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Full Length Research Paper

The role of IgG, IgA and IgM as immunological markers of HIV/AIDS progression

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Patients with human immunodeficiency virus (HIV) infection exhibit a generalized, non-HIV-specific polyclonal B-cell activation resulting in hypergammaglobulinemia of all immunoglobulin isotypes as well as increased production of HIV-specific IgG and IgM. These immunoglobulins have the potential to be used as markers for monitoring the progression of HIV infection. With the inherent challenges of cost and convenience in the use of the conventional markers for HIV monitoring, that is, viral load and CD4^{+} count, there is the need to investigate the possible prognostic role of the above mentioned immunoglobulins in the management of HIV patients in Nigeria. The IgG, IgA and IgM profile as well as the CD4^{+} T cell count of forty HIV seropositive subjects was assayed before and after 3 months follow-up in a case series descriptive study. The Igs were measured using enzyme linked immunosorbent assay (ELISA), while CD4 count was done using flow cytometry. In the determination of concentration/value changes of parameters at baseline and follow up in HIV progression, only IgM, waist and hip circumference showed significant differences ($p < 0.05$) within the period under study. While in the determination of the effect of therapy on the subjects, significant differences ($p < 0.05$) were observed only in the values of CD4 count and BMI. While statistically significantly inverse relationship was observed between the CD4 counts and IgM concentrations, the values of IgG and IgA were inverse but not significant in relation to CD4 count. This study concluded that immunoglobulins (G, A and M) are not reliable in monitoring short term response to therapy unlike CD4 count although IgM has good diagnostic value like CD4 at baseline.

Key words: HIV/AIDS, CD4^{+} count, viral load, antiretroviral, immunoglobulins.

INTRODUCTION

Human immunodeficiency virus (HIV) is a slowly replicating retrovirus of the Genus Lentivirus and family retroviridae that causes acquired immunodeficiency syndrome (AIDS), a clinical condition in humans in which progressive failure of the immune system allows life-threatening opportunistic infections and cancers to subdue the body (Douek et al., 2009). HIV infects vital cells in the human immune system such as helper T cells

(specifically CD4^{+} T cells), macrophages and dendritic cells (Cunningham et al., 2010). Without treatment, average survival time after infection with HIV is estimated to be 9 to 11 years, depending on the HIV subtype (UNAIDS, 2007).

Activation of all components of the immune system is commonly triggered in HIV infected patients. And an important indicator for the manifestation of immune activation is the increase in cytokine production in the body (Chandra et al., 2005). However, Plaeger et al. (1999) reported that the limitation in the ability to quantify numerous circulating cytokines in the body has led to the assessment of downstream products that reflect cytokine activity in lymphoid tissues. Chandra et al. (2005) outlined three categories of immunologic markers as having significant relation to the prognosis of HIV. They are the HIV viral load, the CD4 T-cell levels and plasma levels of soluble markers of immune activation.

HIV infection leads to a progressive reduction in the number of T cells expressing CD4. CD4 counts do not always correlate with clinical outcome, possibly because CD4 lymphocytes are not the only key players at all stages of infection (Helbert, 1992) and because CD4 counts do not reflect function of T cells (Helbert, 2000). However, immunological markers have shown to be very sensitive in disease detection.

Meanwhile, immunological markers have shown to be very sensitive in disease detection. In placental mammals, there are five antibody isotypes known as IgA, IgD, IgE, IgG and IgM. They are each named with an "Ig" prefix that stands for Immunoglobulin, and differ in their biological properties, functional locations and ability to deal with different antigens. The Immunoglobulins G and A are further grouped into *subclasses* (e.g. in Human: IgG1, IgG2, IgG3, IgG4, IgA1 and IgA2) based on additional small differences in the amino acid heavy chain sequences (Fenyo et al., 1996; Moja et al., 2000).

Patients with HIV infection exhibit a generalized, non-HIV-specific polyclonal B-cell activation resulting in hypergammaglobulinemia of all immunoglobulin isotypes (Lane et al., 1983; Shirai et al., 1992), as well as increased production of HIV-specific IgG and IgM (Mizuma et al., 1988). Whilst infection with HIV type 1 (HIV-1) is associated with profound immunologic abnormalities amongst T and B lymphocytes, the specific character and magnitude of this HIV-induced humoral immune response is poorly understood (Fenyo et al., 1996). HIV neutralizing activities have been attributed to IgG and IgA isotypes, whilst IgG subclasses have been associated with virus-specific antibody-dependent cellular cytotoxicity (Subramannian et al., 2002; Burrer et al., 2001; Moja et al., 2000). Serum immunoglobulins (Ig) concentrations have been reported to increase with progression from asymptomatic to symptomatic HIV infection (Lyamuya et al., 1994; Peng et al., 1996).

