The impact of mental health on unintended pregnancies within HIV serodiscordant heterosexual couples in Uganda and Kenya

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Abstract

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Background. Depression among women has important sequelae prior to, during, and after pregnancy. Minimal research has explored the impact of depression on pregnancy incidence.

Methods. We used data from the Partners Demonstration Project, an evaluation of integrated PrEP and ART delivery to 1,013 HIV serodiscordant couples in Kenya and Uganda. We administered socio-behavioral questionnaires, including assessment of fertility intentions, "probable depression", "hazardous" alcohol use, and stigma internalized and perceived, at enrollment and annually for up to 2 years. We used Cox proportional hazards models to assess the association of mental health and incident pregnancy, including separate models for the incidence of unintended pregnancy.

Results. Of 1,013 women, 67.0% were living with HIV, 94.6% were married to their study partner, and 56.4% had no children at enrollment. Nearly 20.0% had probable depression at

some point during the study and “probable depression” was reported at 9.0% of women’s study visits. We observed 238 incident pregnancies, 29.8% of which were unintended. “Probable depression” was associated with an increased rate of intended (adjusted HR=1.62, 95% CI: 1.12-2.36) and unintended pregnancy (adjusted HR=1.48, 95% CI: 0.73-2.98). Stigma and “hazardous” alcohol use were not associated with pregnancy incidence (adjusted HR=1.15, 95% CI: 0.89-1.49), (adjusted HR=0.81, 95% CI: 0.54-1.21)

Conclusions. Women with probable depression were more likely to experience pregnancy. These findings highlight the importance of integrating mental health screening and care into sexual and reproductive health settings in order to reach women who may be experiencing untreated depressive symptoms.

Key words: Depression, pregnancy, unintended pregnancy, women, Africa

Background

The World Health Organization (WHO) estimates that 4.4% of the global population suffers from depression at any given time.[1] Women report mental health disorders 1.5-3 times as often as men,[2-5] representing a disproportionate amount of the burden. Depression among women has been associated with increases in high risk sexual behavior, such as having multiple sex partners, engaging in condomless sex, and reduced adherence to contraception,[6-9] which can lead to greater risk for unintended pregnancy. Compared to intended pregnancy, unintended pregnancy is associated with delayed engagement in prenatal care,[10,11] and missed opportunity for early education about healthy prenatal habits, as well as the opportunity for early detection and treatment of many maternal health concerns, such as sexually transmitted infections.[12] In resource-limited settings, delays in prenatal care are associated with greater likelihood of adverse pregnancy and birth outcomes, including low birth weight and preterm delivery.[13-16]

In resource-limited settings, where the treatment gap for mental health is 75-90%,[17-18] public health officials need to identify ways to screen and engage women in mental health care. Women of reproductive age are often already seeking care for sexual and reproductive health services, which presents an opportunity to screen for depression. Many of these settings also bear a high burden of HIV and people living with HIV report higher rates of depression than their HIV-negative counterparts.[19] For women living with HIV or who have a partner living with HIV (i.e. those in HIV-serodiscordant partnerships), HIV care settings also offer ideal settings to screen for depression and offer treatment.

Prior research has examined the impact of depression during pregnancy and postpartum,[20-24] but there are few studies examining the impact of depression on incident pregnancy, including unintended pregnancy.[25-29] Within a cohort of African women in HIV-serodiscordant partnerships, we compared rates of incident pregnancy during periods when women screened positive for three different measures of mental health: "probable depression," "hazardous" alcohol use, and periods of internalized or perceived stigma.

Materials and methods

Study design and participants. Data were from the Partners Demonstration Project, an open-label evaluation of pre-exposure prophylaxis (PrEP) delivery integrated with antiretroviral treatment (ART) for mutually disclosed high-risk HIV serodiscordant, heterosexual couples, recruited from four sites in Kenya and Uganda.[30] Inclusion was restricted to couples with both members ≥18 years of age, intentions to remain in the partnership for at least 1 year, HIV-positive partners with WHO stage 1 or 2 who had not yet initiated ART, and HIV-negative partners with no prior use of PrEP nor pregnant (if female). At enrollment, PrEP was offered to all HIV-negative participants. ART referrals were provided to HIV-positive partners according to national guidelines of the time. HIV-negative partners were encouraged to discontinue PrEP once the HIV-positive partner had sustained ART use for six months.

