Effect of HIV Infection on Fertility of HIV Positive Women in India:

Analysis based on National Family Health Survey 3

11th August 2008

Master Thesis-Population Studies
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ABSTRACT

Pregnancy and child bearing are important events in the reproductive life of women and HIV can affect fertility in many ways. However, previous studies done to understand the effect of HIV on fertility have yielded inconsistent results. There is dearth of information on the effect of HIV on key biological and behavioral determinants of fertility among Indian women. The present study is an attempt to fill this gap.

The present study analyzes data from National Family Health Survey-3 to understand the effect of HIV on fertility of infected women who did not know their HIV status. The study uses nested case control approach to analyze the birth records and calendar data from the survey by using event history analysis techniques. It uses theoretical framework of proximate determinants of fertility by Bongaarts and Becker's (1993) model of recognizable fecundability.

Acknowledging certain limitations in the data, the study concludes that HIV infection does not affect the fecundability of HIV positive women who do not know their HIV status. It also suggests that pregnancies occurring among HIV positive women are more likely to result into termination and fertility is reduced mainly due to early dissolution of marriages because of widowhood, separation or divorce.

Chapter One

INTRODUCTION

1.1 Background

The Human Immunodeficiency Virus (HIV) affects mainly the young sexually active persons from the reproductive age group. Globally, half of the people living with HIV/AIDS are below the age of 25 years (WHO, 2006). It is estimated that every day over 6800 persons become infected with HIV and 5700 persons die from AIDS (UNAIDS, 2007). AIDS has killed more than 25 million people since 1981 and an estimated 33.2 million people are living with HIV. However, the recent epidemiological trend suggest stabilization in the global epidemic (proportion of new infection) although the number of persons living with HIV is increasing because of ongoing accumulation of new infections with longer survival times, measured over a continuously growing general population (UNAIDS, 2007)

In India, as per the recent estimates, 2-3.1 million (2.47 million) people are living with HIV/AIDS by the end of 2006 (NACO, 2007). The estimated adult HIV prevalence in the country is 0.36% (0.27%-0.47%) (NACO, 2007). The epidemic is spreading predominantly through the heterosexual route resulting into an increasing number of HIV infected women. According to the National AIDS Control Organization (NACO, 2007), women account for around one million out of the estimated 2.5 million people with HIV.

However, the epidemic in India is as diverse as the country. The adult HIV prevalence in the country varies greatly among different states and within state. In the 2006 national sentinel surveillance, six states in the country -Andhra Pradesh, Karnataka, Tamil Nadu, Maharashtra, Manipur and Nagaland- were reported to have high HIV prevalence. There are 11 states that have HIV prevalence which is more than the national average. These states include two northeastern states of Manipur and Nagaland (where the epidemic is primarily driven by Intravenous Drug Use) and Southern states such as Andhra Pradesh, Karnataka, Maharashtra, Tamil Nadu, Goa, Pondicherry etc (NACO, 2007). The highest number

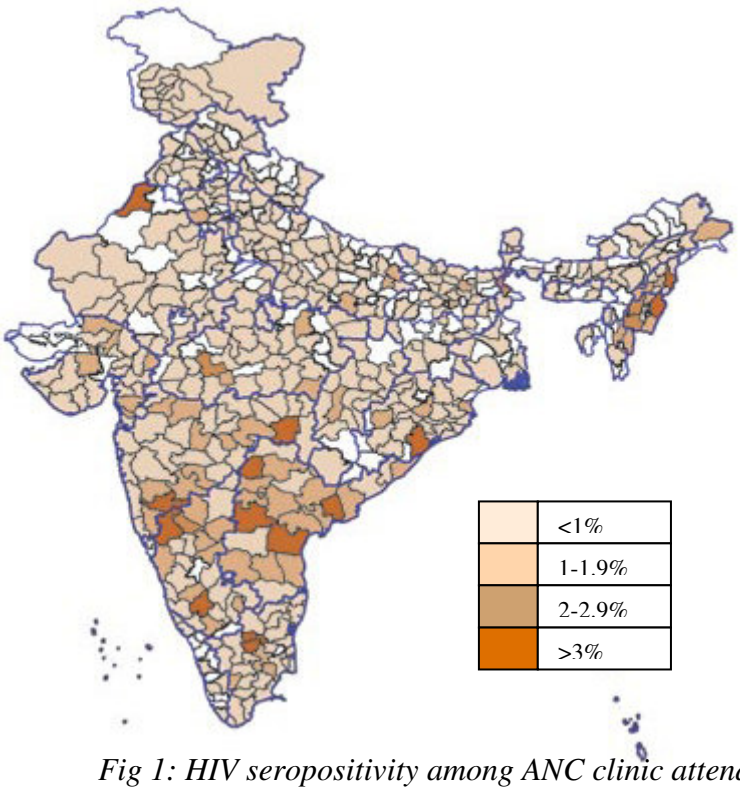


Fig 1: HIV seropositivity among ANC clinic attendees by district, India, 2006 (Source, NACO)

of people living with HIV/AIDS (PLHA) are in Andhra Pradesh and in Maharashtra. Along with Tamil Nadu and Karnataka these four states contribute to 63% of all PLHA in the country (NACO, 2007). As can be seen in the above map (fig 1) there are 118 districts that have more than one percent HIV prevalence among pregnant women attending the antenatal clinics, whereas 16 districts in the country have been identified where HIV prevalence is more than three percent among ANC clinic attendees (NACO, 2007).

HIV epidemic adversely affects women. In the beginning of the epidemic, women sex workers were primarily affected and high HIV prevalence was observed in this group. However, increasing HIV prevalence among pregnant women attending antenatal clinic indicate that the epidemic is no longer restricted to women in high-risk groups but is more generalized. Women are more vulnerable to acquire HIV infection irrespective of their belonging to the typically identified high-risk group or to the so-called general population.

The increasing proportion of HIV infection among women in their reproductive age group also raises important concerns regarding their reproductive health and the health of their children. In India, approximately 27 million pregnancies occur every year. However, the current national program could provide counseling and testing services to only 2.1 million pregnant women even with the recent rapid up scaling of these services (NACO, 2008). Among the pregnant women who were detected HIV positive, only about 45% of women could be given the drug (single dose of Nevirapine) to prevent mother to child transmission of HIV (NACO, 2008). In other words, it means that probably most of the HIV positive women in India do not know about their HIV status and many children of these women are at risk of acquiring HIV infection.

Pregnancy and child bearing are important events in the reproductive life of women. HIV can be transmitted from mother to child during pregnancy, delivery and through breastfeeding. In the absence of any intervention, the chances of such transmissions are 15-45 percent (WHO, 2006). There is a burgeoning attempt to understand the effect of HIV on fertility of infected people. However, there are still uncertainties in establishing the causal effect of HIV on many determinants of fertility. The review of existing literature on the effect of HIV on fertility is presented below.

1.2 HIV/AIDS and fertility

Studies done to understand fertility among HIV positive women have presented conflicting results. Many studies from Sub Saharan Africa suggest that women with HIV infection have lower fertility than HIV negative women (Kaida et al, 2006). In 1998, Zaba and Gregson reviewed six studies in Sub Saharan Africa to conclude that HIV positive women have between 25% to 40% lower fertility as compared to HIV negative women for most age groups. Studies examining the linkages between HIV infection and pregnancy/delivery outcome suggest higher rate of spontaneous abortions and stillbirths (Gray et al, 1997; Miotti et al, 1991; Ryder and Temmerman, 1991; Brocklehurst and French, 1998, cited by Gregson et al 2006) among HIV infected women. However, there are also studies that reported no association of HIV infection with fertility in women and pregnancy loss (see for eg Sedgh et al, 2006).

The potential effect of HIV on fertility can be due to the effect on the biological mechanisms as well as due to the effect on the behavioral determinants of fertility (Department of economic and social affairs, UN, 2002).

Effect on biological mechanisms-

Production of spermatozoa- Several studies have assessed semen quality among HIV infected men. However, the results of these studies are inconsistent. Kreiger et al (1991) have shown no effect on semen parameter among HIV infected men as compared to non infected men whereas Crittenden et al (1992) have reported reduced sperm motility and round cells in infected men (as reported by Bujan et al, 2007). A reduced percentage of morphologically normal spermatozoa has been reported in several studies (Dondero et al, 1996; Muller et al, 1998; Nicopoullos et al, 2004) but not in the study of Dulioust et al (2002) (Bujan et al, 2007). The study by Dulioust et al (2002) also reported decrease in sperm motility and reduction in total sperm count. There has also been studies indicating that the semen quality is affected only in the advanced stage of the disease (Krieger et al 1991, cited by Gray et al 1998)

Spontaneous intrauterine mortality- Studies from Western countries indicate that miscarriages, spontaneous abortions and stillbirths appear to be more common in infected women (Gray et al, 1997; Miotti et al, 1991; Ryder and Temmerman, 1991; Brocklehurst and French, 1998, cited by Gregson et al 2006). Several studies have attempted to understand the association of HIV infection with spontaneous abortion. However, the nature of such association is still uncertain. Carla D'Ubaldo et al (1998) presented a review of literature on HIV infection and spontaneous abortions in their paper. This table is reproduced here.

Table 1: Review of studies on HIV and spontaneous abortions

First Author	Year	Country	Design	HIV +ve	HIV - ve	% spontaneous abortions	Risk
Johnstone	1988	Europe	P	61	75	18.0 Vs 5.3	RR, 3.4
Selwyn	1989	USA	P	52	73	7.7 Vs 5.5	RR, 1.4
Lasley-Bibbs	1990	USA	P	69	276	NR	RR, 4.4
Ryder	1991	Africa	P	197	295	52.1 Vs 51.6 ¶	RR, 0.62
Sunderland	1992	USA	P	37	37	5.4 Vs 8.1	RR, 0.67
Lindsay	1995	USA	P	21	85	4.8 Vs 4.7	RR, 1.0
Stephenson	1996	Europe	P	202	580	16.0 Vs 10.0	RR, 1.6
De Vincenzi	1997	Europe	P	84	110	25.4 Vs 8.3	RR, 3.1
Braddick	1990	Africa	R	177	327	11.0 Vs 8.0	RR, 1.4
Miotti	1990	Africa	R	64	311	28.1 Vs 15.1	OR, 2.2
Lepage	1991	Africa	R	215	216	16.7 Vs 7.9	RR, 2.1
Chirgwin	1993	USA	R	515	2150	9.7 Vs 11.3	RR, 0.86
Temmerman	1994	Africa	R	281	275	7.8 Vs 3.6**	OR, 2.0
De cock	1994	Africa	R	839	1220	7.3 Vs 5.7	RR, 1.3

¶ incidence rate ** no distinction between spontaneous and induced abortions
Design P= Prospective R= Retrospective
RR was not mentioned in the many of these studies and is estimated by the Author

It can be seen in the table-1 that there are a number of studies that calculated greater risk of spontaneous abortions among HIV infected women including the study of

Carla D'Ubaldo et al (1998). However, in many of these studies the association was not significant. Nonetheless, several hypotheses were developed to explain the association of HIV infection with spontaneous abortion such as direct effect of HIV on placenta, increased cytokine production resulting into fetal demise and increased bacterial and viral ascending infection due to immunosuppression etc.

Effect on behavioral determinants of fertility- HIV can have direct or indirect effect on several behavioral factors that determine fertility. These are discussed below.