HIV neutralizing activities have been attributed to IgG and IgA isotypes, whilst IgG subclasses have been associated with virus-specific antibody-dependent cellular cytotoxicity (Subramannian et al., 2002; Burrer et al., 2001; Moja et al., 2000). Serum immunoglobulins' concentrations have been reported to increase with progression from asymptomatic to symptomatic HIV infection (Lyamuya et al., 1994; Peng et al., 1996). Moreover, it is on record that the effect of ARV on immunoglobulin concentrations amongst HIV-infected persons may provide useful information regarding monitoring of drug response and HIV disease progression.

Although, access to ARV drugs in Africa has improved through price reductions, standard monitoring of disease progression using CD4-cell count and viral load measurement remain expensive. CD4-cell count and viral load measurement are only available in a few urban health and research facilities, owing to their technical complexity and the requirement for expensive equipment (Ludaga et al., 2003). The effect of ARV on immunoglobulin concentrations amongst HIV-infected persons may provide useful information regarding monitoring of drug response and HIV disease progression. Immunoglobulin measurement is relatively inexpensive and may potentially serve as simple surrogate markers to evaluate response to ARVs in HIV patients (Ludaga et al., 2003). Lugada et al. (2004) emphasized that studies are required to assess the role of immunoglobulins in the monitoring of patients with HIV in developing countries, including those on anti-retroviral therapy. This study therefore assesses the role of IgG, IgA and IgM in the monitoring of HIV positive patients in selected parts of Oyo State, South-Western Nigeria.

METHODOLOGY

Ethical approval

Ethical approval was obtained for this study from the appropriate authority (Ministry of Health of Oyo State).

Data collection

Anonymized questionnaire was used to collect the socio-demographic characteristics and other relevant information of subjects who were enrolled and followed-up for the study.

Sample collection

A hundred (100) HIV positive baseline blood samples were collected by venepuncture from HIV positive subjects who were yet to be placed on anti-retroviral therapy (ART) and who were attending the PEPFAR clinic at Adeoyo Maternity Teaching Hospital, Ibadan. From these 100 initial samples however, only forty subjects were available for the follow-up phase of data and sample collection which was at least 3 months from the period of first contact. Meanwhile, 48 pre-samples and 40 post-samples were analysed in consonance with the calculated sample size and due to attrition respectively.

3 ml of blood sample were collected from the HIV positive

subjects using potassium (K₃) EDTA vacutainers before and after the commencements of therapy. The suspended plasma was separated and stored frozen with plain bottles at a temperature of -20°C till analysis. 5 ml of blood sample was obtained from 5 apparently healthy, HIV sero-negative individuals and were used as quality control for the study. These control plasma samples were pooled before assaying for their concentration. The control samples were processed and stored in the same way as the HIV positive plasma samples.

CD4 count was obtained by a retrospective enquiry through all the subjects' personal 'green' hospital card at the point of interview. The technique used for the determination of subjects' CD4+ T cell count at the centre was flow cytometry (PartecCyFlow Counter®, Partec GmbH, Münster· Germany). Immunoglobulins G, A and M concentration were measured using enzyme linked immunosorbent assay (ELISA) kit.

HIV staging

Exposure category (staging) was determined using the World Health Organisation (WHO, 2007) staging criteria.

Statistical analysis

The statistical software - Statistical Package for Social Sciences (SPSS Inc., Chicago - version 16.0), was used in the analysis and inference of data collected. Results were expressed as mean ± SD or as median ± (interquartile range), where SD was ambiguous; and values were considered statistically significant at p<0.05. Correlation between the immunological markers under study, that is, IgG, IgA, IgM and CD4+ T-lymphocyte count was assessed by using Spearman's rank correlation coefficient, while statistical significant changes in concentrations at baseline and 3 months follow-up were determined using the Student paired t-test. Changes in concentration of markers/parameters between therapy and non-therapy group were determined using independent sample t-test. Wilcoxon Signed Ranks Test and Mann-Whitney Test were used for the median (interquartile range) t-tests. The Pearson correlation test was used to determine the strength of relationship between CD4 cell count and other immunological markers/parameters. Chi-square test was used to determine the test of association between markers/parameters under study.

