mortality than that found in Kenya[23], but are comparable to those found by Otieno[5] with respect to feeding and health outcomes for the mother and the child.

The findings from a larger study in KwaZulu-Natal among HIV-infected breastfeeding mothers found that infants who were breastfed and also given solids were significantly more likely to be HIV-infected than children who were exclusively breastfed (HR 10.87, 1.51-78.00, p=0.018), in comparison to children who by 12 weeks were fed both breastmilk and formula milk (1.82, 0.98-3.36, p=0.057).[30] Almost none of the mothers in our study were practicing exclusive

breastfeeding. The practice of mixed feeding has been shown to increase the risk of HIV transmission, and their babies were also likely to receive complementary foods by as early as 6 weeks after delivery. In Malawi[223] it was found that even though complementary foods were introduced to 40% of infant diets by 2 months and 65% by 3 months, this still resulted in children displaying a lower weight-for-age at 3 and 6 months ($p<0.05$) and this resulted in an increased risk for respiratory infections($p<0.05$).

Even though antiretroviral therapy can contribute to a significant reduction in MTCT in breast feeding populations, the risk of HIV transmission remains as long as breastfeeding continues[224]. In our study the median duration of breastfeeding in our cohort was 42 days, with the range being 1 to 360 days. As reported in Chapter 5 almost none of the mothers in our study were practicing exclusive breastfeeding and, in fact, complementary foods were introduced as early as 6 weeks after delivery.

It is of interest that despite the recommendation from the PMTCT programme that mothers cease breastfeeding early, there were mothers in our study that continued to breastfeed well beyond the first three or four months of life. One mother who continued to breastfeed for 360 days specifically stated that she was forced to do so by her grandmother. In a review of 14 Demographic and Health surveys from developing countries, Brahmbatt and Gray[225] found mortality to be highest amongst never breastfed children as compared to mothers who had breastfed before and stopped.

Given that our study was not an intervention study, it provides valuable data on the quality of record keeping in the programme within the clinics at the time. The recording of nevirapine administered was an unacceptably low, 8% for the maternal dose and 14% for the neonatal dose. It has been shown within operational PMTCT sites in three provinces in South Africa that women of higher

socio-economic status and those who had received a better quality of counselling were more likely to have received the nevirapine dose within the standard time frames.[226] A study undertaken at Coronation Hospital also highlighted that with good record keeping it was possible to document accurately the HIV transmission rate[227]. Our study highlights that even two to three years after the introduction of PMTCT in South Africa, the record-keeping and data management pertaining to the programme were so poor in the clinics studied that routine monitoring and evaluation aspects of this national programme were severely compromised.

HAART treatment adherence among the mothers in this study was sub-optimal. Similar to our findings, Maskew et al[228] found that the main reasons cited by 182 patients on HAART who failed to return for follow-up visits in Johannesburg included financial reasons (34% of patients) as well as transport and administrative costs entailed in opening a file each time they visited the health facility. We found almost a third (29%) of mothers were not compliant for HAART for similar reasons but also it would appear that non-disclosure could have made them less amenable to the "buddy system" with more than 10% stating they did not have a treatment "buddy".

In this study at four clinics in the Tshwane area we have shown serious defects in the implementation of the national PMTCT programme. This is in line with a published global review of PMTCT programmes and access to paediatric ART, which showed that although PMTCT coverage increased from 7% in 2004 in 58 countries to 11% in 2005 in 71 countries, only 38 countries had complete data on ARV access for mothers on the PMTCT programme and in these countries only 28% of mothers eligible for HAART were accessing it.[229] In order to increase compliance of patients to HAART within a developing country context, efforts should be directed towards making ARV therapy free to those patients requiring it and more accessible by ensuring that treatment is made available at the primary health care facility level[229]. A similar recommendation has also been

made by the World Health Organisation, suggesting that a public health approach is required with less dependence on the physician specialist to administer the drugs.[231]

We have found that almost one third of children born prematurely in our study contracted HIV. Low birth weight and prematurity are known to be a consequence of MTCT.[198,232,233] It is likely that as more HIV-infected mothers are placed on HAART with time there will be fewer low birth weight or preterm deliveries, as has been reported in the USA where over a 15-year period ARV uptake increased from 2% to 84% and the low birth weight prevalence decreased from 35% to 21% and the preterm birth decreased by almost the same percentage.[234]

In this study we attempted to assess the growth pattern of HIV-exposed infants and children over a two-year period and to also determine those factors, such as maternal health, that may impact on growth. It is well established that HIV disease negatively impacts on optimal infant and child growth parameters and may lead to faster disease progression and mortality. Our study emphasised maternal follow-up and we therefore did not achieve adequate regular longitudinal follow-up of the children, having to rely on cross-sectional estimates of growth. It is highly likely that this approach may have missed important trends. It is also possible that those children that did not attend all follow-up visits could have been those who were most ill or malnourished.

