

The link between HIV and reduced fertility among women in Sub-Saharan Africa: Implications for treatment and contraceptive choice.

Virginia Reid¹

¹Undergraduate Student at Duke University, Departments of Biology and Global Health

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Abstract

The effect of viral infections on female fertility is an essential relationship to research in order to properly conduct health interventions and predict population dynamics. Particularly in Sub-Saharan Africa, a relationship between HIV positive status and fertility will have ramifications for how HIV patients are treated and what contraceptive methods they should choose. This paper investigates the hypothesis that viral infections reduce fertility in women due to life history trade-offs and increased susceptibility for co-infections. To investigate this hypothesis, I made the prediction that there is a significant negative correlation between HIV seropositive status and fertility rate among women of reproductive age. In addition, due to key recent studies on the association of injectable contraceptive methods with increased HIV susceptibility, I investigated if injectable contraceptive use modifies this relationship between HIV positive status and fertility. Using linear regression methods, a significant negative correlation between HIV positive status and fertility was found. Additionally, when the modifier of injectable contraceptive use was included in the multiple linear regression analysis, the relationship between HIV positive status and fertility was no longer found to be significant. These results support the hypothesis that viral infections may decrease fertility; however, the inclusion of the modifier of use of injectable contraceptives signals a confounding relationship between injectable contraceptives and HIV risk. The results of this study show that additional research on the effect of HIV and women's fertility is needed, and that contraceptive choice cannot be ignored when examining this relationship.

Introduction

Human Immunodeficiency Virus (HIV) most commonly affects women in their reproductive years, defined generally as the ages between 15 and 49 (Leeuwen 2006). As a result, many HIV-seropositive women consider having offspring, as do women of reproductive age infected with other viral infections (Leeuwen 2006). Examining the effect of viral infections on fertility is essential in order to consider a woman's fertility needs as a key treatment goal in interventions to remedy viral disease. More specifically, the link between HIV and fertility is important to examine in Sub-Saharan Africa because the HIV/AIDS epidemic and the "fertility transition", a shift from high to low birth rates, co-exist in most regions of that area (Terceria 2003). The HIV/AIDS epidemic in Sub-Saharan Africa has contributed to cyclical poverty, increased mortality of women and children, high numbers of orphaned children, deterioration of the health and economic sectors, and reduced agricultural output (Terceria 2003). Individually, HIV and fertility have substantial effects on socio-economic development and health (Shapiro 2015). By uncovering if HIV has a negative effect on fertility for women in Sub-Saharan Africa, researchers will be able to best craft interventions and predict mortality and population dynamics .

HIV is thought to have a negative influence on fertility for several interacting reasons. First, viral infections in general have been shown to have biological effects which may contribute to declining fertility rates, likely due to life history trade-offs, meaning that the body must put significant energy towards fighting off a viral infection, leaving less energy resources available for successful reproduction. Additionally, HIV increases a woman's risk for amenorrhea, miscarriage, and other co-infections which can make birth more risky or impossible (Terceria 2003). To a lesser extent, it is predicted that knowledge of one's HIV positive status may contribute to a decreased desire for pregnancy (Young 2007).

Previous studies have shown negative correlations between HIV and fecundity both at the individual and population level, but given the wide range of confounding social and environmental factors, causation is difficult to prove (Population Bulletin of the United Nations 2002). Most studies which have shown a significant decrease in fertility rates among women who are infected with HIV focus on community-level analyses, as confounding variables abound when examining population level and country-level data, including regional differences in fertility (Fortson 2009). In a population-level study of the effect of HIV on fertility, Juhn et al. found that HIV contributed to a 20-25% decrease in fertility rate among women. This decrease was attributed to direct physiological effects, changes in sexual behavior, and unwillingness to engage in risky sex (Juhn 2013).

As shown by this background research, multiple intersecting factors may contribute to the relationship between HIV and fertility. One possible confounding factor of particular interest to population health researchers is that of injectable contraceptive use. A recent meta-analysis conducted in collaboration with the Population Research Institute reviewed a total of 24 studies published in peer-reviewed journals and found a significant increased risk of acquiring HIV when using Depo-Provera and other injectables (Population Research Institute 2018). Injectable contraceptives are made to mimic naturally occurring progesterone, and work by lessening the inflammatory response of the immune system in order for the body to more easily accept the embryo during pregnancy (Population Research Institute 2018). This reduction in inflammatory response could contribute to the increased susceptibility for HIV virus to cause infection. The possible effect of injectable contraception methods on HIV risk would have major implications for international health interventions, as injectable contraceptives are currently the most-used form of long-acting reversible contraception used in Sub-Saharan African countries with high rates of HIV/AIDS. If injectable contraceptives do pose an increased risk of HIV, the ethics of promoting such contraceptives as a solution to unwanted pregnancies must be immediately considered. Injectable contraceptive use, based on this information, is an essential modifier to consider when examining the link between HIV infection and fertility, due to its possible relationship with both variables.

