HHS Public Access

Author manuscript

AIDS. Author manuscript; available in PMC 2019 November 28.

Published in final edited form as:

AIDS. 2018 November 28; 32(18): 2827–2833. doi:10.1097/QAD.0000000000002025.

Probable antenatal depression at antiretroviral initiation and postpartum viral suppression and engagement in Option B+

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Abstract

Objective—To estimate the association of probable antenatal depression with postpartum HIV care engagement among pregnant women in Malawi.

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AUTHOR CONTRIBUTIONS:

BJH, MCH, BWP, BNG, JM, and WCM designed study. MM, ANJ, NAG, SDW and BJH acquired and processed the data. BJH, BWP, BNG, JM, MM, MCH and WCM analyzed and/or interpreted the data. All authors contributed to and approved the final manuscript.

Conflicts of Interest and Source of Funding:

No authors have conflicts of interest to declare.

Design—We conducted a prospective cohort study of 299 women who were initiating antiretroviral therapy (ART) through Option B+ at a government antenatal clinic in Malawi.

Methods—Probable antenatal depression was assessed on the day of ART initiation with the validated Chichewa version of the Edinburgh Postnatal Depression Scale (EPDS). We estimated crude and adjusted risk differences (RD, aRD) of visit attendance and prevalence differences (PD, aPD) of viral suppression through 12 months post-ART initiation comparing women with versus without probable antenatal depression.

Results—One in ten women had probable antenatal depression. Most women were engaged in care through 12 months post-ART initiation: 85% attended all scheduled ART visits, and 81% were in care and virally suppressed. Women with and without probable antenatal depression had a comparable probability of attending all scheduled visits (RD: −0.02; 95%CI −0.16–0.12; aRD: −0.04; 95%CI −0.18–0.10), and of viral suppression (PD: −0.02; 95%CI −0.17–0.13; aPD: −0.01; 95%CI −0.17–0.15) in crude and adjusted analyses.

Conclusion—Probable antenatal depression was not associated with engagement in HIV care through 12 months post-ART initiation. In a population with high HIV care engagement, antenatal depression may not impair HIV-related outcomes.

Keywords

antenatal depression; HIV; PMTCT; engagement in care; Option B+

Introduction

Long-term engagement in care and viral suppression are necessary for reducing mortality and both heterosexual [1] and vertical [2] transmission of HIV. Consistent with “test and treat” principles, Malawi adopted Option B+ to provide lifelong antiretroviral treatment (ART) to all pregnant or breastfeeding women in 2011 [3]. Despite Option B+’s rapid expansion, sustained patient engagement in care has been challenging and has fallen short of the UNAIDS 90–90-90 goals [4]: 75% remain in HIV care by 6–12 months after ART initiation [5]-[8], and 84% of those are virally suppressed [9].

Engagement in care may be hindered by perinatal depression, but evidence is sparse from sub-Saharan Africa. In higher-resource settings, depression is associated with reduced HIV care engagement among non-pregnant adults [10]–[17]. Among adults in sub-Saharan Africa, depression has a negative or null effect on engagement in HIV care [14], [18]-[20]. However, due to previous ART eligibility guidelines, participants in these studies have had advanced HIV; consequently, generalization to relatively healthy perinatal women is unclear. Moreover, few studies of barriers and facilitators to engagement in Option B+ feature perinatal depression [21].

Antenatal depression is common (prevalence: 11–23%), treatable, and associated with adverse maternal and infant outcomes [22]–[28]. Yet, screening is not routine in sub-Saharan Africa [29]. Understanding how antenatal depression may affect postpartum HIV care engagement is important for programmatic improvement. We quantified the relationship between probable antenatal depression and two measures of engagement in HIV care (visit

attendance and viral suppression) among Malawian women initiating ART through Option B +.

Methods

Study setting and population

In 2015–16, pregnant women living with HIV who sought antenatal care at a government clinic in Lilongwe, Malawi were recruited into an observational cohort study on Option B+ ("Safety, Suppression, Second-line, Survival - S4", ClinicalTrials.gov: NCT02249962). Opt-out HIV testing was performed as part of routine antenatal care with two rapid tests. Study nurses invited a convenience sample of women who tested positive for HIV at their first antenatal visit in any trimester of pregnancy to enroll in S4.