Study procedures. Participants were followed for up to 24 months, with visits occurring at enrollment, 1 and 2 months later, and quarterly thereafter. At each visit, couples were counseled on contraceptive use and HIV prevention, which included condom use, treatment of STIs, and discussions about adherence to HIV medications (PrEP and ART).

Participants were screened for "probable depression" using the 16-item Hopkins Symptoms Checklist for Depression Scale.[31] Mean scores ≥1.75 (range 0-4) were considered an indicator of "probable depression," a cut-off previously validated in sub-Saharan Africa.[32] Individuals who responded with indications of "probable depression" or suicidal ideation were counseled by study staff immediately and referred for further mental health services. Internalized stigma among women living with HIV was measured via an adapted Internalized AIDS-Related Stigma Scale[33] with a greater sum on an 8-item scale indicating greater feelings of internalized stigma. Perceived stigma among HIV-negative women was measured using the modified Berger Scale[34-35] with a higher sum on a 4-item scale indicating greater feelings of perceived stigma. In both populations, women were considered to have internalized or perceived stigma if the sum of their responses was ≥3. Alcohol use was measured using the Rapid Alcohol Problems Screen,[36] with "hazardous" use being determined by an affirmative response to any of the 4 items. All mental health correlates were measured at enrollment and annually thereafter, with scores being carried forward between annual visits for the current analysis.

All women were tested for pregnancy at enrollment using urine rapid tests, with testing at later visits when clinically indicated (e.g., missed or delayed menstrual period). For each pregnancy, the start date of the last menstrual period was captured by self-report and used as the estimated date when pregnancy began. Data indicating pregnancy intention were also captured by self-report when the pregnancy was first discovered at the study site.

Data collection. All clinical data were collected through interviewer-administered questionnaires and recorded on case report forms (CRFs). CRFs were transmitted to the data management center via DataFax (DF/Net Research, Seattle, USA).

Statistical methods. Pregnancy incidence was calculated as the number of pregnancies divided by the amount of time accrued when women were not pregnant. Women who were living with HIV and pregnant at study enrollment had their follow up time left-censored until the pregnancy ended at which point they entered the risk set. The relationship between "probable depression" and first incident pregnancy was estimated using Cox proportional hazards regression. Age was selected *a priori* to be included in multivariable models. Additional potential confounders, including demographic, clinical, and sexual behaviors, were identified through existing literature and any factor that substantially changed the crude hazard ratio (by ≥10%) was included in the final multivariable model. We also considered stigma and "hazardous" alcohol use as additional indicators of suboptimal mental health and ran multivariable models with the same set of confounders since these often share the same demographic and clinical predictors as depression. All data analysis was completed using R Studio (version 3.4.3, Boston).

Ethics. The study protocol was reviewed and approved by ethics review committees overseeing each study site and the institutional review board at the University of Washington. Each study participant provided written informed consent in English or in their preferred local language.

Results

Participant characteristics. A total of 1,013 couples were enrolled, including 679 (67.0%) where the woman was the partner living with HIV and 385 (33.0%) where the woman was the HIV-negative partner (Table 1). Most women (94.6%) were married to their study partner and over half (56.4%) had no children at enrollment. The median age of participants was 28 years (interquartile range [IQR] 22-32), 25 for women who became pregnant during the study and 30 for women who did not. Women who became pregnant had slightly longer relationships with their study partner and more children prior to study enrollment.

Measures of mental health. Overall, 16.3% (165) of women reported symptoms commensurate with "probable depression" at their enrollment visit (Table 1), 6.5% at year 1, and 2.8% at year 2, and 19.7% reported symptoms at any point during the study (Table 2). Women reported "probable depression" at 9.0% of the total study visits. Among women with "probable depression" at enrollment, 76.4% were living with HIV, 20.4% reported "hazardous" alcohol use, and for those living with HIV, their median internalized stigma score was 5 (IQR 3-8).

Nearly half of women (47.3%) reported feelings of internalized stigma at enrollment and 56.9% reported internalized stigma at any point during the study. In total, women reported feelings of internalized stigma at 36.4% of the study visits. At enrollment, 13.2% (134) of women indicated a hazardous use of alcohol, while 21.0% had reported periods of "hazardous" alcohol use at any point during the study. In total, women reported hazardous alcohol use at 11.9% of total study visits.