Sexual intercourse- Sexual behavior and frequency of intercourse may be affected due to HIV because of fear of infecting sexual partner, guilt and shame associated with sex, emotional and psychological distress reducing the desire for sex (Lusti-Narasimhan,2007) and due to resultant morbidity. In cases of sero-discordant couples (when only one partner is HIV positive) the potential risk of transmitting HIV to the uninfected partner as well as the possibility of infection with other STIs should be taken into account. In sero-concordant couples (when both partners are infected with HIV), possible re-infection with HIV has to be considered (Gottlieb et al 2004) although there is still uncertainty regarding the risk and consequences of re-infection (Smith et al 2005). These considerations may also affect the frequency of sexual intercourse among HIV positive women. HIV can also affect sexual behavior and thus fertility of those infected by decreasing the duration of marriage through high rates of separation, divorce or widowhood (Porter et al 2004).

Use and effectiveness of contraception- HIV also affects use and effectiveness of contraception. Overall, studies indicate that contraceptive use is higher among HIV positive couples (who know their HIV status) as compared to HIV negative couples (Ntozi, 2006; Lutalo et al 2000; Okeibunor, 1999 cited by Kaida et al 2006). This can be because HIV positive men and women are advised to use condom for dual protection as it prevents transmission to other partner (in sero-discordant couples) and re-infection (in sero-concordant couples). Generally, the effectiveness of contraceptive methods does not differ in HIV infected women and according to the current WHO guidelines HIV positive women have similar contraceptive options as that of HIV negative women (WHO, 2006). However, some considerations are important in HIV infected women such as drug interactions among hormonal contraceptives and ante-tubercular drug (refampicine) and risk of anemia due to increased menstrual bleeding from copper bearing intrauterine devices (IUDs).

Some studies also indicate that higher percentage of HIV positive women choose permanent method of sterilization as compared to HIV negative women (Hopkins, 2005, Bedimo, 1997). This can be because many women might not desire any further children once they achieve their desired family size. Health care providers can also strongly encourage HIV positive women to go for permanent method of sterilization. This earlier onset of permanent sterility reduces fertility (Bongaarts and Potter, 1983)

Induced abortions- The rate of induced abortion was found higher among HIV positive women as compared to HIV negative women in some of the studies done in Cote d'Ivoire, Cameroon and Kenya (Kaida et al 2006). This may be because HIV positive women are more likely to choose the option of terminating their pregnancies for the fear of transmitting the virus to the unborn.

***Postpartum infecundability*-** Breastfeeding and postpartum abstinence from sexual intercourse contribute to postpartum infecundability (Bongaarts and potter, 1983) and are important determinants of birth interval length. HIV can be transmitted from mother to child through breastfeeding. The risk of such transmission is 7 to 22% (WHO 2006). In an attempt to minimize this risk, HIV positive women may choose not to breast-feed their children or may reduced the duration of breastfeeding. Such reductions in breastfeeding may shorten women's short-term infecundability, leading to earlier pregnancy and higher fertility (Gregson et al, 2006 cited by Kaida et al, 2006)

Based on the current literature it can be said that the effect of HIV on fertility is multidimensional and is a result of complex interplay of various factors such as effect of HIV on health status of the individual, effect of treatment and drugs, social consequences of being diagnosed as HIV positive, stigmatization and discrimination, cultural norms etc. Under such complexities, it is often difficult to estimate the biological impact of HIV infection on fertility as compared to the behavioral impact associated with HIV. One of the ways to understand the biological impact of HIV on fertility is to study women who do not know their HIV status.

There are only two published studies from Africa to our knowledge that have examined fertility and pregnancy outcome among women who do not know their HIV status. Both these studies used retrospective data from women attending antenatal clinics. However, the results of these studies are inconsistent. One study is by Desgrees du Lou *et al (1999)* found that HIV-infected women in the Ivory Coast had up to 13% fewer pregnancies than uninfected women and greater risk of experiencing an abortion or stillbirth. The other study is by Sedgh et al (2006) done in Dar es Salaam, Tanzania concluded that the association of HIV-seropositivity with a woman's reported number of pregnancies was of borderline significance (RR=1.13, 95% CI=1.00, 1.27). They also found out in multivariate analysis that HIV infection was not associated with pregnancy loss. In addition to the socio-demographic characteristics that were included in the analysis by Desgrees du Lou *et al*, the analyses by Sedgh et al (2006) also controlled for other important predictors of fertility, namely contraceptive use, prior exposure to sexually transmitted diseases and recent exposure to sexual intercourse.

Several factors can be associated with the conflicting results in many of these studies. There could be problems related to the methodology of the research such as retrospective study design, inappropriate control group or small sample size. The differences in the findings could also be due to the differences in the epidemiological pattern across different countries and due to the differences in the social, cultural and economic factors that affect the proximate determinants of fertility. The fertility reducing effect of HIV associated factors such as high prevalence of sexually transmitted infections (particularly syphilis and gonorrhea) can also contribute to these differences. In this scenario, the results of these studies cannot be directly extrapolated for Indian women. Currently, there is scarcity of literature on these issues from India. The present study is an attempt to fill this gap.

1.3 Study objective

The overall objective of the study is to understand the effect of HIV infection on fertility of HIV positive women who do not know their HIV status. Fertility can vary among women because of variations in the factors that put the woman at risk of becoming pregnant or it can be due to the variation in the ability of women to conceive. The ability to conceive can be broadly referred as fecundability. At the end of the study we expect that we would be able to explain if fertility among HIV positive women is different than HIV negative women and if so then is it because of the variation in the factors that put the women at risk of becoming pregnant or due to the reduced ability of women to conceive.

To achieve this objective the specific research questions are

1. What is the effect of HIV on the proximate determinants of fertility among HIV positive women who do not know their HIV status?

2. Are the outcomes of pregnancies different among HIV positive women as compared to negative women?

3. Is there any difference in the rate of conception among HIV positive and HIV negative women?

4. Is waiting time to conception different for HIV positive women as compared HIV negative women?

Most of the previous studies done on HIV and fertility have used data from women attending antenatal clinic. Therefore, there is a potential bias of looking at only women who are accessing services at antenatal clinic. The present study is different in that regard as the analysis is based on the data collected in the community based nationally representative sample.

In next chapter, the theoretical framework that guided this research is discussed followed by the discussion on conceptual model. Subsequent chapters give details about the data and the methodology used for analysis and the results and conclusions.

Chapter Two

THEORETICAL FRAMEWORK

The theoretical framework that guided this research is based on the framework of proximate determinants of fertility presented by Bongaarts and Potters (1983) and Becker's model (1993) of waiting time to conception and fecundability. The framework of proximate determinants of fertility is one of the commonly used frameworks for the analysis of fertility differentials due to its usefulness in quantifying these determinants. According to this framework, any difference in the individual level fertility is explained by the differences in the proximate determinants of fertility. In the present study, we analyze the effect of HIV on some of the proximate determinants to compare the fertility differentials among HIV positive and HIV negative women. One of the objectives of the study is to understand the effect of HIV infection on ability of women to conceive. Becker's model (1993) of fecundability (likelihood of conception) is useful to understand the factors affecting the recognizable conception. We use this model mainly to interpret our results on fecundability. These theoretical concepts are explained below. However, before going into the details of the theoretical framework, it would be appropriate to present the definitions of some important terms used in the framework.

2.1 Definitions

Fertility, fecundity and fecundability: Fertility refers to the actual reproduction whereas fecundity denotes the ability to reproduce (Bongaarts and Potter, 1983 pp 3). A woman who is bearing children is considered as fertile and a woman is considered as fecund if she is capable of bearing live offspring. Therefore, a fecund woman may choose to remain infertile by abstaining from sexual activity or by using contraception. The term fecundability is generally defined as the probability of conception, per month or per menstrual cycle, for a women exposed to some risk of conception (Golden et al, 1993). Within this border definition, various terms and concepts are described in association with fecundability, such as total fecundability and recognizable fecundability. Total Fecundability refers to the probability that any conception occurs during a cycle; this include non-implanted fertilized ova and conceptions aborted spontaneously before the end of the cycle. Where as recognizable fecundability refers to the probability of conception, which is recognizable at the end of the conception cycle by the nonoccurrence of menstruation (Golden et al, 1993). Bongaarts (1975) uses the term natural fecundability for non-contracepting population.

Natural fertility: The term natural fertility is defined by Henry (1961) as fertility in the absence of deliberate birth control that is "bound to the number of children already born and is modified when the number exceeds the maximum which the couple does not wish to exceed" (cited by Bongaarts and Potter, 1983 pp 21). In practice, fertility may be considered as natural if no contraception or induced abortion is used (Henry, 1979 cited by Bongaarts and Potter, 1983 p 21)

Spontaneous intrauterine mortality: measures of intrauterine mortality usually include both spontaneous abortions and stillbirths but exclude embryonic deaths before the first missed menses (Bongaarts and Potter, 1983 p 38-39). A spontaneous

abortion is a fetal death before the twenty-eight week of gestation whereas fetal death after twenty-eight week is considered as stillbirth as the fetus is viable after this period.

2.2 Framework of Proximate Determinants of Fertility

Bongaarts (1978) while examining various factors influencing fertility laid down a set of factors, which he termed as proximate determinants that directly influence fertility. His work was based on the previous work of Kingslay Davis and Judith Blake (1956) who described the concept of 'intermediate variables' as a set of factors through which and only through which, social, economic and cultural conditions can affect fertility (Bongaarts, 1982 p. 179). The strength of Bongaarts model is its usefulness in quantifying these determinants. Bongaarts and Potter (1983) laid down seven proximate determinants of fertility. These are 1) Marriage/start of sexual activity 2) Use and effectiveness of contraception 3) Induced abortion 4) Postpartum infecundability (as primarily determined by the duration and intensity of breast-feeding) 5) Fecundability or Frequency of intercourse and 6) Spontaneous intrauterine mortality 7) Onset of permanent sterility (Bongaarts and Potter, 1983). Marriage (which is for practical reasons considered as start of reproductive career instead of menarche) and onset of permanent sterility are the determinants, which mark the beginning and the end of the reproductive life span, and other determinants are related to the rate of birth. The second and third determinant measures the deliberate control of marital fertility and the last four determinants measures the natural marital fertility. Measurement of all these factors together determines the level of fertility.

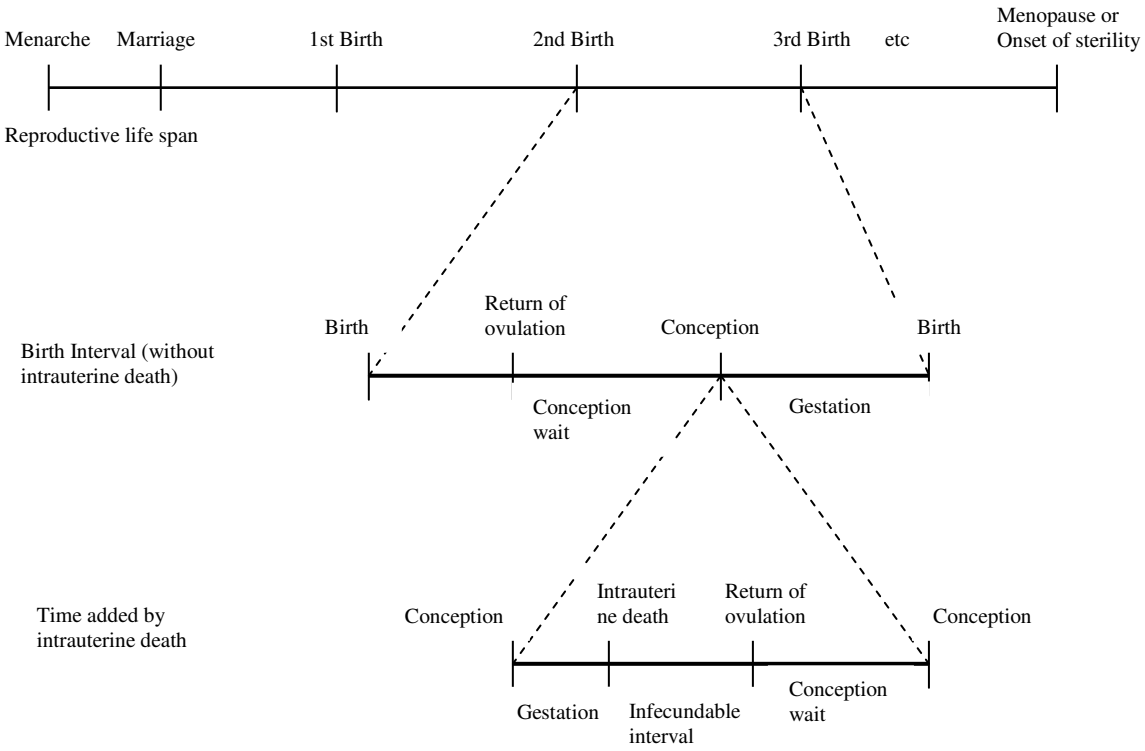


Fig 2: Events determining the reproductive life span and the rate of childbearing, (Bongaarts and Potter, 1983 p. 4)

Figure 2 summarizes the various events that influences the duration of the reproductive period and the rate of childbearing. The potential reproductive years start at menarche or the first menstruation in a woman's life. However, in most societies the actual childbearing starts after marriage, which generally takes place after menarche. Therefore, in practice marriage can be considered as the start of the reproductive career. Once married, a woman may be considered at risk of childbearing until the onset of permanent sterility or menopause, unless her marriage is disrupted due to separation, divorce or widowhood.