Study eligibility criteria included being pregnant, 18 years (or emancipated minor), planning to give birth in Lilongwe, and able to provide informed consent. Study nurses interviewed participants at enrollment, monthly for 6 months, then quarterly thereafter, mirroring standard of care in Malawi. The study was the source of ART for participants unless they officially transferred care to a non-study clinic. All women initiated ART on the day of study enrollment. Interviews were conducted in Chichewa, the predominant local language.

Measures

We evaluated probable antenatal depression at study enrollment with the Edinburgh Postnatal Depression Scale (EPDS) [30], [31], using a score of ≥6 to indicate probable antenatal depression based on the EPDS validation in Malawi in Chichewa [32]. All women answered basic demographic and psychosocial questions at study enrollment, and marital status, history of verbal or physical intimate partner violence (IPV), and self-reported history of depression or anxiety were included as potential confounders in the multivariable model.

Two outcomes of interest were measured at 12 months post-ART initiation: visit attendance and viral suppression. Women who attended all 8 scheduled visits during the first 12 months post-ART initiation were counted as engaged in care. Women who missed any scheduled visit(s) were considered insufficiently engaged in care because missing a visit indicated an ART lapse. In secondary analyses, we defined engagement as attending ≥7 of the 8 scheduled visits, and examined visit attendance through the longer follow-up period of 12 months postpartum, aligning with WHO breastfeeding recommendations [33].

Viral suppression was defined as <1000 copies/mL, per Malawian HIV Treatment Guidelines [33]. Viral loads were assessed at baseline, and 6 and 12 months post-ART initiation. Women who attended their 12 month visit within 30 days and had a viral load <1000 copies/mL were counted as virally suppressed. Women who had a viral load ≥1000 copies/mL or missed the visit were considered unsuppressed.

Statistical analysis

Differences between women with and without probable antenatal depression were tested using Fisher's exact (categorical data) or Wilcoxon rank sum (continuous) tests. Linear binomial regression models estimated crude and adjusted risk differences (RD) for visit

attendance and prevalence differences (PD) for viral suppression at 12 months by probable antenatal depression status. Difference measures were preferred over odds ratios because the absolute scale is more intuitive. Adjusted estimates controlled for potential confounding via standardized mortality ratio (SMR) weights with robust variance estimation for the 95% confidence interval (CI) [34]-[37].

Two sensitivity analyses addressed potential bias from inappropriate selection into the study and from outcome misclassification. First, 28 participants had viral loads ≤400 copies/mL at ART initiation, suggesting they may not have been ART-naïve [38]. Therefore, we repeated our models after excluding these participants. Second, we defined all women lost to study follow up as out of care and unsuppressed, yet other research suggests as many as 36% may have transferred care and remained on ART without our knowledge [39]. To account for potential imperfect outcome sensitivity, we calculated the RD of visit attendance with 36% lower sensitivity, and PD of viral suppression with 32% lower sensitivity, assuming 90% of those in care were virally suppressed (36%*90%=32%), as was found among observed participants.

All analyses were conducted in SAS version 9.4 (SAS Institute, Cary, NC, USA).

Ethical approval—The University of North Carolina at Chapel Hill institutional review board and the Malawi National Health Sciences Research Committee approved the S4 study. Women with an EPDS score ≥6 or who endorsed suicidal ideation were referred to a study clinician or mental health service as appropriate.

Results

Between mid-2015 to 2016, 299 pregnant women started ART and enrolled in the cohort study; approximately 60% of women approached agreed to participate. Three women (1%) died from non-psychiatric causes before reaching 12 months post-ART initiation and were excluded from analyses. Five women (2%) withdrew from the study or relocated before reaching 12 months post-ART initiation; we count them as engaged in care and virally suppressed because they officially transferred care.