Association of "probable depression" and pregnancy incidence. Overall, 238 women became pregnant during the study with an incidence rate of 17.9 per 100 person-years. Among periods with "probable depression", pregnancy incidence was 20.8 per 100 person-years, slightly greater than periods without "probable depression", 17.5 per 100 person-years. Accounting for age, condomless sex and prior children, women with "probable depression" were more likely to experience pregnancy than women without (adjusted hazard ratio [HR] 1.62, 95% confidence interval [CI] 1.12-2.36) (Table 3).

A total of 70.2% of pregnancies were intended, while 29.8% were unintended. "Probable depression" was associated with higher pregnancy incidence for women experiencing an intended (adjusted HR = 1.68, 95% CI 1.08-2.61) and unintended pregnancy (adjusted HR = 1.48, 95% CI 0.73-2.98), although not statistically significant for the latter.

During periods where women identified characteristics aligning with internalized stigma, pregnancy incidence was 19.4 per 100 person-years, similar to the incidence of 16.8 per 100 person-years during times without internalized stigma (adjusted HR = 1.15, 95% CI 0.89-1.49). During periods where women had potentially hazardous alcohol use, pregnancy incidence was 15.8 per 100 person-years, similar to the incidence of 18.1 per 100 person-years when hazardous alcohol use was not reported (adjusted HR = 0.81, 95% CI 0.54-1.21).

Discussion

In this study of Kenyan and Ugandan women in HIV serodiscordant relationships, those with probable depression were more likely to become pregnant, including with an unintended pregnancy. Conversely, reports of internalized or perceived stigma and reports of "hazardous" alcohol use were not associated with pregnancy incidence. Importantly, 16.3% of women

entered the study with probable depression, while 6.5% screened for probable depression at the 1-year mark, highlighting a gap in mental health screening and care for this population.

Our findings align with other studies that have reported associations between depression and unintended pregnancy, though some of these studies lacked power and precision for their estimates[25-29]. Additionally, those studies were largely focused in high-resource settings, making these data some of the first from a low-resource setting.

Lifetime prevalence for depression, while varying by country, frequently shows that around 1 in 10 people will experience depression at some point in their lifetime.[37-39] Women, who report depression at a higher rate than men, are expected to have a higher rate than the population-wide estimate. Depression has the propensity to impact many facets of a woman's life, including her sexual and reproductive health, making this pivotal phase an important research focus. In better understanding how depression can impact a woman during this time, including her ability to engage in care, public health professionals can better tailor care and design interventions that can effectively reach this population.

Over the past decade, global mental health has received increased focus, in large part due to the Lancet's 2007 series dedicated to global mental health.[40-43] Since that time, Grand Challenges in Global Mental Health, which funds and prioritizes mental health, was initiated, WHO created the Sustainable Development Goals, which included a push for good mental health, and WHO also developed its Mental Health Gap Action Program (mhGAP), which serves as the organization's action plan.[44] Yet despite this increased focus, there are important gaps and barriers to accessing mental health services, often related to extreme shortages in mental health service providers in low-resource settings.[45] In response, there has been a growing push

for task shifting the screening and treatment of common mental health disorders to health providers and lay health workers,[44] while referring more complex cases to specialists. Sites that have trialed task shifting, including several within sub-Saharan African communities, found this to be an economically viable option that shows promising outcomes in the populations served.[46-51]

While great changes have been happening in the field of global mental health, the global health community needs to capitalize on the momentum and scale-up the integration of mental health screening and care into settings that service populations with a significant mental health threat, including HIV care and sexual and reproductive health care. Additionally, within discussions about sexual and reproductive health rights, discussions about mental health among women needs to become a greater focal point, as the two are intimately interlaced and have a mutual relationship, in which benefits or harms to one can be similarly beneficial or destructive to the other.

One of our main limitations within this study was that our measures of mental health were only self-reported annually and we were unable to detect a more frequent change in depressive symptoms. However, the measurement tools we utilized within this study were validated measures that have been used in similar settings and our study team included research teams with years of experience in HIV and mental health. Additionally, the generalizability of our results may be limited to women in long-term, stable relationships, and working with this population may have resulted in lower rates of unintended pregnancy than otherwise expected in the general population. Regardless, our study did enroll a large sample of women supporting powered comparisons and some subgroup analyses.