We found that the growth of infected children is comparable to that of uninfected children in our environment and that it is relatively normal up to age 2 years. This may suggest that, overall, the maternal HIV status did not interfere with the mothers' ability to feed and care for their children. Clearly, those mothers who were themselves critically ill or who died and their children were not captured in this approach.

The growth pattern and specifically the weight-for-height Z-score seen in this study correlated with that found in a study conducted among the same communities from which our study population was drawn[235,236,237]. Although that study was not conducted among HIV-exposed infants, it did establish that 92% of the children were exclusively breastfed by 1 month, by 3 months 35% and by 6 months only 7% were exclusively breastfed. This is comparable to the findings among our HIV-negative mothers, and may also illustrate the influence of the counselling received in the PMTCT programme. Delport found in her study that growth faltering was evident from as early as 3 months and continued till 15 months. [237]

In an earlier study assessing the growth of HIV-exposed infants and children participating in routine PMTCT programmes in a peri-urban setting in Kwazulu-Natal, HIV-infected children manifested early and sustained low mean Z-scores for length-for-age and weight-for-age but not for weight-for-length. Those HIV-infected children who died earlier were found to be more severely stunted, wasted and underweight than those who survived[237]. The authors suggested that this may be in part attributable to poor mothering capacity due to the HIV status of the mother and her possible illness. However, it must be noted that none of the children in that study received ARV prophylaxis unlike in our study. In addition, unlike in our study there was evidence of growth faltering in the Durban study among HIV-uninfected children.

The decline in growth (ht/age and wt/age) seen in our study at around the 6 week period may have arisen as a consequence of inappropriate and early introduction of complementary foods at this stage, affecting the optimal growth of the children. There is ample evidence from Africa highlighting that poor infant feeding practices together with low energy and nutrient dense complementary

feeds, coupled with frequent infections can contribute to high infant and young child mortality. [223,238,239]

An earlier study in Uganda found evidence of growth faltering among the HIV-infected children, in particular the mean weight-for-age and length-for-age curves were significantly lower than those of non-infected children over a 25 month period, but more than half (54%) of the HIV-infected infants died prior to 24 months whereas among the HIV-negative group mortality was only 1.6%.[240] That study cannot be compared to our findings because of the much higher mortality rate.

It is possible that we were not seeing evidence of extensive malnutrition among the children in this cross-sectional study as most of the children were asymptomatic or had minor illnesses that were treatable in out-patient hospital departments, and any severely immuno-compromised and malnourished children could be amongst the 33 that died. Others have found that wasting is a common occurrence among children who are categorised as severely malnourished.[243] In Uganda[240] and Tanzania[242] where rates of malnutrition among children (regardless of HIV status) are likely to be higher than in peri-urban settings in South Africa, it was found that wasting, stunting and underweight were strong predictors of mortality among HIV-exposed children.

It has been suggested that given the non-invasive nature of anthropometric measurements, there should be regular nutritional assessment of HIV-exposed children followed by nutritional and energy supplementation where indicated.[243]

More than 11% of the infants and children died during our follow-up period. The main reported causes of death included pneumonia/bronchitis/respiratory infection (60%), foetal distress, stillbirth or congenital malformations (20%), diarrhoea (13%), and other causes, like high fever and sores on the chest (7%).