While married and fecund, women reproduce at the rate inversely related to the average duration of birth interval. Short birth intervals are associated with high fertility and vice versa. In the absence of intrauterine mortality, the length of birth interval is determined by 1) postpartum infecundable interval 2) the waiting time to conception, also called as the fecundable or ovulatory interval, from the first postpartum ovulation to conception and 3) a full term pregnancy. As can be seen in the figure-2 in case a pregnancy ends prematurely in spontaneous or induced intrauterine death then the birth interval is lengthened.

2.3 Becker's Model (1993) of Recognized fecundability

Fecundability is generally defined as the probability of conception, per month or per menstrual cycle, for a women exposed to some risk of conception (Golden et al, 1993). While reviewing the models to estimate fecundability Golden and Millman (1993) described two major categories under which these models can be grouped. Models in the first category treat fecundability as an input that contributes significantly to the level of some empirically observed reproductive outcome, such as the number of live birth, the proportion of women conceiving, or the waiting time to conception. Whereas, models in the second category treat fecundability as an output and attempt to quantify the behavioral and physiological processes underlying it such as coital frequency, length of the fertile period, and the probability of implantation (Golden & Millman, 1993)

In this research we use a model of recognized fecundability suggested by Becker (1993) based on the work of James (1979) and Bongaarts and Potter (1983). This Model is described below. According to Backer (1993) recognized fecundability (F) depends on following probabilities

p_1- Probability that a menstrual cycle is ovulatory- Several studies indicate that the percentage of ovulatory cycles is low right after menarche, then increases slowly and reaches a maximum in the mid and late 19-20s (Hutter et al 2006). In general, fecundability is higher when cycles are regular (Spira et al 1993, cited by Hutter et al. 2006)

p2= Probability that insemination occurs during the fertile period given that ovulation occurs- Frequency of intercourse is an important determinant of fecundability. There are some studies, which indicate that the frequency of sexual intercourse is reduced after the diagnosis of HIV and in the advanced stage of the disease due to illnesses. Though this is an important variable, collecting data on it is difficult. The explanation of fecundability can be limited to a great extent due to lack of data on this variable.

p_3- Probability that insemination leads to fertilization given that it occurs during fertile period-

The frequency of intercourse is not the only factor determining the probability of conception; timing of intercourse is also very important. For women having intercourse within 2 hours of the time of ovulation, the probability of conception given that coitus takes place and that no contraceptives are used, has been estimated to be 0.85 by Hertig,(1967) and 0.95 by Bongaarts and Potters (1983) (cited by Hutter et al, 2006). Use and effectiveness of contraception is an important determinant of the probability of insemination leading to fertilization.

p_4- Probability that conception is recognizable given that fertilization occurs- it is estimated that only half of the fertilized ova yield a recognizable conception (Hertig 1967, cited by Bongaarts and Potters, 1983). The reminders either fail to implant or abort spontaneously before the first missed menses.

Based on this model recognizable fecundability, F is

$F = p_1 p_2 p_3 p_4$

To distinguish pregnancies that result in live births Backer (1993) defines F´ which is the probability that the live birth conception occurs during a menstrual cycle. F´ is also called as effective fecundability and is estimated as

$F' = p_5 F$

Where p_5 is the probability of a live birth given that conception is recognized- Intrauterine mortality (spontaneous abortions, induced abortions and stillbirths) can reduce the probability effective fecundability. There are a number of studies indicate that the rates of intrauterine mortality are higher among HIV positive women.

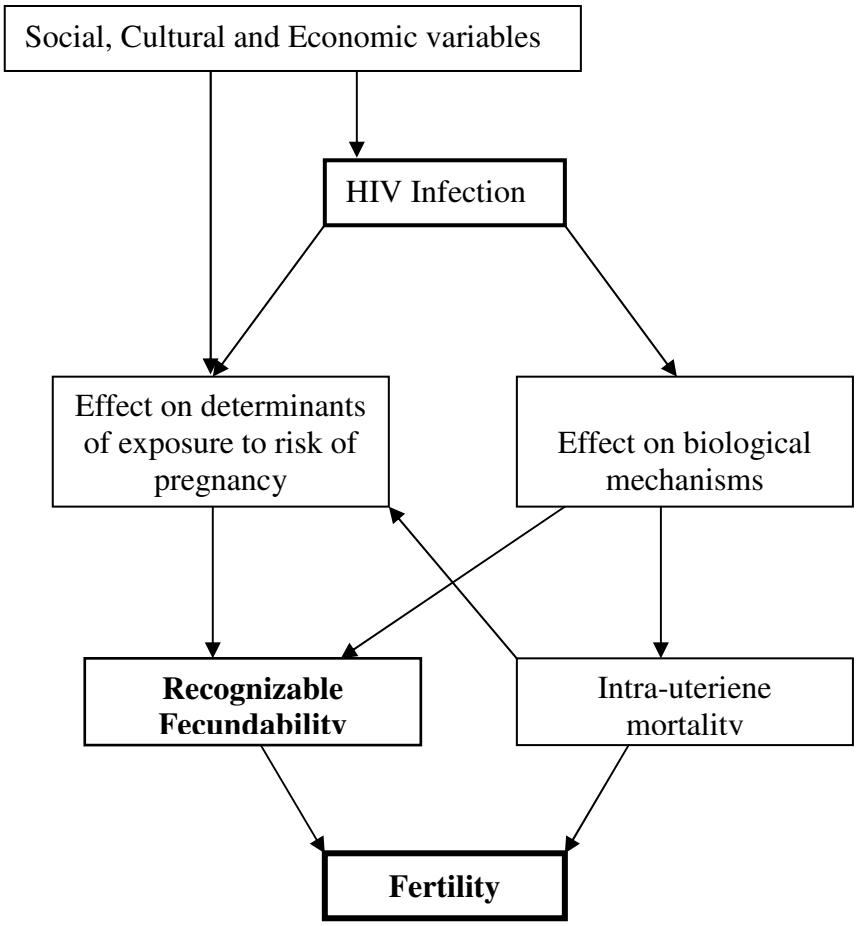
2.4 Conceptual framework

The conceptual model presented in figure-3 explains the relationship between HIV infection and its possible effect on fertility specifically in the situation when women are not aware about their HIV status. HIV can affect fertility by two possible ways. One is by affecting the factors that determines the duration of exposure to the risk of pregnancy. The factors that are considered to influence this duration are -duration of marriage, frequency of sexual intercourse, use of contraception and postpartum infecundability. These factors are the proximate determinants mentioned in the Bongaarts framework. On the other hand, HIV can also influence fertility by its effects on the biological mechanisms. This effect can be on the reproductive mechanisms before the pregnancy is recognized (such unrecognized spontaneous abortions, p1, p2 and p3 of Becker"s Model) or can be after the recognized pregnancy such as spontaneous intrauterine mortality. In our study, we would analyze the biological effect only after the pregnancy is recognized.

Various social, cultural and economic variables can affect fertility by affecting the proximate determinants. In Indian context, fertility is known to differ among women with respect to their age, educational background, economic status, place of residence (rural/urban) etc. The fertility rates are also different in different states due

to difference in the socio-cultural factors. While understanding the effect of HIV on fertility, these factors need to be considered.

Fig 3: Conceptual model: Effect of HIV on fertility



In this framework, explicit distinction is made between recognizable fecundability (ability to reproduce) and Fertility (actual reproduction). This distinction is helpful to understand the effect of HIV on the ability of women to conceive (research question 3 and 4) and on the overall fertility (research question 1 and 2). The terms mentioned in the conceptual model have already been described at the beginning of the chapter.

Hypothesis-
Based on the existing literature and from the epidemiological situation in India, we hypothesize that

HIV reduces fertility but does not have any effect on the recognizable fecundability of Indian women who do not know their HIV status.

Chapter Three

DATA AND METHODOLOGY

The objective of the study is to understand the effect of HIV on fertility of women who do not know their HIV status. To achieve this objective, nested case control study design was used and data from the National Family Health Survey (NFHS -3) of India was analyzed.

3.1 Study design

This is a retrospective case control study. The study design used is the nested case control study design. In the nested case control study, cases of the disease that occur in a defined cohort (here HIV positive women) are identified and for each case a specified number of matched controls is selected from among those in the cohort who have not developed the disease by the time of disease occurrence in the cases (Ernster V, 1994). For many research questions, nested case control design potentially offers impressive reduction in cost and efforts of data collection and analysis compared with the full cohort approach, with relatively minor loss in statistical efficiency (Ernster V, 1994). The number of controls selected per case may vary but it is generally considered that 5-6 controls are enough to achieve more than 90 percent of maximum cohort level power (Cologne et al, 2004). In many epidemiological studies, nested case control design is used particularly to understand the biological effects related to the disease. Since the objective of this study is also to understand the biological effect of HIV (as these women are not aware about their HIV status) use of this study design would be appropriate to answer the research questions.

3.2 Data source

The most common set of data used to study fertility differentials in developing countries are the Demographic and Health Surveys (DHSs). These are large, nationally representative sample surveys collected for many countries around the world that provide information about fertility and family planning, including knowledge and current use of contraceptive methods, and detailed fertility histories with records of children's birth and death dates (Baschieri & Hinde, 2007). In India the first DHS, which is know as National Family Health Survey (NFHS) was conducted in 1992-93. The last survey was the third round of NFHS (2005-6), which was conducted in the year 2005-6. In this study, the data from third round of NFHS was used. In NFHS-3, HIV testing was also conducted among men and women from the household sample to estimate adult HIV prevalence in the country. Therefore, it is possible to analyze these data to compare fertility among HIV positive and HIV negative women.

HIV testing in NFHS-3 –NFHS-3 is the first national survey in India to include HIV testing. Previously, national HIV prevalence estimates were derived primarily from sentinel surveillance among pregnant women attending government antenatal clinics. HIV testing was conducted in NFHS to get a national estimate of HIV in the household population of women age 15-49 and men age 15-54 who are representatives of the adult population in the country. The state level estimation of HIV prevalence was restricted to only seven states. Among these states were the six highest HIV

prevalence states (Andhra Pradesh, Karnataka, Maharashtra, Manipur, Nagaland, and Tamil Nadu) and one low HIV prevalence state, Uttar Pradesh. However, HIV testing could not be conducted in Nagaland due to local opposition.