RESULTS

From the 48 initial samples, there were 40 (83.3%) female subjects and 8 (16.7%) male subjects. 21 (43.8%) had only primary education, 15 (31.2%) had secondary education; while only 4 (8.3%) had tertiary education. But, 8 (16.7%) had no form of formal education. 27 (56.2%) of the subjects were traders, while 5 (10.4%) had no means of income. 12 (25.2%) were artisans and casual workers of various vocations, while 2 (4.2%) were retired pensioners. And, only 2 (4.2%) were engaged in formal jobs. Of these, 45 (93.8%) were little or no income earners, 2 (4.2%) were middle income earner and just one person (2.1%) earns high enough to take good care of himself.

Out of these 48 subjects, 25 (52.1%) were Christians, 22 (45.8%) were Muslims, while 1 subject (2.1%) practised both Christianity and Islam. 38 (79.2%) were married, 8 (16.7%) were single, and 2 (4.2%) were divorced. 34 (70.8%) subjects had symptomatic HIV-1 infection spanning from stages II to IV (3 (6.3%) in stage II; 11 (22.9) in stage III and 20 (41.7%) in stage IV), while 10 (20.8) subjects were still in stage I/asymptomatic infection stage. However, the staging of four (8.3%) subjects could not be ascertained. 23 subjects (57.5%) were already on therapy, while the remaining 17 (42.5%) were yet to be put on therapy. Of the group that commenced treatment, 5 subjects (21.7%) were treated with only anti-retroviral drug (tablets) comprising Tenovirdisoproxil, Fumarate, Lamivudine and Efavirenz at a dosage of 300, 300 and 600 mg, respectively per day, while 18 subjects (78.3%) received 960 mg per day tablets of Septrin (Cotrimoxazole) in addition to the above-mentioned ARV drug. Trimethoprim or Atovaquone was given to those who reacted to Septrin. The paediatrics received lower doses of the ART ad compared to the adults. These also include a fixed dose or triple fixed dose of Zidovudine, Lamivudine and Nevirapinecomprimes at dosage of 60, 30 and 50 or 300, 150 and 200 mg, respectively. The subjects who were put on therapy had been on their respective medications for a period of 2±1 month before the follow-up blood samples were collected.

Among the parameters compared at baseline and follow up, only IgM, waist and hip circumference, weight showed significant differences. There was no significant difference between the baseline and follow up values of CD4, IgG, IgA, BMI, systolic blood pressure, diastolic blood pressure, weight and height of subjects. In the determination of the effect of therapy on the subjects, significant differences (p < 0.05) were observed only in the values of CD4 count and BMI at baseline and follow in the treatment (therapy) group when compared with the non-therapy group (Table 1). Furthermore, within their respective groups in terms of therapy or none, only IgM, weight and BMI showed significant difference (increase, p < 0.05) between baseline and follow up in the group on therapy, while none of the markers observed showed significant changes in the non-therapy group, that is, p>0.05 (Table 2).

Moreover, Table 3 shows a significant direct relationship between the CD4 values at baseline and at follow up. There was also a significant inverse relationship between the CD4 count and IgM concentrations at baseline. Relationships between CD 4 count and IgG and also with IgA were inverse and not significant. IgG and IgA also have inverse relationships that were not significant except for the relationship between the baseline concentrations of IgG and follow up values of IgA that were direct but also not significant. IgG and IgM also have inverse relationships that were not significant at both baseline and follow up. IgA and IgM have direct relationships except at the baseline, where their values have inverse relationships but not significant. Relationship between the baseline concentration and

Table 1. Comparison of changes in levels of immunological markers and physical parameters in treatment and non-treatment group of HIV subjects.

| Parameter | T test for equality of Means | | | |
	Treatment group mean ± SD N=23	Non-treatment group mean ± SD N=17	t value	P Value
CD4 baseline	198.00[a] ± (110.0 – 291.0)[b]	458.00[a] ± (198.50 – 643.0)[b]	-2.804[c]	0.005
CD4 follow-up	201.00[a] ± (105.50 – 368.0)[b]	420.00[a] ± (255.50 – 547.0)[b]	-2.951[c]	0.003
IgG baseline	2782.25 ± 702.05	2878.39 ± 435.53	-0.497	0.622
IgG follow-up	2658.27 ± 764.79	2629.35 ± 654.18	0.126	0.901
IgA baseline	63.09 ± 15.75	67.71 ± 12.91	-0.991	0.328
IgA follow-up	62.03 ± 15.22	63.55 ± 14.21	-0.322	0.749
IgM baseline	218.292[a] ± (141.59 – 480.58)[b]	423.951[a] ± (206.24 – 493.71)[b]	-1.903[c]	0.057
IgM follow-up	491.38[a] ± (280.71 – 493.71)[b]	480.58[a] ± (287.54 – 500.04)[b]	-0.028[c]	0.978
Weight baseline	49.02 ± 16.76	61.82 ± 22.52	-2.063	0.046
Weight follow-up	50.89 ± 15.34	61.79 ± 22.62	-1.818	0.077
BMI baseline	18.99 ± 4.76	25.16 ± 6.72	-3.403	0.002
BMI follow-up	19.86 ±3.82	25.17 ± 6.74	-3.156	0.003

a: Median value; b: (interquartile range); c: Z value.