A positive PCR was found in only 12 of the 33 child deaths, and AIDS was never mentioned as the cause of death in any of our study participants but this could be due to the ongoing stigma about HIV and AIDS when the study was conducted. A study conducted in Malawi found that after two years of follow-up of children born to HIV-infected mothers, 2.2% of mothers and 15.5% of children died.[4] This finding is disturbing considering that in Malawi the socio-economic conditions are likely to be more adverse than in a peri-urban setting in South Africa. Newell has made the point that it will become increasingly important for the monitoring of the PMTCT programmes in future to focus not only on HIV prevention but also on survival of HIV-exposed children as a major outcome.[244]

There are a number of studies that have assessed mortality of children born to HIV-infected women, both within the era of HAART and prior to this. According to Newell et al, in low income countries estimates are that 50% of all HIV-infected infants will die before the age of 2 years if no ARV therapy is made available.[149] In the South African context there is increasing concern over the high rates of child mortality that are attributable to HIV. In a study conducted at community level through a surveillance system in a rural population in KwaZulu-Natal Province, which at the time had the highest prevalence rate of HIV, it was found that HIV and AIDS was attributable to 40% of deaths among children under five. Among these deaths, neonatal deaths accounted for 13% of the total whilst infant deaths accounted for 61% of total deaths. Most deaths were found to occur in the neonatal period and specifically the first day of birth.[245]

A study conducted in Botswana[246] found that after a 24-month follow-up of infants born to HIV-infected mothers the mortality was 29.5% among HIV-infected infants, who were also more likely to have had pneumonia, and this rate declined to 6.7% among HIV-uninfected infants. These findings are comparable

to those of our study, where we found 12 of 39 infected infants to have died (30.7%) compared to 21 of 254 uninfected children (8.3%).

We found that by the end of the 24-month follow-up period a total of 21 children had begun ARV treatment out of 27 surviving HIV-infected children. There is evidence to show that HIV-infected children who are placed on HAART, with a resultant improvement in their viral load and CD4 cell counts, display improvements in weight and height Z-scores when followed up for a period of 96 weeks. The improvements in anthropometry, particularly BMI, were more marked if the children had been of poor nutritional status at baseline.[247] Such a finding raises hopes that with close nutritional-status monitoring and treatment-adherence support, the 21 children on HAART should not experience any deterioration in nutritional status. A global review of the progress in PMTCT and paediatric HAART acknowledges that provision of comprehensive health care packages for HIV-infected children will depend on availability of quality health care services, especially in low income countries.[248]

In this study we set out to assess the impact of HIV-infection on mothering capacity. As previously reported in Chapters 6 and 7, most of the mothers in this study were asymptomatic, not seriously ill and they were not yet at an advanced HIV disease state at the end of the 24-month follow-up. The low breastfeeding rate observed in our study was therefore unlikely to be due to poor maternal health. Studies in some African countries like Zambia have suggested that poor maternal health among HIV-infected women is associated with a shorter duration of exclusive breastfeeding[185]. Other data from Malawi[249] suggest that HIV-infected women themselves believe that breastfeeding may lead to HIV-disease progression, especially if they also believe that their own nutritional status is sub-optimal. Earlier South African and Kenyan data on the influence of infant feeding choices on maternal HIV disease progression were contradictory.[23,50] Given that so few mothers opted to breastfeed in our study, and none of those who were

formula-feeding claimed that they did so for their own health, and that the nutritional health of the mothers as described in Chapter 6 was very good, we have found no linkage between poor maternal health and shorter breastfeeding duration.

By 6 weeks after delivery there were 30 children whose mothers had a CD4 count lower than 200cells/mm³. A large prospective study in Tanzania that followed-up HIV-infected mothers and their children for 24 months after delivery found that the CD4 count of mothers taken during pregnancy was a predictor of increased child mortality among both HIV-infected and non-infected children.[242]

Given that few mothers died during the study period, we were not able to establish any association between maternal death and increased child mortality. This is in contrast to other studies conducted in Uganda, Tanzania and Malawi[15] which found a three times higher mortality rate among children born to HIV-infected women compared to their HIV-negative counterparts. Further, when a mother dies the risk of child mortality is trebled, regardless of the mother's HIV status. The risk of maternal death is higher in these countries as there is greater dependence on breastfeeding.