In these seven states, all women age 15-49 and men aged 15-54 who completed individual interview were eligible for HIV testing. Respondents who consented to participate in the HIV testing provided blood drops from a finger stick that were collected on special filter paper cards and dried overnight. A number of steps were taken to monitor HIV testing including external quality control for HIV testing and formation of an expert group to monitor HIV testing in the laboratory as well as blood collection in the field (for details on HIV testing protocol see NFHS 3 report, chapter one and twelve). HIV testing was conducted for 85% of 62,182 eligible women and 78% of 64,175 eligible men (NFHS-3, 2007). The coverage was 82% for both sexes combined. In NFHS-3, 6 percent of women and 14 percent of men did not complete individual interviews, so they were not eligible for blood tests. In addition, 6 percent of women and 5 percent of men who completed individual interviews refused to provide blood for HIV testing. Only a small number of interviewed women (1 percent) and interviewed men (2 percent) were not at home at the time of the blood collection.

Anonymity of HIV test results-The HIV test results were linked to all other information collected from the tested individual. At the same time, anonymity was promised and assured with regard to all information collected including HIV test results. To assure HIV test anonymity, a number of steps are taken, including the use of randomized barcode IDs; offsite lab testing, independent of data collection and processing; and the scrambling of certain identifiers in the data. The scrambling of the data does not have any effect of the linking of individual data with the HIV data.

Preliminary data set about HIV testing are available through DHS and can be linked to individual recode files for analysis.

Data on fertility determinants- In individual women's interview detailed data on fertility determinants are collected in birth history records and in calendar format. In this study, the birth history records as well as calendar data are used for analysis.

3.3 Quality of birth history and calendar data

In NFHS-3 the data on all live births is recoded under birth history records whereas the monthly status of contraceptive use and pregnancies is collected in a calendar format (annexure 1) for 5-6 years preceding the survey. The data collected under birth histories include information on the date of birth of the child, gender of the child and survival status of the child at the time of interview. During data collection, several measures and procedures were used to obtain complete and accurate reporting of births, deaths, and the timing of these events. First, women were asked a series of questions aimed at recording all the live births that had occurred in their lifetime. Second, for each live birth, information was collected on the age, sex, and survival status of the child. For dead children, age at death was recorded. Interviewers were given extensive training in probing techniques designed to help respondents report this information accurately. For example, interviewers were instructed to check any documents (such as horoscopes, school certificates, or vaccination cards) that might provide additional information on dates of birth, and to probe for any additional

births in each birth interval in order to prevent the omission of births, especially of children who died soon after birth. However, in spite of these measures there can be some errors in data collection, which are known with the retrospective data collection on birth histories such as non-reporting of births especially for children who did not survive.

In NFHS-3 data on pregnancies, contraceptive use and on marriage is also collected in a calendar format. The data set contains four calendars in the women's file. Each of the four calendars run concurrently, starting in the month of interview, and going back in time to January 2000 (phase1) or January 2001 (phase 2). For any woman, the calendar is at least 60 months in length. Each VCAL variable represents the following:

VCAL(1): Births, pregnancies, and contraceptive use (column 1 in the questionnaire)

VCAL(2): Reason for contraception discontinuation (column 4 in the questionnaire)

VCAL(3): Marriage (column 3 in the questionnaire)

VCAL(6): Ultrasound conducted during pregnancy (column 2 in the questionnaire)

Each of the VCAL variables is an 80 character string, with the 80^{th} position in the string corresponding to January 2000 or 2001 (phase 1 or 2).

Studies of the quality of the DHS calendar data on contraception have shown that they are fairly reliable (Baschieri & Hinde, 2007). It is likely that the calendar data quality may vary across countries but it was found that generally the estimates of prevalence obtained retrospectively from the calendar are in very close agreement with the corresponding current status estimates obtained from the earlier survey'(Curtis 1997, cited by Baschieri & Hinde, 2007). With a calendar, the recording of sequence of events is much easier than with the traditional questionnaire, and inconsistencies in the timing of events in different life domains are more easily detected (Khatun, 2005). However, due to its retrospective nature as one goes further back in time the data quality might reduce due to recall bias. Some studies also suggest that the calendar data on contraceptive behavior is fairly reliable at aggregate level but at the individual level the responses are considerably unreliable (Curtis, 1997 cited by Khatun, 2005 p25). These data limitations need to be considered while interpreting the results.

3.4 Selection of Sample

I merged the HIV testing data file with the individual woman's recode file to select the cases of HIV positive women. Several appropriate samples were selected based on the objective of the analysis. Following table summarizes the selection criteria used for sample selection with respect to the research question under consideration.

Table 2: Sample selection criteria

Estimated Parameter	Number of sample	Selection Criteria
Effect of HIV on determinants of exposure to risk of pregnancy	One	Never tested before for HIV Ever married Married for less than 12 years
Effect of HIV intrauterine mortality	One	Same as above
Pregnancy rate	Two	
	First sample	Same as above
	Second sample	Never tested before for HIV Currently married Fecund
Marriage to first birth interval	Two	
	First sample	Same as above
	Second sample	Never tested before for HIV Currently married Fecund Got married after the start of calendar (5-6 years prior to survey)
Interval between last two pregnancies	One	Never tested before for HIV Had at least one pregnancy during calendar period

Matching of cases and selection of HIV negative women

For selection of HIV negative women (control) from the above mentioned samples, every HIV positive cases was matched with respect to five matching variables. These variables were 1) age 2) education 3) state 4) wealth index 5) place of residence. These variables have known influence on the fertility of women. Therefore, these variables were selected for matching so as to control for their effect. The matching was done in SPSS. After matching on the above mentioned variables five controls for each HIV positive case were randomly selected with the help of SPSS (except for analysis of the interval between last two pregnancies where 4 controls were selected for each case due to less number of matches).

The analysis is done with the help of SPSS (14) and MS excel (2003) by using event history analysis techniques.

Chapter Four

RESULTS

4.1 Social, cultural and economic factors affecting fertility

There is a wide diversity in fertility levels in different states in India. Though the national average total fertility rates (TFR) is estimated to be 2.68, it ranges from 1.8 in Goa, Andhra Pradesh, and Tamil Nadu to 4 in Bihar (NFHS-3, 2007). The levels and trends in TFR also differ in urban and rural areas of each state and according to the wealth index of the household. The TFR is 3.9 children for women living in the household with lowest wealth quintile as compared 1.8 children for women living in the highest wealth quintile.

More than half of the women get married before the legal age of 18 years. The median age at marriage is 17.2 years with considerable difference among urban women (median age at marriage, 18.8 years) as compared to rural women (median age at marriage 16.4 years) (NFHS-3, 2007). Due to early age at marriage, there is substantial proportion of teenage pregnancies in India. According to NFHS-3 data, almost 50 percent of the women aged 20-49 had birth before the age of 20. Early child bearing is most common among rural women with no education.

Unplanned pregnancies are also relatively common. NFHS-3 estimated that if all the women were to have only the number of children they wanted then the total fertility rate would be 1.9 instead of 2.7. For most Indian couples the ideal family size is 2 children. However, there is strong cultural influence to have a son. One in five women and men say that they would like more sons than daughters (NFHS-3, 2007)

The contraceptive prevalence rate (CPR) for currently married women in India is 56 percent. However, there is a wide variation in CPR among different states. CPR is more than 70 percent in Himachal Pradesh and West Bengal whereas it is less than 30 percent in Nagaland and Meghalaya (NFHS-3, 2007). Female sterilization is the most preferred contraception accounting for 66 percent of all contraceptive use. Female sterilization is most prevalent in Southern region as compared to other regions in the country. Nationally, the median age at sterilization for women is 25.5 years (lowest 23.3 years in Andhra Pradesh and highest 29.9 years in Manipur) (NFHS-3, 2007). In India as a whole, 77 percent of the women who choose female sterilization never used any other method of contraception.

Comparing fertility among women with such a varied background is challenging. To control for these variations we matched HIV positive cases on following five important demographic variables that are known to influence fertility. These are age of the women at the time of interview (5 years age interval), state, highest education level, wealth index and place of residence (rural, urban). Following is the distribution of the cases based on these matching variables

Table 3. Distribution of cases according to the matching variables

		HIV -Ve (n=345)	HIV +Ve (n=69)	Total	Total %
State	[UP] Uttar Pradesh	20	4	24	5,8%
	[MN] Manipur	50	10	60	14,5%
	[MH] Maharashtra	100	20	120	29,0%
	[AP] Andhra Pradesh	65	13	78	18,8%
	[KA] Karnataka	70	14	84	20,3%
	[TN] Tamil Nadu	40	8	48	11,6%
Age 5-year groups	15-19	40	8	48	11,6%
	20-24	85	17	102	24,6%
	25-29	165	33	198	47,8%
	30-34	45	9	54	13,0%
	35-39	10	2	12	2,9%
Type of place of residence	Urban	160	32	192	46,4%
	Rural	185	37	222	53,6%
Highest educational level	No education	125	25	150	36,2%
	Primary	45	9	54	13,0%
	Secondary	155	31	186	44,9%
	Higher	20	4	24	5,8%
Wealth index	Poorest	45	9	54	13,0%
	Poorer	50	10	60	14,5%
	Middle	55	11	66	15,9%
	Richer	130	26	156	37,7%
	Richest	65	13	78	18,8%

Most of the HIV positive women were from the four southern states (states excluding Manipur and Uttar Pradesh). Since the beginning of the HIV epidemic these states have been identified as high HIV prevalence states. It is estimated that more than 60 percent of people living with HIV are in these four states (NACO, 2007). Majority of the women were in the age group of 20-30. The mean age at the time of interview was 25.5 (SD 4.414) for HIV negative women and 25.4 (SD 4.44) for HIV positive women. The proportion of women living in the household with higher wealth index was more as compared to women living in the household with lower wealth index.

Health status at the time of interview:

Other than the socio-cultural factors, progression of HIV infection to AIDS or presences of other sexually transmitted infections can also affect fertility. Previous studies have highlighted that the fertility among HIV positive women decreases as the disease progresses. To asses the apparent clinical stage of HIV positive women in this sample we analyzed the Body Mass Index (BMI) and Hemoglobin levels among HIV positive women at the time of interview. Weight loss is one of the earlier sign of HIV disease progression and substantial reduction in BMI would indicate

advancement of HIV disease. However, in this sample, there was no significant difference in the absolute value of BMI (Mann Whitney U = 11269, P (2 tailed) = 0.485) and the weight categories (X^2=0.960, 2 df P=0619) among HIV positive women as compared to HIV negative women at the time of interview.

Table 4- Health status of women at the time of interview

		HIV negative	HIV positive	Total
STI in last 12 months	No	343	68	411
	Yes	2	1	3
BMI	Underweight (<18.5 Kg/ m^2)	104	21	125
	Norman range (18.5-24.99 Kg/ m^2)	191	41	232
	Overweight (>25 Kg/ m^2)	50	7	57
Anemia level	Severe	8	2	10
	Moderate	45	12	57
	Mild	140	29	169
	Not anemic	151	26	177

The cut off points for BMI for categorization of nutritional status are adopted from WHO, 2004

Hemoglobin levels of women were assessed at the time of interview. There is no significant difference among HIV positive and HIV negative women in the level of anemia at the time of interview (X^2 =1.394, 3 df P=0.707). Non parametric analysis of Hb values also suggest that there is no significant difference in the level of Hb of HIV positive and HIV negative women (Mann Whitney test P (2 tailed)= 0.280). Based on these data we assumed that HIV positive women in this sample were apparently in the asymptomatic phase of the disease. This assumption can also be supported by the fact that none of these women were tested for HIV. If they were symptomatic then there was a higher chance that they would access health care services and are tested for HIV. In the absence of any direct measure of the health status such as CD4 testing or viral load estimation, we will have to rely of these indicators and interpret our results accordingly.