3 months follow up values of IgM is also inverse but not significant.

DISCUSSION

The use of CD4 count, viral load and immunoglobulins, especially IgG, IgA and IgM in the determination and monitoring of the progression of HIV/AIDS have been established (Ghani et al., 2001; Lugada et al., 2004). However, in practice, physicians depend mostly on the estimation of markers such as the CD4 count and viral load level, to monitor and assess whether or not a patient is at risk of progressing to AIDS, monitor therapeutic efficacy and to help determine an appropriate therapeutic regimen (Ghani et al., 2001).

CD4 count estimation has been established in HIV care as a reliable marker of HIV progression (Phillips et al., 1991; Saah et al., 1992; Whittle et al., 1992; Uppal et al., 2003) because HIV infects and depletes vital cells in the human immune system amongst which are the helper T cells (specifically CD4^{+} T cells), macrophages and dendritic cells (Cunningham et al., 2010). HIV infection leads to a progressive reduction in the number of T cells expressing CD4. So naturally, CD4 count has become a gold standard in monitoring the progression of HIV/AIDS and response to therapy (Mocroft et al., 1997).

HIV neutralizing activities have been attributed to IgG and IgA isotypes, whilst IgG subclasses have been associated with virus-specific antibody-dependent cellular cytotoxicity (Subramannian et al., 2002; Burrer et al., 2001; Moja et al., 2000). Serum immunoglobulins concentrations have been reported to increase with progression from asymptomatic to symptomatic HIV infection (Lyamuya et al., 1994; Peng et al., 1996). However, our findings show no significant difference in IgG and IgA concentrations when comparing the average baseline and follow up samples of all the subjects in both therapy and non-therapy groups as shown in Tables 1, 2 and 3.

Patients with human immunodeficiency virus infection exhibit a generalized, non-HIV-specific polyclonal B-cell activation resulting in hypergammaglobulinemia of all immunoglobulin isotypes' (Lane et al., 1983; Shirai et al., 1992). However, while this hypergammaglobulinemia is expected uninterrupted in the non-therapy group, the reverse was expected in the treatment group. The result of this study as shown in Tables 1 and 2 that there was a decline in IgG and IgA concentrations between the baseline and follow up values and this seem to be contradictory, because, while such a decline is expected in the therapy group, it was not expected in the group without treatment (Lane et al., 1983; Shirai et al., 1992).

Marcelino et al. (2008) reported an inverse association between anti-Env C2C3 IgG and CD4^{+} T cells. Since CD4 count increases in the group on therapy, it is expected that the immunoglobulins concentrations decline. However, the pattern observed in the non-therapy group (Tables 1, 2, and 3) where instead of hyperglobulinaemia, a decline is observed; seem to support studies that found a decrease in anti-HIV IgG3 during disease progression (Lugada et al., 2004). And anti-Gag IgG3 appears early in acute infection and then declines (Wilson et al., 2004).

In contrast however, in Table 1, there was significant increase in IgM. In Table 2, amongst the groups on therapy, a significant increase in IgM was also observed.

Table 2. Comparison of changes in levels of immunological markers and physical parameters in therapy (N=23) and non-therapy (N=17) groups of HIV subjects at baseline and 3 months follow up.