One of the benefits of the Serithi Project was to enable periodic and regular follow-up of mothers and infants so as to be able to facilitate speedy referral to the paediatric ART clinic at Kalafong for management and treatment where indicated. However, the development of a project that is geared toward close follow-up of mothers and children and is designed to reinforce existing PMTCT programmes is not representative of the "typical" situation in South Africa and highlights the question of generalisability of this study. For example, it has been documented[229] that more than 30% of infants and more than 70% of children were lost to follow-up by four months due to poor follow-up rates at Government PMTCT sites, with consequently poor ability to assess the efficacy of local PMTCT

programmes[227]. The lack of follow-up of HIV-exposed and infected children denies them access to adequate medical care. Understanding the socio-economic factors that affect the ability of communities to comply with PMTCT and long-term ARV programmes is critical in assisting resource-poor countries to develop strategies to achieve follow-up of HIV-exposed infants.[250]

8.7 SUMMARY

Our study findings show that PMTCT in this cluster of clinics in Tshwane resulted in a poor outcome, given the high HIV transmission rate, missed doses of NVP to mother and missed doses of NVP to the baby. It is disappointing that our findings are not too dissimilar to other developing countries in Sub-Saharan Africa in the early stages of the PMTCT programme implementation. At the time that our study was conducted there was no dual ARV therapy or HAART for pregnancy. Yet, it is known that if this was available it would have contributed to improved outcomes for mothers and their children. Poor record-keeping in hospitals was noted and would need to be addressed by ensuring that personnel is better trained and held accountable for recording administration of any ARV medication. It is also clear that at the time this study was conducted mothers on HAART were not fully sensitised on the risks of non-adherence to treatment on the long-term efficacy of the therapy, given that almost a third had treatment interruption.

Our study has shown the continuing risk of HIV transmission through breast feeding, but has also highlighted serious problems with the way in which mothers respond in their feeding choices. Exclusive breastfeeding is seldom practised and mothers commonly choose mixed feeding options, recognised to be the most risky for HIV transmission.

In order to increase HIV-free survival among HIV-exposed children it will be important to increase the access to dual therapy, improve the documentation of the programme, ensure that eligible mothers are placed on HAART without much delay and that frequent quality counselling is provided postnatally on exclusive infant feeding practices. Optimal effectiveness and scaled-up coverage of the PMTCT programme interventions will be assured if there is detailed and consistent follow-up and early HIV diagnosis of all infants born to HIV-infected mothers at the primary health care level. This will minimise missed opportunities for the children to be placed onto ARV therapy as deemed necessary and for those eligible mothers to be referred for HAART initiation.

CHAPTER 9 - CONCLUSIONS AND RECOMMENDATIONS

The overall objective of the study was to determine prenatal and postnatal infant feeding practices of HIV-infected women and the factors that determined choices and adherence. Futhermore, the study set out to determine the longitudinal changes in anthropometry and micronutrient status and the determinants thereof from six weeks after delivery until 24 months. To assess whether maternal HIV status influences her mothering capacity, the study determined the growth patterns of children born to HIV-infected mothers over a two-year follow-up period and the influencers thereof.

In order to achieve the main objective it was necessary to conduct a series of interlinked assessments, each of which contributed to the main objective. This Chapter will summarise each of these studies and assess the extent to which they assist in meeting the main objective.

9.1. CONCLUSIONS

9.1.1. Prenatal and Postnatal infant feeding choices and practices of HIV-infected women

This study re-affirms that counselling on feeding choices for HIV-exposed infants must be extremely sensitive to numerous internal and external factors impacting on that decision. We found that HIV-infected women who had better coping skills, more education (though not statistically significant), who were married and who had disclosed to their partners tended to choose formula-feeding after undergoing the routine PMTCT counselling process. This study further emphasises the importance of support to HIV-infected women in their infant

feeding decisions, to enable disclosure and improved coping. Community-wide efforts are needed to enable HIV-infected women to independently make their infant feeding choices, relative to their own household circumstances. Such support may be in the form of frequent counselling sessions, regular antenatal contact with the mother and including, where possible, home visits. Without this package of interventions, mothers will continue to find it difficult to address the psychosocial issues pertaining to their status and to make truly independent and informed infant feeding decisions.

Our findings on postnatal infant feeding practices in comparison to antenatal choices have highlighted the serious challenges posed by the application of PMTCT guidelines to the socio-cultural complexity of advice on infant feeding. The poor adherence to exclusivity of either infant feeding choice reflects either poor maternal knowledge on the importance of exclusive feeding, or limited knowledge of counsellors. The support that HIV-infected women need in making their infant feeding decisions will entail psychosocial, community-wide interventions, and frequent counselling sessions to assist them in coping with and disclosing their status. Improving the quality of infant feeding counselling for all mothers and promotion of exclusive breastfeeding at family level are key to enhancing HIV-free survival.