Conclusion

Women with poorer measures of mental health were more likely to become pregnant in our study, highlighting opportunity to integrate mental health screening and treatment into sexual and reproductive health programming and other existing health services, such as HIV care, for women. As the global burden of mental health problems continues to be substantial, capitalizing on new opportunities for mental health research and programming can greatly impact health outcomes for women and their families.

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Table 1. Study demographics among African women in serodiscordant partnerships

	All women N=1,013 N (%) or Median (IQR)	Women who became pregnant during the study N=385 N (%) or Median (IQR)	Women who did not become pregnant during the study N=628 N (%) or Median (IQR)
Age (Mean, IQR)	28 [22, 32]	25 [21, 28]	30 [23, 35]
18-24	383 (37.8%)	202 (52.5%)	181 (2.%)
25-34	447 (44.1%)	163 (42.3%)	284 (45.2%)
35-44	152 (15.0%)	20 (5.2%)	132 (21.0%)
45+	31 (3.1%)	0 (0.0%)	31 (4.9%)
Years in school	8 [6, 11]	8 [7, 12]	8 [6, 10]
No monthly income	387 (38.2%)	174 (45.2%)	213 (33.9%)
Male partner demographics			
Age (Mean, IQR)	34 [27, 39]	30 [26, 34]	36 [28, 42]
18-24	141 (13.9%)	69 (17.9%)	72 (11.5%)
25-34	473 (46.7%)	225 (58.4%)	248 (39.5%)
35-44	266 (26.3%)	74 (19.2%)	192 (30.6%)
45-54	101 (10.0%)	14 (3.6%)	87 (13.9%)
55+	32 (3.2%)	3 (0.8%)	29 (4.6%)
Years in school	8 [7, 12]	9 [7, 12]	8 [6, 12]
No monthly income	30 (3.0%)	15 (3.9%)	15 (2.4%)
Couple characteristics			
Married to study partner	958 (94.6%)	366 (95.1%)	592 (94.2%)
Partnership length, years	2 [1, 7]	1 [0, 4]	3 [1,9]
Number of children with study partner	0 [0, 1]	0 [0, 1]	0 [0, 2]
Proportion of couples with no children	571 (56.4%)	253 (65.7%)	318 (50.6%)
Number living in household	3 [2, 4]	3 [2, 4]	3 [2, 5]
Male partner has more than one wife	142 (14.0%)	40 (10.4%)	102 (16.2%)
Woman is the partner with HIV	679 (67.0%)	297 (77.1%)	382 (60.8%)
WHO stage 1	503 (49.7%)	239 (62.1%)	265 (42.2%)
WHO stage 2	176 (17.4%)	59 (15.3%)	117 (18.6%)
ART eligible	365 (36.0%)	192 (49.9%)	173 (27.5%)
Sexual behavior, last month			
Number of sex acts with study partner	5 [3, 10]	7 [3, 12]	4 [3, 10]

Number of sex acts without a condom	2 [0, 5]	3, [0, 6]	2 [0, 5]
Used a condom every time	317 (31.3%)	112 (29.1%)	205 (32.6%)
Women who have had sex with someone other than their partner	12 (1.2%)	8 (2.1%)	4 (0.6%)
Women who reported having anal sex	17 (1.7%)	8 (2.1%)	9 (1.4%)
Women who reported using no form of birth control	503 (49.7%)	164 (43.6%)	339 (54.0%)
Clinical factors			
Probable depression[1]	165 (16.3%)	75 (19.5%)	90 (14.3%)
Hazardous alcohol use[2]	134 (13.2%)	37 (9.6%)	97 (15.4%)
Social support[3]	3.6 [3.2, 3.9]	3.6 [3.1, 3.9]	3.6 [3.2, 3.9]
Reported domestic violence with study partner, last 3 months	3 (0.3%)	0 (0.0%)	3 (0.5%)
Internalized stigma score[4]	3 [2,5] – HIV-positive women 0 [0,1] – HIV-negative women	3 [2,5] 0 [0,1]	3 [2,5] 0 [0,0]

