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Factors associated with the lack of antiretroviral therapy initiation among eligible HIV-positive pregnant women in Swaziland

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Background. Antiretroviral therapy (ART) initiation is critical for the prevention of mother-to-child transmission (PMTCT) of HIV.
Objectives. To quantify factors that were barriers or facilitators to the initiation of ART in pregnant HIV-infected women in Swaziland.
Methods. We conducted a cross-sectional survey in HIV-infected women with at least one antenatal care (ANC) visit, who had delivered in maternity wards between April and August 2013 in Swaziland. Variables collected included intrapersonal, interpersonal and organisational factors. Logistic regression models were used to calculate univariate and adjusted multivariate measures of association between ART initiation and the independent variables.
Results. Among the 163 pregnant women who were eligible for ART, 110 (67.5%) were initiated on ART by the time of delivery. The most commonly cited reason for not initiating ART (n=53) was women not being ready to initiate life-long treatment (24.5%). On multivariate logistic regression, favourable perceptions of the benefits of ART (adjusted odds ratio (AOR) 3.04; 95% CI 1.55 - 5.96) and presence of partner support (AOR 4.75; 95% CI 2.11 - 10.67) remained significantly and independently associated with ART initiation.
Conclusion. ART initiation among ART-eligible pregnant women in Swaziland was independently associated with the presence of partner support and favourable perceptions of the benefits of ART. Stronger counselling and education for pregnant women and male involvement strategies need to be implemented as universal life-long ART for all HIV-infected pregnant women is implemented.

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Prior to 2013, antiretroviral therapy (ART) was recommended by the World Health Organization (WHO) for HIV-infected pregnant women with CD4 cell counts of <350 cells/μL or those who were at WHO clinical stage III or IV Women who did not meet these criteria,were advised to use one of two options. Option A: antepartum zidovudine, with single-dose nevirapine during labour, and a 7-day zidovudine/lamivudine 'tail' alongside daily infant nevirapine during breastfeeding. Option B: ART during pregnancy and through cessation of breastfeeding to prevent mother-to-child HIV transmission (PMTCT.)[1]

Many countries, including Swaziland, chose to implement option A; a CD4 cell count was performed on all women identified to have HIV infection to determine those who should be initiated on life-long ART for both maternal health and PMTCT. In Swaziland, 88% of facilities that provide antenatal care (ANC) services also provide PMTCT services.[2] In 2009, 73% of women attending ANC facilities were tested for HIV, and 88% of HIV-infected pregnant women received a complete course of PMTCT prophylaxis in 2009.[3] However, a review of the data in the Early Infant Diagnosis (EID) database in Swaziland at the time of the introduction of option A guidelines, showed that ~50% of HIV-infected women who were eligible for ART actually initiated treatment.[4]

In Kenya, pregnancy has been identified as one of the risk factors for ART non-initiation.[5] A number of studies identified barriers to ART initiation during pregnancy in southern and eastern Africa, including fear of knowing one's HIV status, lack of male partners' support, negative attitudes of healthcare workers, late presentation in pregnancy, advanced HIV disease, lack of finances, fear of stigma and discrimination, non-disclosure of HIV status and long waiting times.[6-11]

New WHO guidelines now recommend initiation of life-long therapy in all HIV-infected pregnant and breastfeeding women. Obtaining a better understanding of the factors associated with the acceptance of ART will be critical to implement these recommendations effectively.[12] We conducted a study to quantify factors that were barriers or facilitators to the initiation of ART in HIV-infected women in Swaziland who were identified as eligible for ART under option A.

Methods

Study design and setting

An analytical cross-sectional study was performed through administration of a pre-tested questionnaire to HIV-infected pregnant women after delivery, with a review of antenatal care cards, in all 11 public hospital and health centre maternity wards in Swaziland.

Participant selection

Participants were selected consecutively from April to August 2013. The inclusion criteria for the study were: HIV-infected women who

were eligible for ART (i.e. CD4 cell counts of <350 cells/μL or WHO clinical stage III or IV) as documented in the patient ANC card; and the women should have attended at least one ANC.