9.1.2. Maternal outcomes

We observed a well-maintained nutritional state amongst most HIV-infected mothers in this study over a period of two years after giving birth. A tendency to develop obesity was noted, and the micronutrient status was well maintained or even improved.

We noted a high postnatal maternal mortality of 3.6% over two years. While more mothers who ever breastfed had died (5.9%) compared with formula-feeding mothers (2.9%), the possibility of sicker mothers choosing to formula-feed was not excluded and small numbers precluded statistical comparison. We also noted a poor compliance rate of only 71% with HAART among those mothers who were eligible and who had started treatment.

9.1.3. Child outcomes in relation to maternal health

Our study has identified several missed opportunities in the delivery of optimal PMTCT services for both mothers and their children in select clinics in Tshwane during our two-year follow-up period. Poor recording of both the mother and child nevirapine dose, poor infant feeding practices such as mixed breast- and formula-feeding, together with early introduction of complementary feeds, are all factors that have compromised the PMTCT services and led to high HIV transmission rates. We found a 15% vertical transmission rate of HIV infection by 2 years of age.

We found that 11% of the children in this cohort had died by age 2 years. This included both HIV-infected and uninfected children. Nearly one third of the HIV-infected children (30.7%) had died, compared with 8.3% of uninfected children. This illustrates the very high risk to children of HIV-infected mothers, even though on the whole there was no evidence in our cross sectional data of extensive malnutrition among the children in this study.

On the positive side, of the 27 surviving HIV-infected children, more than 75% had begun ARV therapy. This is the only hope for an improved outcome for the infected children of this cohort following the failure of the PMTCT programme for

them. Given the poor compliance with HAART by the mothers, a special effort is needed to guarantee child compliance.

9.2 RECOMMENDATIONS

Enhancement of the quality of infant feeding counselling offered antenatally and postnatally to HIV-infected women. It is essential that HIV-infected women gain access to several counselling opportunities focusing on infant feeding choices and adherence during pregnancy and soon after delivery. The counselling process needs to address the family context and be tailor-made to suit the individual context of the mother being counselled, bearing in mind that infant feeding-related stigma is still prevalent in the society. Counsellors will need to receive continuous training and skills development to ensure that the quality of the counselling they are rendering is applicable to the socio-economic and cultural background of each mother that has to decide the optimal feeding option for their children.

Monitoring at regular intervals maternal anthropometric indices and determining HIV disease progression is important. Within a peri-urban environment it is important to prevent both undernutrition and overnutrition and ensure reinforcement of the prudent diet in the HIV context. Evidence-based nutrition messages on healthy lifestyles (including exercise and physical activity) and the food-based dietary guidelines need to be emphasised for persons living with HIV in order to minimise their vulnerability to consuming unprescribed supplements and immune boosters.

As more mothers become eligible and enroll for HAART, it will be essential to **ensure adherence to treatment** by making such services more affordable and accessible at the primary health care level. Health systems management may have to review the fee structure for patients to access their files as the cost

inherent in this hinders patient compliance with HAART. **Counselling on stigma** and disclosure for mothers on HAART will continue to be an essential and continuous element of the Comprehensive Care, Management and Treatment Plan on HIV and AIDS in South Africa.

More intense efforts should be made to address the high levels of mortality among HIV-exposed infants and their infected mothers, and more PMTCT programme managers need to view "HIV-free survival" as an outcome indicator. All HIV-infected mothers need to be encouraged to bring their children for regular growth monitoring after delivery and to also be aware of the availability of the DBS PCR test for determination of the child's HIV. Whilst we found that the follow-up to ensure access of children to HAART was good, there is still a need to ensure that at each clinic visit a thorough assessment of the children's growth pattern is performed to detect any growth faltering or changes in disease state. Along with this, reinforcement of adherence to exclusive formula-feeding or exclusive breastfeeding and access to prophylactic treatment especially for the first 6 months of life should be enforced. Every effort should be made to increase maternal awareness of the dangers of mixed feeding and early introduction of poor nutrient-quality complementary food on optimal growth of the children.