Ten percent of women (n=30) screened positive for probable antenatal depression at ART initiation (Table 1). Most women (85%) attended all 8 scheduled ART-dispensing visits, including 83% of women with probable antenatal depression and 85% of women without.

Participants with and without probable antenatal depression at ART initiation had comparable visit attendance through 12 months in both crude (RD: −0.02; 95%CI −0.16–0.12) and adjusted (aRD: −0.04; 95%CI −0.18–0.10) analyses (Figure 1).

Viral loads 12 months after ART initiation were available for 91% (n=269/296) of women, of which 241 (90%) had viral loads <1000 copies/mL, meaning 81% (241/296) both presented to care and were virally suppressed. Proportions of women in care with viral suppression were comparable by probable antenatal depression status at 12 months post-ART initiation: 80% among women with probable antenatal depression and 82% among women without. In crude and adjusted analyses, the probability of viral suppression at 12

months did not differ by antenatal depression status (PD: −0.02; 95%CI −0.17–0.13; aPD: −0.01; 95%CI −0.17–0.15) (Figure 1).

Estimates from secondary analyses that relaxed the definition of 100% visit attendance, and extended the time on follow up through 12 months postpartum, were similar to the main analyses. 88% of women attended ≥7 ART-dispensing visits in the first 12 months, without a difference in visit attendance by antenatal depression status (RD: −0.02; 95%CI: −0.14–0.11; aRD: −0.02; 95%CI −0.15–0.11). Through 12 months postpartum, fewer women (82%) attended all visits compared to through 12 months post-ART initiation (85%), but the probability of visit attendance was similar by probable antenatal depression status (RD: −0.06; 95%CI: −0.21–0.10; aRD: −0.08; 95%CI: −0.24–0.08).

For both visit attendance and viral suppression through 12 months post-ART initiation, point estimates did not differ substantively from the main analyses when women who may have not been ART-naïve were excluded (n=28 with viral load ≤400 copies/mL), ($aRD_{visit\ attendance}$: −0.08; 95%CI −0.26–0.09; $aPD_{viral\ suppression}$: −0.06; 95%CI −0.25–0.13), and when potential outcome misclassification among those lost to follow up was accounted for ($RD_{visit\ attendance}$: −0.07; 95%CI: −0.19–0.06; $PD_{viral\ suppression}$: −0.01; 95%CI: −0.15–0.13).

Discussion

Among pregnant women initiating ART in Malawi, 10% had probable antenatal depression, and engagement in care was high at 12 months post-ART initiation. Probable antenatal depression at ART initiation did not appreciably affect postpartum engagement in care. Similarly, a study of women living with HIV in the Democratic Republic of the Congo (DRC) evaluated visit attendance at 6 weeks postpartum found no difference in visit attendance by antenatal depression status [40]. Although depression is widely cited as a barrier to engagement in HIV care [16], [41]–[46], the relationship of probable antenatal depression with engagement in care has not been quantified outside of the DRC study and the current study, which also includes viral load data.

Compared to recent studies from Malawi, a similar or higher proportion of our participants were engaged in care 12 months post-ART initiation [5], [7], [47], [48]. Engagement in care was approximately consistent between 12 months post-ART initiation and the longer 12 months postpartum, but more women missed any visits through 12 months postpartum. Our results were consistent under two sensitivity analyses addressing potential inappropriate selection into the study and outcome misclassification, and under two secondary analyses that extended the period of follow up, and relaxed the visit attendance definition.

Crudely, our participants met all three 90–90-90 targets at 12 months post-ART initiation [4]. However, engagement in care is complex, and may be influenced by numerous facilitators and barriers [21], [49]–[57]. Isolating any single factor, such as antenatal depression, may fail to capture the nuance of a complex health behavior like engagement in HIV care [58], [59]. Women who were not engaged in care may have specific needs and are not likely a random sample of ART-eligible women.

The EPDS is a screening rather than diagnostic assessment, so some women may have been misclassified. Many participants received their HIV diagnosis, started ART and answered the EPDS on the same day, which may have influenced EPDS scores. Among women who screened positive for antenatal depression, none started counseling or medication as part of the study; no information exists on whether women accessed mental health services outside the study.