Parameters (N = 23) (N=17)	Baseline (before therapy) Mean ± SD	3 Months follow-up (after therapy) Mean ± SD	P value
CD4 count (cells/mm^3)			
Therapy	198.00^a ± (110.0 – 291.0)^b	201.00^a ± (105.50 – 368.0)^b	0.088
Non-therapy	458.00^a ± (198.50 – 643.0)^b	420.00^a ± (255.50 – 547.0)^c	0.850
IgG (mg/dl)			
Therapy	2782.25 ± 702.05	2658.27 ± 764.79	0.556
Non-Therapy	2878.39 ± 435.53	2629.35 ± 654.18	0.166
IgA (mg/dl)			
Therapy	63.07 ± 15.75	62.03 ± 15.22	0.826
Non-Therapy	67.71 ± 12.92	63.55 ± 14.21	0.382
IgM (mg/dl)			
Therapy	218.292^a ± (141.59 – 480.58)^b	491.38^a± (280.71 – 493.71)^b	0.011
Non-Therapy	423.951^a ± (206.24 – 493.71)^b	480.58^a ± (287.54 – 500.04)^b	0.463
Weight (kg)			
Therapy	49.02 ± 16.76	50.89 ± 15.34	0.043
Non-Therapy	61.82 ± 22.52	61.79 ± 22.62	0.975
BMI (kg/m^2)			
Therapy	18.99±4.76	19.86 ± 3.82	0.041
Non-Therapy	25.16 ± 6.72	25.17 ± 6.74	0.993

a: Median Value; b: (interquartile range).

Table 3. Pearson correlation of concentrations of immunological parameters at baseline and follow-up.

(N = 40)	Coefficient of correlation, r P value							
Parameter	CD4 pre	CD4 post	IgG pre	IgG post	IgA pre	IgA post	IgM pre	IgM post
CD4 Pre								
r	1	0.870	-0.084	-0.050	-0.132	-0.053	-0.410	-0.085
p		0.000	0.605	0.760	0.416	0.745	0.009	0.603
CD4 post								
r	0.870	1	-0.124	-0.133	-0.214	-0.197	0.318	-0.008
p	0.000		0.460	0.427	0.197	0.236	0.052	0.962
IgG pre								
r	-0.084	-0.124	1	0.114	-0.239	0.150	-0.025	-0.077
p	0.605	0.460		0.484	0.114	0.355	0.869	0.639
IgG post								
r	-0.050	-0.133	0.114	1	-0.129	-0.160	-0.252	-0.182
p	0.760	0.427	0.484		0.428	0.325	0.116	0.262
IgA pre								

Table 3. Cont'd

r	-0.132	-0.214	-0.239	-0.129	1	-0.034	-0.034	0.257
p	0.416	0.197	0.114	0.428		0.834	0.822	0.110
IgA post								
r	-0.053	-0.197	0.150	-0.160	-0.034	1	0.238	0.006
p	0.745	0.236	0.355	0.325	0.834		0.139	0.969
IgM pre								
r	0.410	0.318	-0.025	-0.252	-0.034	0.238	1	-0.231
p	0.009	0.52	0.869	0.116	0.822	0.139		0.152
IgM post								
r	-0.085	-0.008	-0.077	-0.182	0.257	0.006	-0.231	1
p	0.603	0.962	0.639	0.262	0.110	0.969	0.152	

. This corroborated the earlier study that chronic state of B-cell hyper activation continues 2 to 3 years after highly active anti-retroviral therapy (HAART) initiation (Lugada et al., 2004). This continuous, chronic immune hyper activation due to HAART must be responsible for the significant increase in the median concentrations of the IgM from the baseline to 3 months follow up in this study. This agrees with Wilson et al. (2004) who reported that there is an increased production of IgM in HIV infections.

Table 3 shows that there is a significant direct relationship between the baseline and 3 months follow up values of CD4 count, establishing the reliability of our test method and it also shows an inverse relationship between the baseline values of CD4 count and IgM concentrations. This agrees with previous studies that show that the primary IgM response does not persist beyond 3 months (Gaines et al., 1988; Lange et al., 1988; Joller-Jemelka et al., 1987). This inverse relationship between the baseline values of CD4 count and IgM concentration suggests that at baseline, IgM concentrations can be used to enhance the prognostic value of CD4 count. However, since there is no significant relationship between the two parameters at 3 months follows up, it will be safe to suggest that at 3 months or beyond, IgM concentration might not be used independently, interchangeably or along with CD4 count in assessing HIV progressions and response to therapy.

Conclusion

This study concluded that IgG and IgA cannot be used as independent, complementary or CD4 associated markers in the monitoring of HIV/AIDS progression or response to therapy and IgM might be useful in enhancing the diagnostic and staging value of CD4 count in HIV/AIDS management; it cannot be safely used in monitoring progression or response to treatments.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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Full Length Research Paper

Childbearing intentions among sexually active HIV-infected and HIV-uninfected female adolescents in South Africa

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Women of reproductive age account for nearly half of all HIV-infected people worldwide. Childbearing intention among HIV-infected women is complicated by social and reproductive concerns related to their HIV status. We conducted a cross-sectional study of HIV-infected and HIV-uninfected sexually active South African women aged 17 to 21 in order to compare their childbearing intentions and to identify predictors of the desire to have children among women with HIV. We found the rate of childbearing intention to be similarly high among both HIV-infected and HIV-uninfected study participants (80 and 79% respectively, p=0.81). History of previous parity was found to be associated with decreased intention to have children. No difference in childbearing intention was found between HIV-infected women on anti-retroviral therapy (ART) and women not on ART. High rates of childbearing intention among HIV-infected women require integration of reproductive health services with comprehensive HIV/AIDS care in order to mitigate the risks of sexual and vertical transmission of HIV.