Based on this prior data, I hypothesize that viral infections reduce female fertility due to life history trade-offs and increased susceptibility for co-infections. To investigate this hypothesis, I will make the prediction that there is a significant negative correlation between HIV seropositive status and fertility rate among women of reproductive age in Sub-Saharan Africa. In addition, I will investigate if injectable contraceptive use modifies this relationship between HIV and fertility.

Materials and Methods

All data was collected from the Demographic and Health Surveys (DHS) public website. DHS Surveys are conducted in conjunction with local governments to collect and share key population health information. Data from 73 separate DHS Surveys, conducted over the time period of 1986-2016, was initially used, and was eventually parsed down based on my specifications. Each DHS survey was conducted in a separate year and country. DHS surveys from Sub-Saharan Africa were chosen for this analysis for multiple reasons; they provided the most complete data on both fertility and HIV status, and Sub-Saharan Africa is the geographical area in which most previous studies on the effect of HIV seropositive status on fertility have been conducted (Population Bulletin of the United Nations 2002).

The two indicators used to compare the effect of HIV status on fertility were:

1. “HIV Status Among Women Age 15-49”, which the DHS defined as the percentage of women aged 15-49 in the survey who tested positive to HIV.
2. “Fertility Rate”, which the DHS defined as the total fertility rate for the three years preceding the survey for age group 15-49 expressed per woman.

Additionally, the third variable, “Ever Use of Injections”, which was included as a possible confounding variable in the multiple linear regression analysis, was defined by the DHS as the percentage of women surveyed who reported ever having used injectable contraceptives (Demographic and Health Surveys 2018).

Restrictions were placed on the data set in order to select for relevant data points. Only surveys which contained values in both the “HIV Status Among Women Age 15-49” and “Fertility Rate” were selected for the linear regression, which resulted in a data set containing 55 surveys among 29 countries in Sub-Saharan Africa. A linear regression analysis was then conducted using R-studio. All statistical tests were conducted with a significance level of $\alpha=0.05$.

Studies of the effect of HIV on fertility are difficult to quantify due to HIV seropositive status likely having multiple interacting effects on fertility, including possible biological factors which may lead to decreased fertility, confounding effects of contraceptive choice, and behavioral factors which may cause a women to choose not to seek pregnancy. Based on past data on the association of injectable contraceptives both with fertility and HIV risk, I chose an additional confounding variable of “Ever Use of Injections” for use in a multiple linear-regression. For the multiple linear regression of HIV and Fertility Rate + Injectable Contraceptive Use, the data were again restricted to include only surveys which had values for all three indicators. This resulted in a data set of 23 DHS Surveys containing all 3 variables. A multiple linear regression was conducted in R-Studio to find the association of injectable contraceptive use on the linear relationship between HIV and fertility.

Results

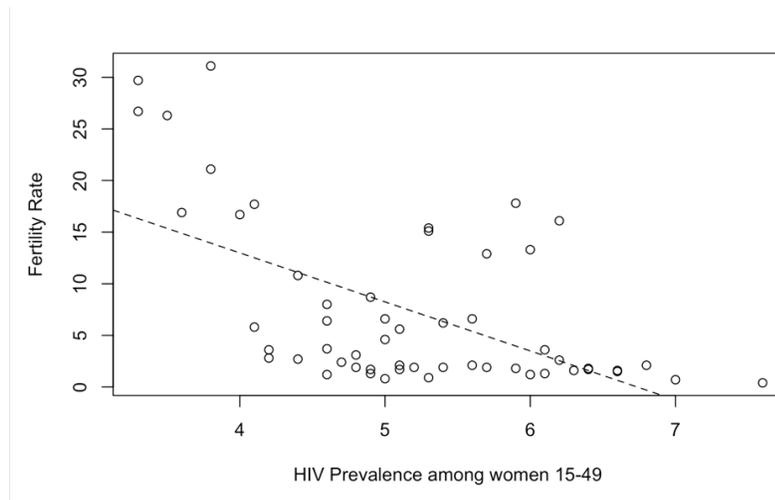


Figure 1: Linear regression model of HIV Prevalence Among Women 15-49 and Fertility Rate. Generated using Demographic and Health Surveys data.