Although the present analysis does not suggest an association between probable antenatal depression and engagement in HIV care, identifying and treating antenatal depression may reduce other adverse outcomes for the mother and child [24]–[27], [60], [61]. Antenatal depression predicts postpartum depression and could be treated in the context of antenatal care [62], and most Malawian women have an antenatal visit [63], which lends support for implementing depression screening antenatally.

Conclusion

Most Malawian women initiating ART through Option B+ remained engaged in care through 12 months, and probable antenatal depression was not associated with HIV care engagement. Our finding that 10% of women had probable antenatal depression suggests depression screening in Option B+ could be appropriate.

ACKNOWLEDGMENTS

The authors gratefully acknowledge research funding to support the operational costs of cohort study from the NICHD [grant R01HD080485] (MCH). The following funding sources supported the trainee (BJH) who carried out the analysis: the UNC Medical Scientist Training Program [grant T32GM008719], the NIMH individual fellowship [grant F30MH111370], the Fulbright-Fogarty U.S. Student fellowship, and the NIH Fogarty International Center Grant [grant R25TW009340]. Regulatory support was provided through the UNC Center for AIDS Research (CFAR) [grant P30AI50410]. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. The funding sources had no role in the study design, data collection and analysis, interpretation of results, or preparation of the manuscript for publication.

We are appreciative of our S4 study collaborators (the Malawi Ministry of Health HIV/AIDS Unit, Baobab Health, Lighthouse Trust, Baylor College of Medicine), Bwaila Hospital Family Health Unit, and UNC Project-Malawi. Special thanks to the S4 study participants, and the S4 research team: Trywin Phiri, Mark Maluwa, Clement Mapanje, Gift Sambiri, Linda Chikopa, Agness Gumbo, Jane Kilembe, Alvis Mvula, Juliana Ngwira, Lusubiro Paile, Chimwemwe Baluwa, Limbikani Chimndozi, Madawa Kumwenda, Chalimba Lusewa, Alice Maluwa, Kingsley Msimuko, Victoria Chilembwe, Tiyamike Itaye, Rob Krysiak, Gerald Tegha, Christopher Mwafulirwa, Kelvin Maziya, Frank Chimbwandira, Portia Kamthunzi, Maganizo Chagomerana, Sam Phiri, Atupele Kapito-Tembo, Nora Rosenberg, Irving Hoffman, Innocent Mofolo, Francis Martinson, Valerie Flax, Saeed Ahmed, Maria Kim, Deborah Demster Kamwendo, Michael Herce, Julie Nelson, Lameck Chinula, Robert Flick, Austin Wesevich, Caroline G. Melhado, Lua Samimi, Laura Limarzi, and Bethany DiPrete.

The authors gratefully acknowledge research funding to support the operational costs of cohort study from the NICHD [grant R01HD080485] (MCH). The following funding sources supported the trainee (BJH) who carried out the analysis: the UNC Medical Scientist Training Program [grant T32GM008719], the NIMH individual fellowship [F30MH111370], the Fulbright-Fogarty U.S. Student fellowship, and the NIH Fogarty International Center Grant [R25TW009340]. Regulatory support was provided through the UNC Center for AIDS Research [grant P30AI50410]. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. The funding sources had no role in the study design, data collection and analysis, interpretation of results, or preparation of the manuscript for publication.