Key words: HIV, childbearing intention, South Africa, anti-retroviral therapy.

INTRODUCTION

Decisions about childbearing among HIV-infected women are complicated by concerns regarding family planning methods, sexual transmission of HIV, risk of maternal orphanhood, community expectations, and vertical transmission of HIV. Childbearing intentions may be influenced by a number of variables including age, time since diagnosis of HIV, treatment with anti-retroviral therapy (ART), and history of parity. To achieve the goals of comprehensive HIV care, childbearing intentions require regular evaluation in order for women to make informed decisions regarding this complex reproductive health scenario. Nearly half of all HIV-infected people globally are women of reproductive age (UNAIDS, 2016).

Approximately 66% of all new HIV infections occur in sub-Saharan Africa with the highest incidence occurring in Southern Africa (UNAIDS, 2016). In South Africa, an

estimated 29% of pregnant women are living with HIV (Goga et al., 2016). Although ample evidence exists that many HIV-infected women desire children, the identified predictors of childbearing intention have varied among previous studies.

In addition, little prior research has directly compared childbearing intention between HIV-infected and HIV-uninfected women from the same community. Finally, there is a paucity of research specifically aimed at evaluating the fertility desires of HIV-infected adolescents. Young women are the key drivers of the HIV epidemic in South Africa (Murray et al., 2014), the country with the largest population of people living with HIV (Murray et al., 2014). We compared childbearing intentions between HIV-infected and HIV-uninfected sexually active South African adolescent females, ages 17 to 21. In addition, among our HIV-infected participants, we compared childbearing intentions between those on anti-retroviral therapy (ART) and those not on ART. Finally, using bivariate and multiple logistic regression analyses, we assessed predictors of these intentions.

MATERIALS AND METHODS

Between October 2013 and March 2015 we conducted a cross-sectional study of 50 HIV-infected and 50 HIV-uninfected young, sexually active, South African women, ages 17 to 21 years. Cohort enrollment occurred sequentially until the goal of 50 participants in each group was met.

Study participants were surveyed in English and/or Xhosa regarding their childbearing intentions, contraception use, sexual history, HIV care (HIV-infected only), and demographic variables. The primary outcome, childbearing intention, was defined as an affirmative answer to the question, "Do you intend to have children at any time in the future?" Responses of "don't know" were considered lack of affirmative childbearing intention.

All participants were recruited from a youth community center and clinic in two indigent township communities in Cape Town, South Africa where surveys were interview-administered by staff. These study sites offer HIV testing and counseling, treatment for sexually transmitted infections, and free contraceptives and condoms. Informed consent (age 18 years or older) or parental consent along with signed adolescent assent (age 17 years), was obtained from all participants. In order to confirm HIV status, all study participants underwent HIV testing on the same day as survey administration. The University of Rochester's Research Subject Review Board and the University of Cape Town's Human Research Ethics Committee granted ethical approval for this study.

Descriptive statistics were calculated separately for HIV-infected and HIV-uninfected women using means and standard deviations (for continuous variables) and frequencies and percentages (for categorical variables). Comparisons between HIV-infected and HIV-uninfected women were performed using independent measures t-tests and χ^2 tests for independence. All analyses were performed in SPSS 23.

RESULTS

Demographic and behavioral variables of our cohort are presented in Table 1. Childbearing intention was high among both HIV-infected and HIV-uninfected members of our cohort (80 and 79% respectively, p=0.81). No significant differences between number of past pregnancies and number of past live births were identified between groups and approximately two thirds of the cohort was nulliparous. Likewise, HIV-infected and HIV-uninfected members of our cohort had similar numbers of lifetime sexual partners and most were monogamous over the previous six months. Contraception use was nearly universal in our cohort although HIV-infected women were more likely to report condom use.