Linear Correlation between Fertility and HIV in Sub-Saharan Africa

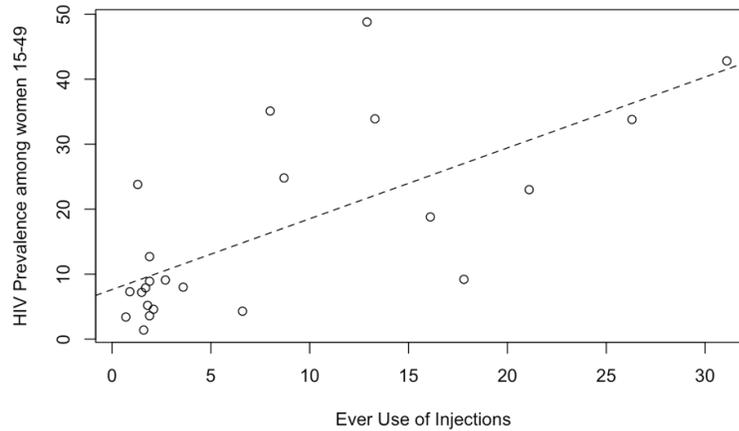


Figure 2: Linear regression model of Ever Use of Injections and HIV Prevalence Among Women 15-49. Generated using Demographic and Health Surveys Data.

Graphical results of the linear regression between Fertility and HIV Prevalence among women 15-49 are shown in Figure 1. The linear regression resulted in a negative correlation between the variables Fertility and HIV Prevalence (p-value:4.957e-06, Adjusted R-squared: 0.315).

Multiple Linear Regression Analysis with Modifier “Ever Use of Injections”

The results of the multiple linear regression analysis of the relationship between HIV and Fertility including the modifier “Ever Use of Injections” resulted in non-significant p-values (p-value for Fertility vs. HIV Prevalence: 0.128, p-value for Fertility vs. Ever Use of Injections: 0.371, Adjusted R-squared: 0.2762).

In order to further assess the relationship between these variables, a simple linear regression of HIV Prevalence vs. Ever Use of Injections was conducted and resulted in a significant positive correlation (p-value: 0.0002358, Adjusted R-squared: 0.4577). This regression is shown in Figure 2.

Discussion

The link between HIV and fertility represents key missing knowledge in the global health and development sector (Gregson 1993). My research found a significant negative correlation between HIV-seropositive status and fertility in women of reproductive age in Sub-Saharan Africa, as shown in Figure 1. This negative correlation supports the hypothesis that viral infections such as HIV have a negative impact on a woman’s fertility. The reasons for this negative correlation occurring in the Demographic and Health Surveys data may be widely varied and likely include physiological and behavioral reasons.

One weakness of this analysis is the fact that many confounding variables likely contribute to the negative correlation between HIV and fertility, most of which are impossible to control for within the bounds of available data. Thus, it is difficult to pinpoint exactly why this significant negative correlation between HIV positive status and fertility was found, but it is unlikely that it was due to a single variable, and likely involved both biological predictors, such as life-history trade offs and co-infections, as well as behavioral changes a HIV-infected individual may make, including making the decision not to attempt pregnancy. For this reason, more research must be done on the true relationship between viral infections as a physiological predictor of fertility.

Additionally, my research found that when the modifier of injectable contraceptive use was included in my

analysis of the relationship between HIV positive status and fertility, the negative relationship between these two variables was rendered insignificant. This effect signals that any correlation between fertility and HIV prevalence cannot be disentangled from both variables' association with injectable contraceptive use. These results suggest first that there is a negative association between fertility and injectable contraceptive use, which we should expect, since injectable contraceptives are a highly effective form of pregnancy prevention. Second, they suggest that there is also an association between HIV positive status and the modifier of injectable contraceptive use, supporting past data that injectable contraceptives may increase susceptibility to HIV through a physiological response.

This research supports previous findings that viral infections, particularly HIV, likely lead to reduced fertility among women. However, the inclusion of the modifying variable of injectable contraceptive use which led to a non-significant correlation between HIV and fertility demands that more research on the link between contraceptive choice, HIV, and fertility be conducted. The Population Institute and similar organizations are conducting meaningful research on the link between injectable contraceptives and HIV risk, but this research should be put into the context of HIV's negative correlation with fertility. In order to best treat HIV-seropositive women, we must know if their ability to reproduce is affected by their viral status. With this knowledge, fertility assistance can be integrated into HIV treatment, and population health researchers will be able to best predict the effects of the "fertility transition" in Sub-Saharan Africa. In a broader sense, the effect of any viral infection on a woman's fertility will have significant implications for treatment and intervention. Though straightforward relationships between variables have not been found in this study, the results provide an important jumping-off point for conversations regarding fertility and viral infection.

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