Another important condition, which is known to be associated with reduced fertility is the presence of sexually transmitted infection (STI). Some STIs such as syphilis and gonorrhea are associated with reduction in fertility. Ideally the presence (or absence) of these STI should be measured at the time of the pregnancy under consideration. However, it is often not possible in retrospective data collection. In NFHS-3 data there was no information about the STIs in each pregnancy though the question about STIs in past 12 months was asked to the women. As can be seen in the table-4 the history of STIs in past 12 months is negligible among both HIV positive as well as HIV negative women.

Based in these result we can say (or assume) that in this sample, the results on fertility and fecundability would not be affected by the differences in the health status or presences of STIs.

4.2 Effect of HIV on determinants of exposure to risk of pregnancy

HIV and union dissolution

Marriage is considered as the beginning of reproductive career of women. As mentioned earlier, in Indian context most women acquire HIV after marriage, mainly from their husbands. From the epidemiological point of few, since men acquire the infection prior to women, they are likely to die earlier. This is also reflected in these data presented in table-5 There are considerably high numbers of HIV positive women who are widowed. The dissolution of marriage, either due to widowhood, divorce or separation appears higher among HIV infected women as compared HIV non-infected women. This is an important variable determining fertility as marriage dissolution reduces the risk of pregnancy.

Table 5 Current martial status

	HIV negative	HIV positive	Total
Married	333 (96.5%)	50 (72.4%)	383
Widowed	4 (1.1%)	14 (20.2%)	18
Divorced	1 (0.2%)	1 (1.4%)	2
Not living together	7 (2%)	4 (5.8%)	11
Total	345	69	414

For women who were currently married, for most it was their first marriage. Only 6 women out of 333 HIV negative and 2 out of 50 HIV positive women were married twice.

In this sample, there was no significant difference (Mann Whitney test P (2 tailed)= 0.966) in the age at marriage and the mean duration since marriage for HIV positive women compared to HIV negative women. This also indicates that the variation in the duration of exposure to the risk of pregnancy in both these groups would be mainly due to dissolution of marriage and not due to differences in the age at marriage.

The mean age of partners of HIV positive women were 31.82 years whereas that of HIV negative women is 31.57 years. On average husbands were 6 years older than their wives.

Majority of women in the sample (both HIV positive and HIV negative) were monogamous and reported to have only one lifetime sexual partner (husband). Only seven HIV negative and three HIV positive women reported to have total two lifetime sexual partners

Frequency of sexual intercourse

For most women the initiation of sexual activity was only after marriage. Therefore, the mean age at first sexual intercourse was same as the mean age at marriage (18.4 years) and there was no significant difference in both the groups.

Frequency of sexual intercourse is an important determinant of fertility. The frequency of intercourse depends on various personal, interpersonal, physical and social factors and it is often difficult to estimate it retrospectively for a longer period. In NFHS-3 women were asked about their sexual activity in last four weeks. Recent sexual activity was significantly less among HIV positive women (X^2 (1) =5.631 P= 0.18) as compared to HIV negative women. However, this significance was mainly due to more number of HIV positive women who were not in union. When the sexual activity among currently married women was compared then there was no significant difference between both these groups (X^2 (1) =0.413 P= 0.520). Among women who were currently married and are not practicing postpartum abstinence, 82% of HIV positive women and 77% of HIV negative women were sexually active four weeks prior to survey.

Table 6 – Recent sexual activity

All women	HIV negative	HIV positive	Total
Active in last 4 weeks	260 (81.5%)	43 (68.2%)	303 (79.3%)
Not active in last 4 weeks	59 (18.5%)	20 (31.8%)	79 (20.7%)
Total	319	63	382
Currently married women	HIV negative	HIV positive	Total
Active in last 4 weeks	259 (82%)	42 (85.7%)	301 (82.4%)
Not active in last 4 weeks	57 (18%)	7 (14.3%)	64 (17.6%)
Total	316	49	365

For more than 94% of the women in both the groups the husband was living in the same house. Based on these data we assumed that there was no difference in the frequency of sexual intercourse among HIV positive and HIV negative women and when in union the risk of exposure to pregnancy is the same (without use of contraception)

Use of contraception

Use and effectiveness of contraception is one of the most important determinants of the regulated fertility. The table 7 shows ever use and current use of contraception among HIV positive and negative women.

Table 7 – Contraception use

Ever used a method		**HIV -ve**	**HIV +ve**	**Total**
	Never used	**163** (47.2%)	**39** (56.5%)	**202** (48.7%)
	Used modern method	**167** (48.4%)	**28** (40.5%)	**195** (47.1%)
	Knows only traditional method	**15** (4.3%)	**2** (2.9%)	**17** (4.1%)
Current use	**Not using**	**188** (54.4%)	**42** (60.8%)	**230** (55.5%)
	Female sterilization	**106** (30.7%)	**17** (24.6%)	**123** (29.7%)
	Pill	**6** (1.7%)	**1** (1.4%)	**7** (1.6%)
	IUD	**9** (2.6%)	**2** (2.9%)	**11** (2.6%)
	Condom	**16** (4.6%)	**3** (4.3%)	**19** (4.5%)
	Other	**20** (5.7%)	**4** (5.7%)	**24** (5.7%)
	Total	**345**	**69**	**414**

In general, 51.3% of the women ever used contraception. The use of one of the modern methods is quite high among women who ever used any method. However, in India by far the most preferred method is female sterilization and it accounts for 58 percent of modern method use. Among women who opted for female sterilization, almost 70% of them were below the age of 25 years. There is no significant difference in the ever use of contraception (X^2 (1) =1.732 P= 0.188) among HIV positive and HIV negative women.

Postpartum infecundability

Postpartum infecundability is a period after birth when the woman is not susceptible to the risk of pregnancy. Postpartum infecundability is primarily a function of postpartum amenorrhea, which mainly results from the duration and intensity of breastfeeding and postpartum abstinence.

In this sample, the mean duration of postpartum amenorrhea was 6.2 months (SD 5.4 months) among HIV negative women and 7 months (SD 8.0 months) among HIV positive women. There was no significant difference in the duration of amenorrhea in both these groups (Mann Whitney test P (2 tailed) = 0.901). When HIV positive women are not aware about their HIV status, then there is no apparent reason for change in the duration and intensity of breastfeeding among them and therefore it is expected that in a group of apparently asymptomatic HIV positive women the duration of postpartum amenorrhea would be similar to that of HIV negative women.

The information on postpartum abstinence was available for 38 pregnancies among HIV positive women and 283 pregnancies among HIV negative women. The mean duration of abstinence among HIV negative women was 5.6 months (95% CI 4.7, 6.4, SD 7.43) and for HIV positive women it was 9 months (95% CI 4.8, 13.1, SD 12.6).

Though the duration appeared to be longer among HIV positive women it was not statistically significant (Mann Whitney test P (2 tailed) = 0.065).

From the analysis of effect of HIV infection on the determinants of exposure to risk of pregnancy it appears that dissolution of marriage is the only significant way in which HIV can affect the risk of conception.

4.3 Effect of HIV on biological mechanisms

While estimating the effect of HIV on biological mechanisms we would consider the effect only after the pregnancy is recognized. That is the effect on intrauterine mortality.

HIV and Spontaneous intrauterine mortality

Measures of intrauterine mortality usually include both spontaneous abortions and stillbirths but exclude embryonic deaths before the first missed menses (Bongaarts and Potter, 1983). A spontaneous abortion is a fetal death before the twenty-eight week of gestation whereas fetal death after twenty-eight week is considered as stillbirth. The overall risk of intrauterine mortality is estimated to be 20% after the fourth gestational week. The risk is much higher before the forth week and declines steeply from a high of 8.1% in the second month of gestation to a low of 0.2% around 8^{th} month of gestation (Bongaarts & Potters, 1983)

Estimation of risk of spontaneous intrauterine mortality is fraught with several challenges. Among the important problems encountered is the incomplete reporting of early fetal deaths in retrospective studies and inclusion of induced abortion resulting into overestimation of spontaneous abortions and small samples.

The data used in the present study is also not free of these problems. Being retrospective in nature, there is a possibility of under-reporting of early fetal loss. Another important limitation of these data in NFHS-3 is the lack of distinction between induced abortion and spontaneous abortions. In the data set, any pregnancy, which is terminated either due spontaneous abortion, induced abortion or due to stillbirth, is noted as 'T', indicating pregnancy termination. This lack of distinction in data does not allow us to estimate the risk spontaneous abortions (by excluding induced abortions from the data) among HIV positive women. Therefore, we use the indicator of risk of termination of pregnancy among HIV positive women. Calendar data is used for this estimation.

During the calendar period, 58 pregnancies occurred among HIV positive women and 427 pregnancies occurred among HIV negative women. By excluding pregnancies without any outcome, 92 percent of HIV negative pregnancies and 81 percent of HIV positive pregnancies resulted in live births. By analyzing the pregnancies with the outcome (either as live birth or termination), it was observed that termination of pregnancies was significantly higher among HIV positive women (18%) (X^2 = 6.257 (1) P<0.05) as compared to HIV negative women (8.5%). Pregnancies occurring among HIV positive women are 2.62 times more likely to be terminated because of miscarriage or still births (OR 2.62 95% CI 1.20-5.74).

Table 8- Intra-uterine mortality

	HIV Negative	HIV positive	Total
Live birth	347 (92%)	44 (81.5%)	391 (90.7%)
Termination	30 (18%)	10 (8.5%)	40 (9.3%)
Total	377	54	431

Among the 40 pregnancies that were terminated, six were stillbirths and 34 were abortions (spontaneous or induced). Of these six stillbirths, one was in HIV positive woman and five were among HIV negative women. Therefore, the higher risk of termination among HIV positive women is mainly related to spontaneous or induced abortions. Our findings are consistent with some of the previous studies that found higher risk of spontaneous abortions among HIV positive women (Gray et al, 1997; Miotti et al, 1991; Ryder and Temmerman, 1991; Brocklehurst and French, 1998). However, the data limitations should be considered while interpreting the results.

4.4 Recognizable fecundability

In this section the findings of recognizable fecundability are presented, that is the likelihood of HIV positive women to become pregnant if they are exposed to similar risk of pregnancy as compared to HIV negative women. For this analysis, Birth rate, pregnancy rate and waiting time to conception were estimated.

4.4.1 Birth rate

In this sample, eighteen HIV positive women and fifty-six HIV negative women did not give birth to any living child. In total, there were 107 live births among HIV positive women and 613 live births among HIV negative women. On an average total number of children ever born to HIV positive women were 1.5 as compared to 1.7 for HIV negative women

Table 9- Total children ever born

Number of children	HIV negative	HIV positive	Total
0	58 (16.8%)	18 (26%)	76 (18.3%)
1	82 (23.7%)	16 (23.1%)	98 (69.5%)
2	127 (36.8%)	22 (31.8%)	149
3+	77 (22.3%)	13 (18.8)	90
Total	345	69	414

The mean age at first birth was 19.9 years for HIV positive women whereas it was 19.7 years for a HIV negative woman.

However, to understand the difference in the likelihood of becoming pregnant, a micro level approach is needed where the exact duration of exposure is taken into account. Calendar data is used to estimate the rates of pregnancies where the denominator is the person years of exposure to the risk of pregnancy.