Measurements

Variables were collected using an interviewer-administered structured questionnaire and a record review of clinical information from the ANC cards. The socio-ecological model (SEM) was used to study the factors associated with ART initiation among eligible pregnant women. The model outlines multiple levels of influence for the actions of individuals that include intrapersonal, interpersonal, organisational, community and policy levels.[13,14] Intrapersonal variables collected included sociodemographic factors (age, parity, level of education, employment status); disease factors (CD4 cell count, clinical staging); and perceptions of ART (fear that ARV might harm the baby, lack of understanding of the need for ART, fear of side-effects from ART, and fear of commitment to life-long ART). Interpersonal variables collected were marital status, HIV disclosure, partner support, and being a member of a support group. The main organisational variable collected was pregnant women's perceptions of healthcare workers' attitudes toward them.

Sample size, data collection, management and analysis

The planned sample size was calculated to be 380, with α set at 0.05 and 80% power to detect a 15% difference in ART initiation between women who had disclosed their status and those who had not, assuming that the ART initiation was 50% in those who did not disclose their status.

Data collection was performed by trained midwives at the identified maternity units. Training for the midwives consisted of a one-day training session onsite involving presentations and role-play. Data were entered using EpiData 3.1 software (EpiData Association, Denmark). Double data entry was done using EpiData 3.1. Data were exported to Stata version 11 (StataCorp LP, USA) for analysis.

Women's characteristics were described using percentages and proportions for categorical data and means, medians, standard deviation, ranges and interquartile ranges for continuous data. The proportion of eligible women initiating ART was also computed. Logistic regression was used to calculate crude and adjusted measures of association between the outcome and the independent variables (intrapersonal, interpersonal and organisational variables) which were measured as odds ratios with χ^2 test (univariate analyses) or *z*-test (multivariate analyses) *p*-values. The Cronbach alpha statistic was calculated for each construct variable, i.e. variables that consisted of scores derived from responses to a number of questionnaire items. Construct variable scores were included as predictor variables if their Cronbach alpha statistics were 0.70 or higher. Additional potential predictor variables were included in the model if there was information from other studies that the variable was associated with ART initiation and also if the χ^2 test *p*-value was ≤0.25 in univariate analysis as recommended by Hosmer and Lemeshow.[15] Stepwise backward hierarchical elimination was used to produce a parsimonious model; the likelihood ratio test, with an alpha value of 0.05, was used to decide on the elimination of statistically non-significant variables. Post regression analysis consisted of estimation of the receiver operating characteristic (ROC) area under the curve[16] and the Hosmer-Lemeshow goodness-of-fit test.[15]

Table 1. Demographic characteristics of the participants

	Total (*N*=163)		ART initiated (*N*=110)		ART not initiated (*N*=53)	
Characteristic	***n* (%)**	**Median (IQR)**	***n* (%)**	**Median (IQR)**	***n* (%)**	**Median (IQR)**
Age (years)		26 (23 - 30)		26 (23 - 31)		25 (22 - 29)
Parity		2 (1 - 3)		2 (1 - 3)		2 (1 - 3)
Level of education						
Some primary	43 (26.4)		28 (25.5)		15 (28.3)	
Completed primary	10 (6.1)		7 (6.4)		3 (5.7)	
Some secondary	46 (28.2)		32 (29.1)		14 (26.4)	
Completed secondary	52 (31.9)		34 (30.9)		18 (34.0)	
Tertiary	4 (2.5)		2 (1.8)		2 (3.8)	
Never attended school	8 (4.9)		7 (6.4)		1 (1.9)	
Employment status						
Professional	4 (2.5)		3 (2.7)		1 (1.9)	
Semi-skilled	35 (21.5)		21 (19.1)		14 (26.4)	
Self-employed	8 (5.0)		4 (3.6)		4 (7.5)	
Not employed	116 (71.2)		82 (74.5)		34 (64.2)	
Religion						
Pentecostal	34 (20.9)		21 (19.1)		13 (24.5)	
Protestant	67 (41.1)		48 (43.6)		19 (35.8)	
Zionist	41 (25.2)		27 (24.5)		14 (26.4)	
Other	19 (11.6)		13 (11.9)		6 (11.4)	
Not stated	2 (1.2)		1 (0.9)		1 (1.9)	

ART = antiretroviral therapy; IQR = interquartile range.
*Fisher's exact test for categorical variables and Mann Whitney (Wilcoxon rank-sum) test for continuous variables.