1 From the 16-item Hopkins Symptoms Checklist. Individual scores are calculated based on the average of responses to 16 questions (minimum average score = 1, maximum average score = 4, cutoff for probable depression = 1.75).
2 From the 4-item Rapid Alcohol Problems Screen. "Yes" on any item indicates hazardous alcohol use.
3 From the 10-item Functional Social Support Questionnaire. Individual scores are calculated based on the average of responses to 10 questions (minimum average score = 1, maximum average score = 4).
4From the adapted Internalized AIDS-Related Stigma Scale. Individual scores are calculated based on the sum of questions (8 questions for the index, 4 questions for the partner, cutoff for stigma = 3).

Table 2 – Mental health among women who became pregnant and women who did not become pregnant during follow up

		Pregnant during the study	Not pregnant during the study	Total
Proportion of women				
Probable depression		46/238 (19.3%)	152/768 (19.8%)	198/1006 (19.7%)
Internalized stigma				
	Internalized (index) stigma	117/159 (73.6%)	400/513 (78.0%)	517/672 (77.0%)
	Perceived (partner) stigma	15/79 (19.0%)	40/255 (15.7%)	55/334 (16.5%)
Hazardous alcohol use		33/238 (13.9%)	178/768 (23.2%)	211/1006 (21.0%)
Proportion of study visits				
Probable depression		46/307 (15.0%)	156/1930 (8.1%)	202/2237 (9.0%)
Internalized stigma				
	Internalized (index) stigma	125/206 (60.7%)	625/1238 (50.5%)	750/1444 (51.9%)
	Perceived (partner) stigma	16/101 (15.8%)	48/689 (7.0%)	64/790 (8.1%)
Hazardous alcohol use		36/307 (11.7%)	231/1930 (12.0%)	267/2237 (11.9%)

Table 3 – Association of probable depression and pregnancy incidence

	Pregnancy incidence (# pregnancies/# years not pregnant)[1]	HR (95% CI) p-value	Adjusted[2] HR (95% CI) p-value
All pregnancies			
Probable depression	20.8 (32/154)	1.28 (0.88 – 1.86) p=0.195	1.62 (1.12 – 2.36) p=0.011
No probable depression	17.5 (206/1179)	REF	REF
Unintended pregnancies			
Probable depression	5.8 (9/154)	1.19 (0.59 – 2.40) p=0.624	1.48 (0.73 – 2.98) p=0.275
No probable depression	5.3 (62/1179)	REF	REF
Intended pregnancies			
Probable depression	14.9 (23/154)	1.31 (0.85 – 2.90) p=0.224	1.68 (1.08 – 2.61) p=0.022
No probable depression	12.1 (144/1179)	REF	REF
All pregnancies			
Internalized stigma	19.4 (107/552)	1.22 (0.94 – 1.58) p=0.127	1.15 (0.89 – 1.49) p=0.288
No internalized stigma	16.8 (131/781)	REF	REF
Unintended pregnancies			
Internalized stigma	5.8 (32/552)	1.22 (0.77 – 1.95) p=0.400	1.58 (0.72 – 1.86) p=0.541
No internalized stigma	5.0 (39/781)	REF	1REF
Intended pregnancies			
Internalized stigma	13.6 (75/552)	1.22 (0.90 – 1.65) p=0.209	1.14 (0.84 – 1.55) p=0.406
No internalized stigma	11.8 (92/781)	REF	REF
All pregnancies			
Hazardous alcohol use	15.8 (27/170)	0.89 (0.60 – 1.34) p= 0.584	0.81 (0.54 – 1.21) p= 0.306
No hazardous alcohol use	18.1 (211/1163)	REF	REF
Unintended pregnancies			
Hazardous alcohol use	4.1 (7/170)	0.76 (0.35 – 1.67) p= 0.500	0.73 (0.33 – 1.61) p= 0.437
No hazardous alcohol use	5.5 (64/1163)	REF	REF
Intended pregnancies			

Hazardous alcohol use	11.7 (20/170)	0.95 (.060 – 1.52) p= 0.835	0.85 (0.53 – 1.35) p= 0.488
No hazardous alcohol use	12.6 (147/1163)	REF	REF
1 per 100 person years 2 adjusted for age, condomless sex, and number of children			