The first column of the calendar (VCAL$1- pregnancies, birth and contraception) is used to estimate total number of pregnancies and third column (VCAL$3) of

marriage and union is used to estimate the person years of exposure. In this sample, 33 (47%) HIV positive women 153 (44%) HIV negative women had at least one child before the start of calendar period. Whereas 4 HIV positive women and 50 HIV negative women were pregnant at the time of interview (at the end of calendar)

4.4.2 Pregnancy rate

Estimation of total number of pregnancies- Total number of pregnancies were calculated as the pregnancies that occurred during the calendar period excluding the pregnancies at the start date of the calendar (since the exposure to these pregnancies will not be during the calendar period)

Estimation of exposure to risk of pregnancy in person years- The risk of pregnancy is defined as the duration for which all ever married women were in union and were not using contraception. For women who were sterilized or who were not in union (widow, divorced and separated) the date of sterilization or dissolution of marriage was considered as the ending point of exposure

For women using one of the modern contraception such as pill or IUD, the duration of use of these contraceptives was subtracted from the duration of exposure. And for women who were pregnant at the time of start of calendar, the duration of this pregnancy was subtracted from the duration of exposure

Pregnancy rate was then calculated as

$$\frac{\text{Total number of pregnancies in last five years}}{\text{Number of person years exposed to the risk of pregnancy in last five years}}$$

The results of the pregnancy rates, pregnancy incidence rate ratios and their confidence intervals are presented in the table below

Table 10. Pregnancy rate

Event	HIV Negative	HIV positive
Total births	347	44
Pregnancy terminations	30	10
Pregnant when interviewed	50	4
Pregnancies at the start of calendar	48	5
Total Pregnancies	379	53
Person years of exposure (excluding female sterilization)	1189.58	214.75
Pregnancy rate	0.319 (0.292, 0.345)	0.247 (0.189, 0.304)
Person years without contraception*	1123.5	202.16
Pregnancy rate without contraception	0.337 (0.310, 0.365)	0.262 (0.202,0.323)

* only use of IUD and Pill is considered; number in parenthesis indicate 95% CI

Pregnancy incidence rate ratio is 1.18 (95% CI 0.895, 1.555). Since the use of temporary contraception method (Pill and IUD) is low, there is no difference in the

pregnancy incidence rate ratio among women who used contraception versus women who did not use.

Therefore, based on the results it can be said that there is no statistical difference between the pregnancy rate for HIV positive women as compared to HIV negative women. In other words, HIV positive women will have similar number of pregnancies as HIV negative women when exposed to the same duration of risk.

While calculating the person years of exposure, dates were imputed for three cases whose marriages were dissolved due to widowhood and there was no sufficient information available. Following is the description of these three cases.
Case ID 27 31 27 3 HIV positive woman. She was married in the year 2002 and also had a pregnancy in late 2003 (which was terminated in 5th month). However, there was no data in her marriage and union column. For calculation of number of person years contributed in union, we assumed the time from marriage till her pregnancy which was 24 months

Case ID 29 27 14 7 HIV positive woman. She was married in the year 2002 and had two live births, first in the year 2002 and second in the year 2004. However, all the columns in her calendar have value 0 which indicate that she was not in union. Since we did not know the date when her husband died, we considered the date of her last child birth as the end of union. This interval was 44 months.

Case ID 27274 24 3 HIV negative woman. No data in the marriage column on the union. However, she had one live birth during the calendar therefore that date is considered as last date of exposure. This interval was 26 months

Pregnancy rate among currently married and fecund women

It is estimated that 3% of couples are sterile from the beginning of the reproductive period and will consequently remain childless (Bongaarts and Potters, 1983) Inclusion of such women while estimating the pregnancy rate for five years might also affect the results. Therefore, a separate estimations of pregnancy rate was made for currently married and fecund women. In NFHS-3 data, women are defined as being infecund if they are not menopausal and not postpartum amenorrhic and not pregnant, have had no birth in the five years preceding the survey continuously married and have not used contraception in the five years preceding the survey.

A separate sample of currently married and fecund women was selected as per the selection criteria mentioned in the second chapter. After this selection, 55 HIV positive women and 275 HIV negative women were considered for analysis.

Table 11 -Pregnancy rates among currently married and fecund women

	HIV Negative	HIV positive
Total Pregnancies	164	24
Person years without contraception	548.92	92.58
Pregnancy rate	**0.298** (0.260, 0.337)	**0.259** (0.170, 0.348)

Pregnancy incidence rate ratio for fecund women is 1.15 (95% CI 0.750; 1.767).

Therefore, it can be said that there is no statistical difference between the pregnancy rate for HIV positive women as compared to HIV negative women. With both these samples, the results are consistent.

Some discrepancies in the data

There are some inconsistencies in the data. Women who were classified as infecund were not consistent with the definition provided under NFHS-3. In NFHS-3 data, women are defined as being infecund if they are not menopausal and not postpartum amenorrhic and not pregnant, have had no birth in the five years preceding the survey continuously married and have not used contraception in the five years preceding the survey

As per V623 women with following ID were categorized as infecund. However, their data in the birth history and in the calendar is not consistent with the definition.

ID 28 37 10 2- this woman was married at the time of interview and had one live birth in 2000 and one pregnancy termination in the year 2006. As per the data from her birth history she also had one live birth before calendar period in the year 1997. Therefore, in our analysis we did not consider this woman as infecund

ID 9307 40 2 is a currently married woman who has one live birth in the year 1998 and also had one pregnancy during calendar period (which was terminated immediately in next month of her pregnancy)- We have not considered this woman as infecund

I D 27152 15 2 is a currently married women who has one live birth in the year 2000. This birth was during the calendar year

ID 28153 12 3 is a currently married women who has one live birth in the year 2000. This birth was during the calendar year

ID 27245 8 3 is a currently married women who has one live birth in the year 2000. This birth was during the calendar year

ID 33120 22 2 is a HIV positive women currently married women who had four live births (1996, 1998, 2000 and 2004) the last birth was in the calendar period

4.4.3 Waiting time to conception and fecundability

Fecundability is inversely related to the duration of conception wait. Noncontracepting fecundable women who engage in regular sexual intercourse take an average of several months to conceive (Bongaarts & Potters, 1983). The duration of waiting time to conception is determined by the rate of conception. Typical value of fecundability is estimated to be 0.2 that means that in a group of fecundable women 20% can be expected to conceive in the first month of exposure to the risk of conception (Bongaarts & Potters, 1983).

The most reliable estimates about conception wait can be made by analyzing the interval from marriage to first birth or first conception. Here the term conception refers to the conception recognized by the woman after she misses her menses. Fertilized ova that fail to implant or abort spontaneously before the women realize that she is pregnant are not counted as conception. However, for the present study where we do not know when the women acquired HIV infection the estimate of interval between marriage to first birth may not be reliable to understand the effect of HIV infection on fecundability. Alternative strategy is required. One can fairly assume that if the pregnancy is closer to the date of interview or is as late after marriage as possible then the chances that the woman is infected with HIV at the time of this pregnancy are high. Therefore, in this study we also estimate the interval between last two pregnancies that occurred in 5-6 years prior to the date of interview (during the calendar period)

Interval between marriage and first birth

To understand the effect of HIV on fecundability of women we first analyzed the interval between marriage and first birth. In the absence of intrauterine mortality and induced abortion, this interval would depend on the use and effectiveness of contraception. However, as mentioned earlier it is uncommon among Indian women to use contraception after marriage to delay first birth.

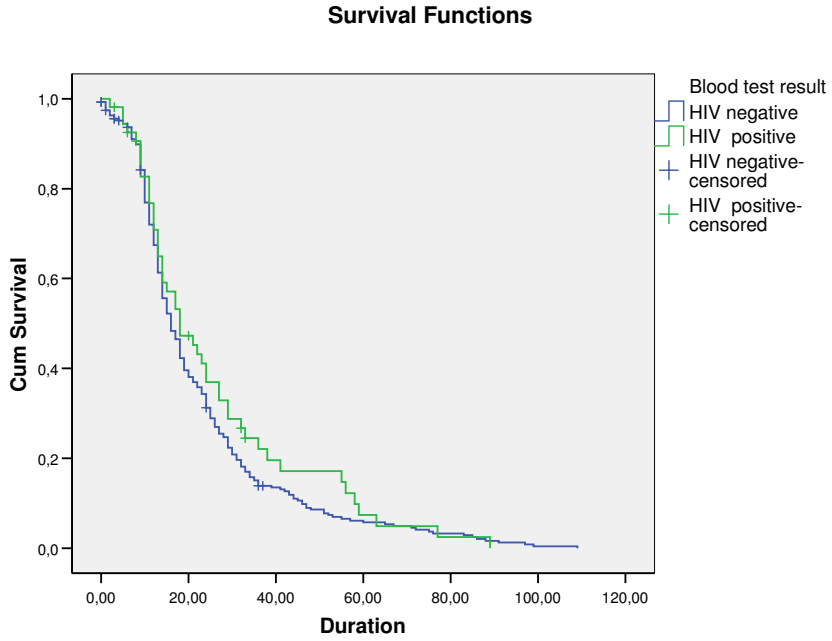
This analysis is done on the sample of currently married and fecund women. We used the data from birth history record. The event was defined when the woman had live birth after marriage. The duration was censored when the woman did not have live birth after marriage. In this case the duration is calculated from the date of marriage to the date of interview. The analysis was done using Kaplan Meier technique. Following table shows the distribution of events and censoring in the data.

Table 12 – Interval between marriage a birth-distribution of events

Blood test result	Total N	Number of Events	Censored
HIV negative	271	260 (95.9%)	11 (4.1%)
HIV positive	54	48 (88.9%)	6 (11.1%)
Overall	325	308 (94.8%)	17 (5.2%)

The median waiting time to firth birth for HIV negative women was 16 months (95% CI 14.1, 17.8) and 18 months for HIV positive women (95% CI 11.1, 24.8).

Fig 4- Interval between marriage and first birth- survival function



The difference in the survival functions in both the groups was not statistically significant (log rank X^2 = 1.072 (1) P=0.300). In the absence of contraception, intrauterine mortality (spontaneous or induced) is known to increase the length of the birth interval. However, in these data the information on the occurrence of intrauterine mortality before first live birth was not available. As we saw earlier that intrauterine mortality was higher among HIV positive women, the higher median duration can be due to possibly more case of intrauterine mortality if not due to chance.

As mentioned earlier, it is also possible that some of the women will not have been infected at the time of their first birth, which can also affect the results. Therefore, a separate analysis was done on another sample of women where the date of marriage is less than the date of calendar (5-6 years preceding the survey). In this way, it is more likely that these women were HIV infected at the time of their first birth. Not many women in this sample used contraception to space the first birth interval. Hence, this would not affect the first birth interval. After selecting the cases on this basis, there were 26 HIV positive women and 129 HIV negative women in the sample. In this sample too the duration was not significantly different in both these groups (log rank X2= 2.112 (1) P= 0.146). The median duration for HIV negative women was 18 months (95 % CI 14. 3 , 21. 6) where as for HIV positive women it was 29 months (95 % CI 14.4 , 43.5). However, due to smaller sample size the confidence intervals for the median were high.

Analysis of both these samples suggest that there is no significant difference in the interval between marriage to first birth among HIV positive and HIV negative women. In other words, HIV positive women are equally likely to become pregnant as compared to HIV negative women when exposed to similar risk of pregnancy.

However, the analysis of inter pregnancy interval between last two pregnancies would give us more reliable estimate of waiting time to conception when all the known variable affecting this interval are controlled.