Ethical considerations

All patients were asked to provide written informed consent before inclusion into the study. This study was approved by the University of Pretoria Ethics Committee (ref. no. 217/2011) and by the Swaziland Ministry of Health's Scientific and Ethics Committee (ref. no. MH/599C).

Results

Participants enrolled in the study

Of the 1 371 HIV-infected pregnant women delivering at the study sites, 6 had no ANC cards, 431 were already on ART before the current pregnancy, 549 were not eligible for ART, 204 had no documented CD4 cell count results, 16 decided not to participate in the study, and 2 were missed by the data collectors (Fig. 1). Therefore, 163 women were enrolled in the study.

ART initiation

Among the 163 pregnant women who were eligible for ART, only 110 (67.5%) had been initiated on ART by the time of delivery.

Sociodemographic characteristics

The demographic characteristics of the participants are summarised in Table 1. The median age was 26 years. The women who did not initiate ART were slightly younger (median age of 25 years) than those who initiated ART (median age of 26 years) but this difference was not statistically significant (p=0.2253). Only 4.9% of the women never attended school. The majority of the women (71.2%) were not employed. A higher proportion of women who initiated ART were unemployed compared with the women who did not initiate ART. The median parity for the women was 2 and this was not different between women who initiated ART and those who did not (p=0.2735). The most common religion among the women was Protestant followed by Zionists (a Christian religious group that generally does not believe in the efficacy of Western medicines).[17]

Clinical characteristics

The median baseline CD4 cell count for participants was 248 cells/μL and was slightly higher in women who initiated ART compared with those who did not; however, the difference was not statistically significant (p=0.6413) (Table 2). Excluding women who were already known HIV-infected at the time of conception, the median gestational age at HIV diagnosis was 19 weeks; women who did not initiate ART were diagnosed with HIV later in pregnancy compared with women who initiated ART. More than 90% of the women were at WHO clinical stage I or II. The majority of clients (88%) were seen at

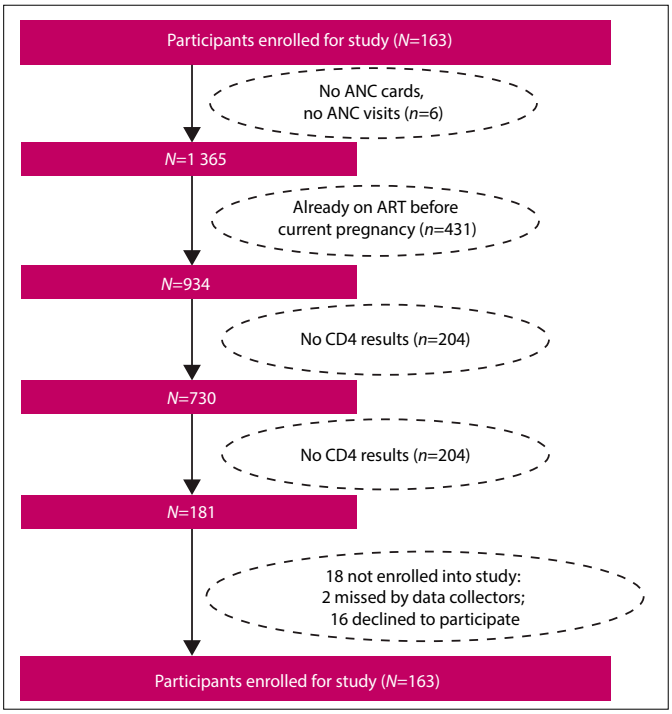

Fig. 1. Flow chart for patients enrolled into study. (ANC = antenatal care; ART = antiretroviral therapy.)