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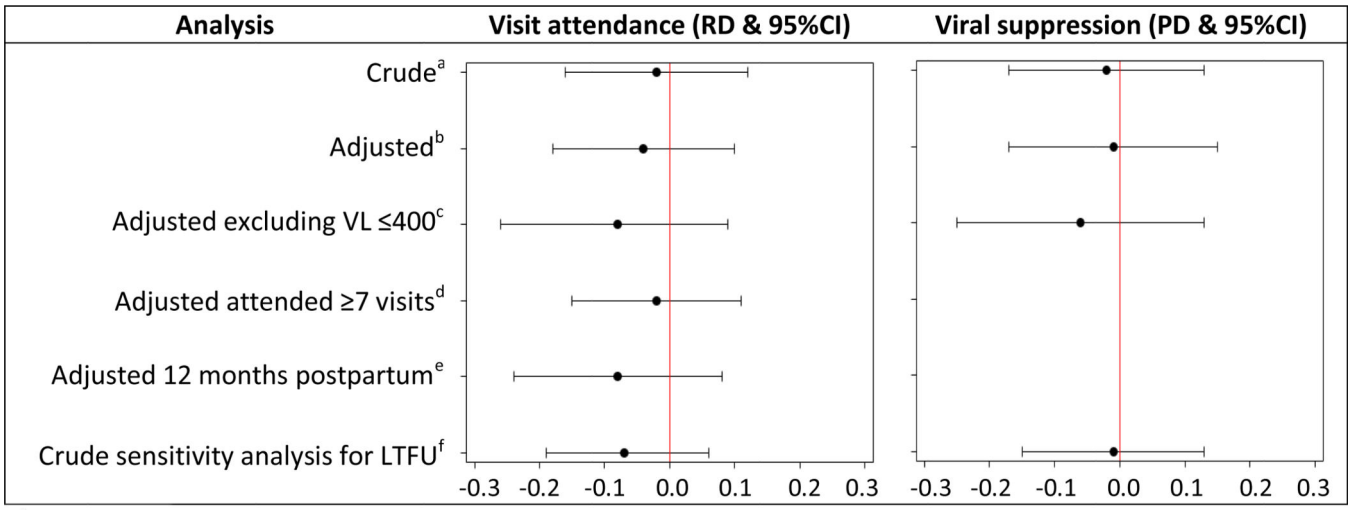

Figure 1. Risk and prevalence differences of engagement in HIV care outcomes comparing women with and without probable antenatal depression at time of ART initiation: crude, adjusted, and sensitivity analyses

[a] Crude estimate featuring all n=296 women participants who initiated ART through Option B+ (referent group: women without probable antenatal depression)

[b] Adjusted for potential confounding by marital status at enrollment, history of self-reported depression or anxiety, and history of intimate partner violence (IPV)

[c] Adjusted for marital status, history of depression or anxiety and history of IPV, excluding women (n=28) whose baseline viral load (VL) was ≤400 copies/mL and may have already been taking ART at study enrollment

[d] Adjusted for marital status, history of depression or anxiety and history of IPV, with adequate visit attendance defined as attending ≥7 visits in the first 12 months post-ART initiation

[e] Adjusted for marital status, history of depression or anxiety and history of IPV, with adequate visit attendance defined as attending all scheduled visits through 12 months postpartum

[f] Sensitivity analysis accounting for potential outcome misclassification for those lost to follow up (LFTU)

Table 1:

Participant demographics (n=299)

Characteristic at enrollment	EPDS <6 (n=269)	EPDS ≥6 (n=30)	*p* value
	Median (IQR)		
Age in years	26 (22–30)	27 (24–32)	0.08
Weeks gestation	22 (18–26)	23 (17–25)	0.80
	N (%)		
Marital status			0.17
Currently married	241 (90)	22 (73)	
Not currently married	28 (10)	8 (27)	
Education attained			0.70
None/some primary	121 (45)	12 (40)	
Finished at least primary	148 (55)	18 (60)	
Employment status			0.01
Unemployed	178 (66)	12 (40)	
Employed	91 (34)	18 (60)	
Current pregnancy intendedness			0.44
Intended	121 (45)	11 (37)	
Not intended	148 (55)	19 (63)	
Ever experienced intimate partner violence			0.01
No	223 (83)	19 (63)	
Yes	46 (17)	11 (37)	
History of depression or anxiety			<0.01
No	173 (64)	11 (37)	
Yes	96 (36)	19 (63)	
WHO HIV Clinical Stage			0.68
Stage 1	254 (94)	28 (93)	
Stage 2–4	15 (6)	2 (7)	

IQR: interquartile range

WHO: World Health Organization