Pregnancy interval between last two pregnancies-

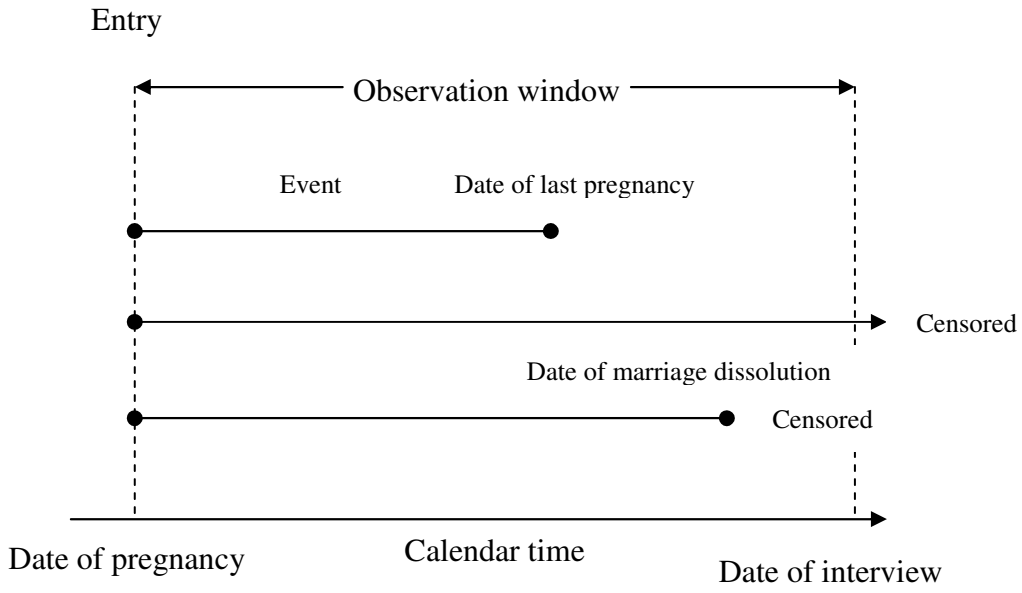
We conducted analysis of last two pregnancies that took place in last 5-6 years preceding the survey. In this analysis, we used data from the calendar where we had information on the outcome of pregnancies and the duration of post partum infecundity. We used Cox regression to analyze these data.

Selection of women

For this analysis we selected women who had at least one pregnancy during the calendar period irrespective of the outcome of this pregnancy. With this selection process, we had 45 HIV positive women and 180 HIV negative women for analysis.

Event was defined as the occurrence of pregnancy after the index pregnancy. If the woman did not become pregnant after the index pregnancy then the observation was censored. Here index pregnancy is defined as the last but one pregnancy in the calendar period.

Fig. 5 Observation window for analysis of interval between last to pregnancies



The cases when event has occurred, duration was defined as the interval between index pregnancy and last pregnancy and in cases of censoring, it was considered as the interval between the index pregnancy and the date of interview for currently married women. When the marriage was dissolved due to widowhood, separation or divorce then the date of marriage dissolution was considered as the end of observation for censored cases.

The interval between two pregnancies depends on three factors-post partum infecundable period, mainly determined by the post partum amenorrhea, use and effectiveness of contraception and the duration of conception wait. The duration of post partum amenorrhea is mainly determined by the duration and intensity of breastfeeding. I included these variables as predictor variable in our model along with HIV status. I will first describe the data on these variables.

The following table-13 shows the outcome of the index pregnancy among HIV positive and HIV negative women. The outcome of index pregnancy is particularly important as it influences the duration of amenorrhea and thus affect the length of the inter-pregnancy interval.

Table 13- Outcome of index pregnancy

Pregnancy outcome	HIV negative	HIV positive	Total
Abortion/stillbirth	23 (12.7%)	8 (17.7%)	31 (13.7%)
Live birth	157 (87.3%)	37 (82.3%)	194 (86.3%)
Total	180	45	225

Duration of amenorrhea- The duration of amenorrhea after the index pregnancy was calculated from the birth history. The information on the duration was available only for 147 live births. The minimum duration was 1 month and maximum duration was 30 months. The mean duration was 7.2 months (SD 6.2, 95% CI 6.2, 8.3). The cases where the duration was reported as inconsistent were eliminated from analysis.

Duration of breastfeeding- The data on duration of breastfeeding was taken from the birth history records. The information was available for 153 pregnancies that resulted in live births. The mean duration of breastfeeding was 17.9 months (SD 12.0 95% CI 16.0, 19.8). The duration of breastfeeding was recoded as 0 for women who never breast fed their babies.

Use of contraception- The use of contraception was calculated as a binary variable (Yes/No) from the data in the contraceptive use calendar. In this sample 36% of the women used some contraception after the index pregnancy. The following table-14 shows the distribution of the contraception used according to the type of contraceptive method.

Table 14- Contraception use according to different methods

Use of contraception	Frequency	Percent
No use	142	63,1%
Pill	6	2,7%
IUD	13	5,8%
Condom	11	4,9%
Female sterilization	40	17,8%
Periodic abstinence/rhythm	4	1,8%
withdrawal	9	4,0%
Total	225	100%

Most women preferred female sterilization as method of contraception, which is consistent with the overall trend. Barring the methods like periodic abstinence and withdrawal the efficacy of most other contraceptive methods is known to be quite high.

After including these variables and HIV status in the Cox model, we obtained following results. All the variables were entered in one-step.

Table 15- Cox model for pregnancy interval between last two pregnancies

Parameter	B	SE	Wald	Df	Sig.	Exp(B)	95,0% CI for Exp(B)	
							Lower	Upper
Duration of Breastfeeding	-,028	,012	5,505	1	,019	,972	,950	,995
Duration of Amenorrhea	-,021	,025	,725	1	,394	,979	,933	1,028
HIV Negative	-,251	,342	,537	1	,463	,778	,398	1,521
No contraception	2,423	,474	26,132	1	,000	11,275	4,454	28,544

*Values of EXP(B) if less than one reduces the hazards of becoming pregnant thus increases the length of inter-pregnancy interval. However values more than one increases the hazards of becoming pregnant and thus reduces the inter-pregnancy interval

As expected duration of breastfeeding and use of contraception were significant predictor of the inter-pregnancy interval. Women who breastfeed for longer duration are less likely to become pregnant and women who do not use contraception are much more likely to become pregnant as compared to women who use contraception when the effect of other variables is controlled. However, HIV status was not significantly related to the duration of inter-pregnancy interval. As can be seen in the graph below, there is no significant difference in the survival function among HIV positive and HIV negative women. The hazards in both the groups were proportional.

Fig 6 Survival function

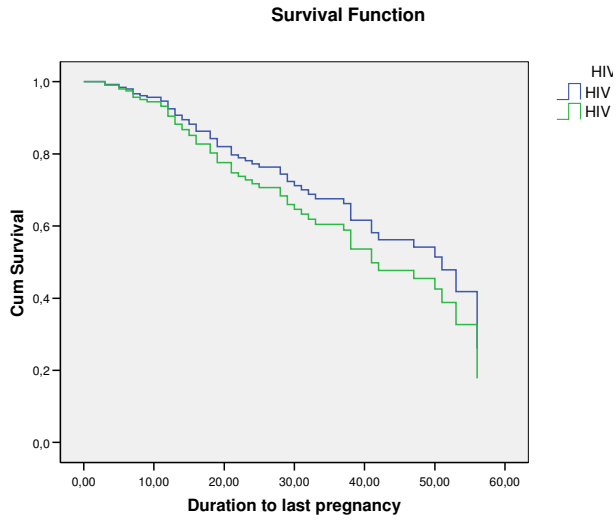
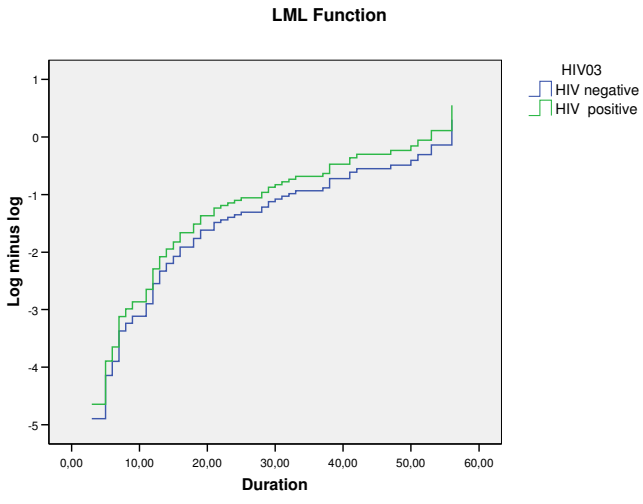


Fig 7 Hazard function



Similar analysis was done by Desgr'ees Du Lau et al (1999) among clinic based sample of HIV infected women in Abidjan, Cote d'Ivoire. In their analysis the hazard ratio was 0.83 (95% CI 0.69, 0.99). They concluded that HIV positive women experience fewer pregnancies and the interval between last two pregnancies were longer among HIV positive women as compared to HIV negative women when the effect of other factors were controlled. It was hypothesized that difficulty in conceiving or increased number of miscarriages going unnoticed might be the reason for the longer duration of conception wait. However, in our study we did not find any association to support that. It is possible that the effect of other confounding variables such as advanced stage of the disease or infection with other sexually transmitted diseases will be significant factors in explaining the differences in the results in different studies.

Based on the analysis of the data related to fecundability it can be concluded that HIV does not affect the likelihood of becoming pregnant when there is no difference in the exposure to the risk of pregnancy.

Chapter Five

CONCLUSION

Certain limitations in the data have to be kept in mind while interpreting the results of this study. The data collected are retrospective in nature and therefore can affect the results due to errors such as recall bias or under reporting of events. The other important limitation is the lack of information about the time of HIV infection among women. Small sample size imposed some restrictions on the analysis. With this consideration, based on the results of the study we can conclude that

1. HIV infection does not affect the fecundability among women who do not know their HIV status. There is no significant difference in the pregnancy rate among HIV positive women as compared to HIV negative women. And there was no difference in the time of conception wait for both the groups. In other words, HIV positive women would have similar number of pregnancies as compared to HIV negative women when exposed for similar duration of risk. Linking this finding with the Becker's (1993) model of fecundability, it can also be expected that there might not be a significant difference in the regularity of menstrual cycle or the process of fertilization and implantation among HIV positive and HIV negative women.

2. Fertility among HIV positive women might be reduced mainly due to early dissolution of marriages because of widowhood, separation or divorce. Here fertility refers to actual reproduction

3. Pregnancies occurring among HIV positive women are more likely to result into termination (stillbirth, spontaneous abortions or induced abortions) as compared to HIV negative women

Understanding fertility and fecundability among HIV positive women is also important for public health programs, mainly HIV disease surveillance when it is done among antenatal clinic attendees. As mentioned earlier, in India majority of the HIV surveillance sites are in the antenatal clinics. Based on these findings we suggest that reduction in fertility or fecundability among HIV positive women is not a significant factor that would affect their attendance in the antenatal clinics. However, this study is inadequate to evaluate if women coming to ANC clinics would be representative of the women in the community and if HIV prevalence among ANC can be considered as HIV prevalence among women in the general population.

Owing to the difference in the findings of various studies done to understand the effect of HIV on pregnancy outcomes and fertility it can be concluded that the findings of the studies done in Africa and other regions can not be directly extrapolated for India. There is a need for well-designed and in-depth prospective study to explain the relationship of HIV and fertility among Indian women.

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ANNEXURE ONE- Calendar used in NFHS-3

INSTRUCTIONS:

ONLY ONE CODE SHOULD APPEAR IN ANY BOX.
FOR COLUMNS 1 AND 3, ALL MONTHS SHOULD BE FILLED IN.