Table 2. Clinical characteristics of the women (*N*=163)

Characteristic	Total *n/N* (%)	Total Median (IQR)	ART initiated *n/N* (%)	ART initiated Median (IQR)	ART not initiated *n/N* (%)	ART not initiated Median (IQR)	*p*-value*
CD4 cell count (cells/μL)	n/a	248 (190 - 300)	n/a	247 (179 - 300.5)	n/a	254 (199 - 300)	0.6413
Known positive at entry, *n/N* (%)	38/161 (23.6)	n/a	n/a	25/108 (23.1)	n/a	13/53 (24.5)	n/a
GA at HIV diagnosis (weeks)	n/a	19 (7 - 23)	n/a	19 (7.5 - 22)	n/a	21 (7 - 24)	0.2302
WHO clinical stage, *n/N* (%)							
I	117/163 (71.8)	n/a	81/110 (73.6)	n/a	36/53 (67.9)	n/a	n/a
II	35/163 (21.5)		23/110 (20.9)		12/53 (22.6)		
III	10/163 (6.1)		5/110 (4.5)		5/53 (9.4)		
IV	1/163 (0.6)		1/110 (0.9)		0/53 (0)		
Client referred for ART, *n/N* (%)							
Yes	15/163 (9.2)	n/a	11/110 (10)	n/a	4/53 (7.5)	n/a	0.3460
No	4/163 (2.5)		0/110 (0)		4/53 (7.5)		n/a
ART available at site	144/163 (88.3)		99/110 (90)		45/53 (84.9)		n/a

ART = antiretroviral therapy; IQR = interquartile range; GA = gestational age; n/a = not applicable.
*Fisher's exact test for categorical variables and Mann-Whitney (Wilcoxon rank-sum) test for continuous variables.

Table 3. Women's perceptions towards ART*

	Total		ART initiated		ART not initiated		Cronbach's alpha	p-value†
	N	Median (IQR)	*N*	Median (IQR)	*N*	Median (IQR)		
Perceptions on benefits of ART	163	4.0 (3.6 - 4.6)	110	4.2 (3.8 - 4.8)	53	3.8 (3.6 - 4.2)	0.71	0.0001
Perceptions on harms/difficulties with ART	162	3.9 (3.4 - 4.4)	109	4.0 (3.6 - 4.6)	53	3.6 (3.0 - 4.0)	0.63	0.0011
Perceptions on need for ART	162	4.5 (4.0 - 5.0)	109	4.5 (4.0 - 5.0)	53	4.0 (3.8 - 4.8)	0.61	0.0155
Fear of stigma and discrimination	162	4.0 (3.8 - 4.8)	109	4.0 (3.8 - 4.8)	53	4.0 (3.3 - 4.5)	0.54	0.0280

ART = antiretroviral therapy; IQR = interquartile range.
*Maximum score = 5 (positive perception). Scores for harms of ART, stigma and need for ART were reversed so that values closer to 5 indicate less harm and stigma; and greater need for ART.
†Mann-Whitney (Wilcoxon rank-sum) test.

Table 4. Interpersonal factors

Characteristic	Total (*N*=163), *n* (%)	ART initiated (*N*=110), *n* (%)	ART not initiated (*N*=53), *n* (%)	p-value*
Disclosed HIV status (*N*=163)				
Yes	150 (92)	107 (97.3)	43 (81.1)	<0.0001
No	13 (8)	3 (2.7)	10 (18.9)	
Member of support group (*N*=163)				
Yes	10 (6.1%)	9 (8.2)	1 (1.9)	0.117
No	153 (93.9)	101 (91.8)	52 (98.1)	
Religion supports ART (*N*=163)				
Yes	120 (73.6)	84 (76.4)	36 (67.9)	0.252
No	12 (7.4)	7 (6.4)	5 (9.4)	
Unknown	31 (19)	19 (17.3)	12 (22.6)	
Knows HIV status of partner (*N*=163)				
Yes	91 (55.8)	65 (59.1)	26 (49.1)	0.227
No	72 (44.2)	45 (40.9)	27 (50.1)	
Partner supportive of ART (*N*=139)				
Yes	117 (84.2)	94 (91.3)	23 (63.9)	<0.0001
No	22 (15.8)	9 (8.7)	13 (36.1)	

* Fisher's exact test.