Bivariate analyses were conducted to identify potential predictors of childbearing intention. Among the entire cohort, women with no history of pregnancy were more likely to have childbearing intentions than those with one or more past pregnancies (76 versus 24%, p=0.001). Similarly, women with no history of live births had greater childbearing intentions than those who had given birth to one or more children (78.5 versus 21.5%, p<0.001). This finding held true when analyzing HIV-infected women only, with 72.5% of never pregnant participants reporting positive childbearing intention compared to 27.5% of women with a history of pregnancy (p=0.038). Age of the participant was not found to be predictive of childbearing intention. Multiple logistic regression analyses supported these findings - the likelihood of childbearing intentions was significantly higher for individuals with no history of live births (Odds Ratio = 12.35, p<0.001) or with no history of past pregnancy (Odds Ratio = 7.19, p=0.002) when controlling for patient age, HIV status, and contraception use.

A comparison of demographic and behavioral variables between HIV-infected participants on ART and not on ART is presented in Table 2. No difference was identified between groups regarding childbearing intention. Pregnancy history, contraception use, and number sexual partners also did not significantly differ between groups. Time since HIV diagnosis (among HIV-infected participants) was not found to be predictive of childbearing intention.

DISCUSSION

This study identified similarly high levels of childbearing intention among HIV-infected and HIV-uninfected young women. This high proportion of intention among HIV-infected African women (80%) exceeds that reported in previous literature. A survey study of HIV-infected Malawian women aged 18 to 40 years found a proportion of childbearing intention of 50.4% (Kawale et al., 2014).

Similar studies of HIV-infected women aged 18 to 49 in Ethiopia and Ghana identified intention proportions of 44% (Asfaw and Gashe, 2014) and 58% (Gyimah et al., 2015), respectively. Past research among HIV-infected South African women also reported childbearing intention that was lower than identified in our study: a 45%

Table 1. Participant Demographics and Behavioral Variables.

Variables	HIV-infected (n = 50)	HIV-uninfected (n = 50)	P-value
Age	19.6 (SD 1.40)	18.4 (SD 1.40)	<0.001
Childbearing Intention	40 (80%)	39 (78%)	0.81
Number of Past Pregnancies			
0	33 (66%)	34 (68%)	
1	15 (30%)	15 (30%)	0.84
2	2 (4%)	1 (2%)	
Number of Live Births			
0	33 (66%)	36 (72%)	
1	16 (32%)	13 (26%)	0.80
2	1 (2%)	1 (2%)	
Current Contraception			
Condom	49 (98%)	41 (82%)	0.008
Injection	29 (58%)	32 (64%)	0.54
Pill	1 (2%)	4 (8%)	0.17
None	1 (2%)	1 (2%)	1.00
Lifetime Sexual Partners			
1	11 (22%)	4 (8%)	
2-5	34 (68%)	44 (88%)	0.054
>5	5 (10%)	2 (4%)	
Sexual Partners - Last 6 Months			
1	48 (96%)	47 (94%)	0.65
2-5	2 (4%)	3 (6%)	

proportion of intention was found among a Cape Town cohort aged 25 to 34 (Cooper et al., 2009), and 30% proportion was identified in a cohort aged 18 to 44 in Soweto (Kaida et al., 2011).

The only study we identified of HIV-infected African women with a level of childbearing intention similar to our findings was from Burkina Faso and reported as an intention proportion of 70% (Lemoine et al., 2011). The high proportion of childbearing intention among our HIV-infected participants may be related to the young age of our cohort. Most previous research on this subject has included all adult women of childbearing age whereas our cohort comprised of women aged 17 to 21, of whom the majority (67%) had not yet had children.

With the increased life expectancy of HIV-infected persons in the era of ART, it is understandable that HIV-infected women have childbearing intentions that may be equal to those of their HIV-uninfected counterparts, despite additional reproductive and social complications associated with their HIV status, most notably the risks of sexual and vertical transmission of HIV. Still, there is a paucity of literature comparing childbearing intentions between these groups from within the same community.

One such study from South Africa found HIV-infected women to have less than half of the childbearing intention compared to HIV-uninfected women residing in the same township (Kaida et al., 2011). Our finding of no difference in childbearing intention between these two groups contrasts notably with this prior work from South Africa. These divergent findings may reflect age differences between the two study cohorts (child-bearing intention was higher among the younger participants in the Soweto study), cultural differences between these geographically and socially distinct communities (Cape Town versus Soweto), or possibly a change over time in childbearing intention among women with HIV.

Contradictory evidence regarding predictors of childbearing intention among women with HIV has been presented in prior research. While several studies have found younger age to be associated with increased childbearing intention (Asfaw and Gashe, 2014; Haddad et al., 2016; Kawale et al., 2014; Lemoine et al., 2011), some have identified increased age as a positive predictor of childbearing intention (Gyimah et al., 2015; Laar et al., 2015). A meta-analysis of fertility desires among HIV-infected men and women identified age less than 30 to be strongly associated with fertility intention (Berhan and Berhan, 2013). Given the very young age

Table 2. HIV-infected participant demographics and behavioral variables.