ANC healthcare facilities where ART services were available. There was no difference in ART initiation between women at ANC facilities with ART services (*n*=144) and those without ART services (*n*=15; 69% v. 73%, respectively; *p*=0.346).

Perceptions towards ART

Perceptions towards initiating ART were estimated by the scores obtained for the construct variables; the median scores were statistically significantly different between those initiated on ART and those not initiated for all the domains. The median scores and Mann-Whitney (Wilcoxon rank-sum) test *p*-values are presented in Table 3.

Interpersonal factors

More than 90% of the participants had disclosed their HIV status to at least one individual. However, among those who did not initiate ART, 18.9% had not disclosed their status compared with 2.7% among those who initiated ART ($p<0.0001$). A higher proportion of women who initiated ART were members of a support group compared with women who did not initiate ART (8.2% v. 1.9%), but this difference was not statistically significant. More than 40% of participants did not know the HIV status of their partner and this proportion was higher among women who did not initiate ART compared with those who initiated ART, although the difference was not statistically significant. Of the 139 women who consulted their partners on ART initiation, 84.2% said that their partners supported the decision to start ART. This proportion was lower (63.9%) among women who did not initiate ART compared with women who initiated (91.3%; $p<0.0001$). Interpersonal factors are summarised in Table 4.

Organisational factors

Women who did not initiate ART reported a less favourable attitude from healthcare workers compared with those who did initiate ART (median score for healthcare workers' (HCWs') attitude towards pregnant women of 3.5 v. 3.61, $p=0.0045$) (Table 5).

Reasons for not initiating ART

The most common reason cited for not initiating ART (*n*=53) despite being eligible for ART, was that they were not yet ready to commit to life-long treatment (24.5%). There were, however, numerous other reasons (Table 6).

Univariate analysis

On univariate analysis, factors that were associated with ART initiation were: perceptions of the benefits of ART (OR 3.49; $p<0.001$), perceptions on the harms of/difficulties with antiretrovirals (OR 2.14; $p=0.002$), perceptions on the need for ART (OR 1.94; $p=0.011$), fear of stigma and discrimination (OR 1.70; $p=0.011$), HIV status disclosure (OR 8.29; $p=0.002$), partner support for ART (OR 7.66; $p<0.001$).

Multivariate logistic regression

The following variables were included in the initial regression model: employment status; perceptions on the benefits of ART; HIV disclosure status; member of a support group; partner support for ART; and knowledge of partner status (Table 7). The other variables were not included, either because of a *p*-value of >0.25 or Cronbach's alpha <0.70, or because of many missing variables. The final model had two variables as independent predictors of ART initiation among pregnant women: partner support and perceptions of the benefits of ARVs.

Table 5. Organisational factors

Characteristic	Total		ART initiated		ART not initiated		Cronbach's alpha	*p*-value†
	N	Median (IQR)	*n*	Median (IQR)	*n*	Median (IQR)		
HCWs' attitudes towards pregnant women*	108	3.57 (3.16 – 3.86)	78	3.61 (3.27 – 3.88)	30	3.5 (2.98 – 3.73)	0.86	0.045

ART = antiretroviral therapy; HCW = healthcare worker; IQR = interquartile range.
*Expected score = 4 (excellent attitude).
†Mann-Whitney (Wilcoxon rank-sum) test.

Table 6. Reasons for not initiating ART (*N*=53)*

	n (%)
Not ready	13 (24.5)
Delayed by clinic procedures	9 (17.0)
Partner/family refused	7 (13.2)
Limited ANC visits	7 (13.2)
Not offered ART by nurses	7 (13.2)
Lack of food/finances	4 (7.6)
Fear of ART	3 (5.7)
Felt healthy	2 (3.8)
Work challenges	1 (1.9)

ART = antiretroviral therapy; ANC = antenatal care.
*Respondents were asked to select one reason for not initiating ART.

Table 7. Multivariate logistic regression results for the final model (*N*=158)*

Variable	Univariate OR	AOR	95% CI	*p*-value
Perceptions of benefits of ART	3.49	3.04	1.55 - 5.96	0.001
Partner support for ART	7.66	4.75	2.11 - 10.67	<0.001

OR = odds ratio; CI = confidence interval; AOR = adjusted odds ratio; *p*-value = double-sided *z*-test *p*-value; ART = antiretroviral therapy.
*Area under the receiver operating characteristic (ROC) curve = 0.77; Hosmer-Lemeshow goodness-of-fit test *p*-values for 8, 10 and 12 groupings were 0.47, 0.54 and 0.71, respectively.

Discussion

In this study we found that only 67.5% of HIV-infected pregnant women who met the eligibility criteria for ART, actually initiated ART before they delivered. This rate was comparable with those reported globally.[18-23]

The sociodemographic, HIV disease (WHO clinical stage or CD4 cell count), and gestational age at HIV diagnosis were not associated with ART initiation in our study. Data on the importance of these factors in ART acceptance have been questionable, with conflicting results between studies.[10,11,24-31]

Partner support was strongly and independently associated with ART initiation among eligible pregnant women in our study, with the odds of initiating ART 4.8-fold higher in women whose partners supported ART initiation compared with those women whose partners did not support ART initiation ($p<0.001$). Our study contributes to the body of literature that shows that men's support influences women's decisions to accept ART and PMTCT interventions.[32-38]

Disclosure of HIV status has been associated with the acceptance of ART for PMTCT in studies in South Africa and Zimbabwe.[26,33,39] In univariate analysis, the odds of ART initiation among women who had disclosed their HIV status to their respective partners were higher than those of women who had not disclosed. However, in multivariate analysis, disclosure of HIV status was not associated with ART uptake when controlling for employment status, presence of male support, being a member of a support group, perceptions of the benefits of ARVs, and knowledge of partners' HIV status.

In a study in Zimbabwe, women who were members of an HIV support group were more than twice as likely to access HIV care and treatment as those who did not belong to any group.[11] In our study, being a member of a support group was not significantly associated with ART initiation, but only 6% of women were members of a support group during pregnancy. This might be attributed to the fact that pregnancy is short and women might not have the time to join a support group before they deliver. Owing to small numbers, we lacked sufficient power to draw a correlation between ART initiation and support group memberships.

The odds of initiating ART among eligible pregnant women in Swaziland increased threefold for every one unit score increase in the positive perceptions of women regarding the benefits of ART ($p=0.001$). This was consistent with other studies which showed that women may refuse ARVs for PMTCT because they doubted their efficacy or they feared that ARVs could harm the unborn child.[40-43]

In our study, both healthcare workers' attitudes towards pregnant women and women's perceptions of access to ART were associated with ART initiation in univariate, but not multivariate, analyses. Other studies have reported that negative interactions between healthcare staff and pregnant women, negative staff attitudes and poor access to ART services can serve as barriers to the uptake of and adherence to PMTCT services by pregnant women.[6,10,40,42,44,45]

Study limitations

Our study had some limitations. It only focused on women who were delivering at the healthcare facilities and this might have introduced some bias as women delivering at healthcare facilities might be motivated and committed individuals who are also likely to initiate ART. The interviews were conducted by healthcare workers and this might introduce bias especially on questions asking about healthcare workers' attitude towards pregnant women. However, efforts were made through training and supervision of healthcare workers to minimise this. Finally, the cross-sectional nature of the study posed some difficulty in defining the temporal relationships

Conclusion

The most commonly cited reason given by women who did not initiate ART was that they felt they were not ready for a life-long commitment to ART. In multivariate analysis, positive perceptions of the benefits of ART and partner support were significantly associated with ART initiation. These results suggest that universal

ART in HIV-infected women should be accompanied by improved counselling and education programmes. Strategies to implement male involvement and support could be to the advantage of both the women and PMTCT.

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Author contributions. CC designed the study, wrote the protocol, supervised study implementation, conducted data analysis and wrote the manuscript. BN and MAM helped in designing and supervising study implementation. GL helped in study design, protocol writing and article review. BVG helped with data analysis and article editing. All authors read and approved the final manuscript.

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