Variables	On ART (n = 22)	Not on ART (n = 28)	P-value
Childbearing Intention	18 (82%)	22 (79%)	0.78
Number of Past Pregnancies			
0	15 (68%)	18 (64%)	
1	5 (23%)	10 (36%)	0.20
2	2 (9%)	0 (0%)	
Number of Live Births			
0	15 (68%)	18 (64%)	
1	6 (27%)	10 (36%)	0.46
2	1 (5%)	0 (0%)	
Current Contraception			
Condom	22 (100%)	27 (96%)	0.37
Injection	17 (77%)	12 (43%)	0.014
Pill	0 (0%)	1 (4%)	0.37
None	0 (0%)	1 (4%)	0.37
Lifetime Sexual Partners			
1	7 (32%)	4 (14%)	
2-5	13 (59%)	21 (75%)	0.33
>5	2 (9%)	3 (11%)	
Sexual Partners in the Past 6 Months			
1	22 (100%)	26 (93%)	0.20
2-5	0 (0%)	2 (7%)	

and narrow age range of our cohort we did not identify age as a predictor of childbearing intention in our study.

Previous parity has also been found to be associated with childbearing intention. Some prior research has found a history of giving birth to be associated with decreased prospective childbearing intention among HIV-infected women (Abbawa et al., 2015; Asfaw and Gashe, 2014; Kawale et al. 2014; Melaku et al., 2014). A study of HIV-infected Ghanaian women, however, found childbearing intention to be positively associated with a history of childbearing (Gyimah et al., 2015). Our findings were consistent with the bulk of prior literature reporting greater childbearing intention among nulliparous HIV-infected women compared to those with a history of giving birth.

ART became widely available in South Africa in April 2004. Since that time, access to ART in South Africa has increased very substantially and is available in the township communities in which this study was conducted. In addition, the Western Cape Government has a three-phase program for the prevention of mother-to-child transmission of HIV that includes antenatal testing, ARTs, and post-natal ARTs for babies until HIV-status is determined. Still, not all women in our cohort were on ART therapy at the time of our study. In addition to incomplete access to ART, high rates of ART refusal in

this population may also have contributed to incomplete coverage in our cohort (Katz, et al., 2011). We did not find a difference in childbearing intention between HIV-infected women on ART and those not on ART. This is similar to prior findings among South African women (Kaida et al., 2011) and in the aforementioned meta-analysis (Berhan and Berhan, 2013). Some studies, however, have found being on ART to be correlated with increased childbearing intention (Abbawa et al., 2015; Asfaw and Gashe, 2014; Cooper et al., 2009).

While the level of childbearing intention among the HIV-infected women in our cohort may be higher than that presented in previous work, it is clear that many HIV-infected African women desire to have children, despite the complications that their medical condition may present. Contraceptive counseling has long been an essential component of comprehensive AIDS care but it is also important to assist HIV-infected women to achieve their reproductive goals. Integration of HIV care and reproductive health care, focusing on safe conception, is essential. Pre-exposure prophylaxis, for example, has been shown to be an effective method to decrease the risk of HIV transmission during condomless sex (Ndase et al., 2014). Optimizing reproductive outcomes for HIV-infected women will require family planning and counseling services to transit successfully to services

aimed at safe conception, prevention of mother-to-child transmission, and safe feeding of the newborn.

Our study has several important limitations. Due to the relatively small sample size, our ability to identify important differences between groups and sub-groups may be limited. Although our cohort included only sexually active women who are thus engaged in decision-making regarding reproduction, the overall young age of our study participants limits the generalizability of our findings. The generalizability of our findings may also be limited by cultural and geographic factors. Self-reporting of childbearing intention may not represent actual intention and may be influenced by perceived community expectations. Finally, our study did not include men and therefore cannot reflect their contribution to childbearing intention among HIV-infected women in their community.

Conclusion

In our cohort, childbearing intention was high among both HIV-infected and HIV-uninfected participants. Having no history of pregnancy and never having given live birth were identified as predictors of childbearing intention. Among HIV-infected women, being on ART was not found to be associated with childbearing intention.

Given the high rate of childbearing intention, comprehensive HIV/AIDS care for women of reproductive age requires both family planning and conception counseling to manage the risks of sexual and vertical transmission of HIV.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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