INFORMATION TO BE CODED FOR EACH COLUMN

COL. 1: BIRTHS, PREGNANCIES, CONTRACEPTIVE USE
- B BIRTHS
- P PREGNANCIES
- T TERMINATIONS

- 0 NO METHOD
- 1 FEMALE STERILIZATION
- 2 MALE STERILIZATION
- 3 PILL
- 4 IUD/LOOP
- 5 INJECTABLES
- 6 IMPLANTS
- 7 CONDOM/NIRODH
- 8 FEMALE CONDOM
- 9 DIAPHRAGM
- J FOAM OR JELLY
- L RHYTHM METHOD
- M WITHDRAWAL
- X OTHER _____ (SPECIFY)

COL. 2: ULTRASOUND CONDUCTED DURING PREGNANCY
- Y YES
- N NO

COL. 3: MARRIAGE
- X MARRIED
- N MARRIED, GAUNA NOT PERFORMED
- 0 NOT MARRIED

COL. 4: DISCONTINUATION OF CONTRACEPTIVE USE
- 0 INFREQUENT SEX/HUSBAND AWAY
- 1 METHOD FAILED/BECAME PREGNANT WHILE USING
- 2 WANTED TO BECOME PREGNANT
- 3 HUSBAND/PARTNER DISAPPROVED
- 4 WANTED MORE EFFECTIVE METHOD
- 5 HEALTH CONCERNS/PROBLEMS
- 6 SIDE EFFECTS
- 7 LACK OF ACCESS/TOO FAR
- 8 COSTS TOO MUCH
- 9 INCONVENIENT TO USE
- F FATALISTIC
- A DIFFICULT TO GET PREGNANT/MENOPAUSAL
- D MARITAL DISSOLUTION/SEPARATION
- L LACK OF SEXUAL SATISFACTION
- M CREATED MENSTRUAL PROBLEM
- G GAINED WEIGHT
- N DID NOT LIKE METHOD
- P LACK OF PRIVACY FOR USE
- X OTHER _____ (SPECIFY)
- Z DON'T KNOW

				1	2	3	4			
	12	DEC	01					01	DEC	
	11	NOV	02					02	NOV	
	10	OCT	03					03	OCT	
	09	SEP	04					04	SEP	
2	08	AUG	05					05	AUG	2
0	07	JUL	06					06	JUL	0
0	06	JUN	07					07	JUN	0
6	05	MAY	08					08	MAY	6
	04	APR	09					09	APR	
	03	MAR	10					10	MAR	
	02	FEB	11					11	FEB	
	01	JAN	12					12	JAN	
	12	DEC	13					13	DEC	
	11	NOV	14					14	NOV	
	10	OCT	15					15	OCT	
	09	SEP	16					16	SEP	
2	08	AUG	17					17	AUG	2
0	07	JUL	18					18	JUL	0
0	06	JUN	19					19	JUN	0
5	05	MAY	20					20	MAY	5
	04	APR	21					21	APR	
	03	MAR	22					22	MAR	
	02	FEB	23					23	FEB	
	01	JAN	24					24	JAN	
	12	DEC	25					25	DEC	
	11	NOV	26					26	NOV	
	10	OCT	27					27	OCT	
	09	SEP	28					28	SEP	
2	08	AUG	29					29	AUG	2
0	07	JUL	30					30	JUL	0
0	06	JUN	31					31	JUN	0
4	05	MAY	32					32	MAY	4
	04	APR	33					33	APR	
	03	MAR	34					34	MAR	
	02	FEB	35					35	FEB	
	01	JAN	36					36	JAN	
	12	DEC	37					37	DEC	
	11	NOV	38					38	NOV	
	10	OCT	39					39	OCT	
	09	SEP	40					40	SEP	
2	08	AUG	41					41	AUG	2
0	07	JUL	42					42	JUL	0
0	06	JUN	43					43	JUN	0
3	05	MAY	44					44	MAY	3
	04	APR	45					45	APR	
	03	MAR	46					46	MAR	
	02	FEB	47					47	FEB	
	01	JAN	48					48	JAN	
	12	DEC	49					49	DEC	
	11	NOV	50					50	NOV	
	10	OCT	51					51	OCT	
	09	SEP	52					52	SEP	
2	08	AUG	53					53	AUG	2
0	07	JUL	54					54	JUL	0
0	06	JUN	55					55	JUN	0
2	05	MAY	56					56	MAY	2
	04	APR	57					57	APR	
	03	MAR	58					58	MAR	
	02	FEB	59					59	FEB	
	01	JAN	60					60	JAN	
	12	DEC	61					61	DEC	
	11	NOV	62					62	NOV	
	10	OCT	63					63	OCT	
	09	SEP	64					64	SEP	
2	08	AUG	65					65	AUG	2
0	07	JUL	66					66	JUL	0
0	06	JUN	67					67	JUN	0
1	05	MAY	68					68	MAY	1
	04	APR	69					69	APR	
	03	MAR	70					70	MAR	
	02	FEB	71					71	FEB	
	01	JAN	72					72	JAN	

Source-http://www.nfhsindia.org/pdf/Woman_QRE.pdf,
Accessed-10 Aug 2008

ANNEXURE TWO-

SPSS Syntax used for analysis

Merging of HIV data file with Individual woman's file

```
GET
  FILE='D:\Data Shirish\IAIR50FL.SAV'.
DATASET NAME DataSet1 WINDOW=FRONT.

SORT CASES BY
  CASEID (A) .

GET
  FILE='D:\Data Shirish\IAar50fl.SAV'.
DATASET NAME DataSet2 WINDOW=FRONT.
```

Variable HIVID was renamed as CASE ID

```
SORT CASES BY
  CASEID (A) .


MATCH FILES /FILE=*
 /TABLE='D:\Data Shirish\IAar50fl.SAV'
 /BY CASEID.
          EXECUTE.
```

Selecting cases as per the selection criteria

```
* Deleting cases- women never married

FILTER OFF.
USE ALL.
SELECT IF(V513 > 0).
EXECUTE .

*Selecting cases of women who were married for less than 12 years
FILTER OFF.
USE ALL.
SELECT IF(V512 < 13).
EXECUTE .

*Selecting cases of women who were never tested for HIV before

FILTER OFF.
USE ALL.
SELECT IF(V781=0).
EXECUTE .
```

In the all India file there were women who were not tested for HIV (24183) for many states so the value under HIV testing was missing therefore these cases were eliminated

```
FILTER OFF.
USE ALL.
SELECT IF(HIV03 = 0 OR HIV03 =1).
EXECUTE .
```

Matching HIV Positive cases with Negative cases

Recode for matching the cases **** base file is allIndia_filtered_unmatched.sav

```
RECODE
  V024  (27=27)  (28=28)  (29=29)  (33=33)  (14=14)  (ELSE=35) INTO StateGr .
EXECUTE .

RECODE
  V130  (1=1)  (2=2)  (ELSE=96) INTO ReligionGR  .
EXECUTE .

RECODE
  V445
  (Lowest thru 1850=1)  (1851 thru 2499=2)  (3000 thru Highest=3)  INTO
  BMI_Group .
EXECUTE .

* Identify Duplicate Cases.
SORT CASES BY V013(A) V025(A) StateGr(A) V106(A) V190(A) HIV03(D) .
MATCH FILES /FILE = * /BY V013 V025 StateGr V106 V190
 /FIRST = PrimaryFirst /LAST = PrimaryLast.
DO IF (PrimaryFirst).
COMPUTE MatchSequence = 1 - PrimaryLast.
ELSE.
COMPUTE MatchSequence = MatchSequence + 1.
END IF.
LEAVE MatchSequence.
FORMAT MatchSequence (f7).
COMPUTE InDupGrp = MatchSequence > 0.
SORT CASES InDupGrp(D).
MATCH FILES /FILE = * /DROP = PrimaryFirst PrimaryLast InDupGrp.
VARIABLE LABELS MatchSequence 'Sequential count of matching cases' .
VARIABLE LEVEL MatchSequence (SCALE).
EXECUTE.
```

After the matching was done then the number of cases were randomly selected. Following is the example of the SPSS syntax for random selection of cases

```
USE ALL.
do if $casenum = 1.
  compute #s_$_1=5.
  compute #s_$_2=25.
  end if.
  do if #s_$_2 > 0.
  compute filter_$ = uniform(1)* #s_$_2 < #s_$_1.
  compute #s_$_1 = #s_$_1 - filter_$.
  compute #s_$_2 = #s_$_2 - 1.
  else.
  compute filter_$ = 0.
  end if.
VARIABLE LABEL filter_$ '5 from the first 25 cases (SAMPLE)'.
FORMAT filter_$ (f1.0).
FILTER BY filter_$.
EXECUTE .
```

After this selection the file with HIV cases and their controls were ready for analysis

Analysis of Effect of HIV on the determinants of exposure to the risk of pregnancy

```
  FILE='F:\Data Shirish\NFHS_3\Final data set without religion'+
 ' matching\AllIndia_complete.sav'.
DATASET NAME DataSet1 WINDOW=FRONT.

CROSSTABS
  /TABLES=V013 V024 V025 V106 V190 BY HIV03
  /FORMAT= AVALUE TABLES
  /CELLS= COUNT
  /COUNT ROUND CELL .
DESCRIPTIVES
  VARIABLES=V012
  /STATISTICS=MEAN STDDEV MIN MAX .
MEANS
  TABLES=V012  BY HIV03
  /CELLS MEAN COUNT STDDEV  .

COMPUTE BodyMassIndex = V445/100 .
EXECUTE .

RECODE
  BodyMassIndex
  (0 thru 18.5=1)  (18.5 thru 24.99=2)  (25 thru Highest=3)  INTO  BMI_Gr .
EXECUTE .

CROSSTABS
  /TABLES=BMI_Gr  BY HIV03
  /FORMAT= AVALUE TABLES
  /STATISTIC=CHISQ
  /CELLS= COUNT
  /COUNT ROUND CELL .

EXAMINE
  VARIABLES=BodyMassIndex
  /PLOT BOXPLOT STEMLEAF NPPLOT
  /COMPARE GROUP
  /STATISTICS DESCRIPTIVES EXTREME
  /CINTERVAL 95
  /MISSING LISTWISE
  /NOTOTAL.

NPAR TESTS
  /M-W= BodyMassIndex   BY HIV03(0 1)
  /K-S= BodyMassIndex   BY HIV03(0 1)
  /MISSING ANALYSIS
  /METHOD=EXACT TIMER(5).
CROSSTABS
  /TABLES=V457  BY HIV03
  /FORMAT= AVALUE TABLES
  /STATISTIC=CHISQ
  /CELLS= COUNT
  /COUNT ROUND CELL .
NPAR TESTS
  /M-W= V453   BY HIV03(0 1)
  /K-S= V453   BY HIV03(0 1)
  /MISSING ANALYSIS
  /METHOD=EXACT TIMER(5).
CROSSTABS
  /TABLES=HIV03  BY V501
```

```
  /FORMAT= AVALUE TABLES
  /STATISTIC=CHISQ
  /CELLS= COUNT
  /COUNT ROUND CELL .

RECODE
  V201
  (0=0)  (1=1)  (2=2)  (3 thru 8=3)  INTO  Total_children .
EXECUTE .

RECODE
  V208
  (0=0)  (ELSE=1)  INTO  birthlast5yrs_yes_no .
EXECUTE .
SORT CASES BY
  HIV03 (D) .
```

Marriage to first birth interval

```
RECODE
  B3$01 B3$02 B3$03 B3$04 B3$05 B3$06 B3$07 B3$08 B3$09 B3$10 B3$11
  (SYSMIS=0)  .
EXECUTE .

COMPUTE one = B3$11 .
EXECUTE .

IF (B3$07=0) two = B3$06 .
EXECUTE .

IF (B3$06=0) three = B3$05 .
EXECUTE .

IF (B3$05=0) four = B3$04 .
EXECUTE .

IF (B3$04=0) five = B3$03 .
EXECUTE .

IF (B3$03=0) six = B3$02 .
EXECUTE .

IF (B3$02=0) seven = B3$01 .
EXECUTE .

RECODE
  one two three four five six seven  (SYSMIS=0)  .
EXECUTE .
COMPUTE CMCfirstbirth = one + two + three + four + five + six + seven .
EXECUTE .

IF (CMCfirstbirth ~= 0) dur_mar_firstbrith = CMCfirstbirth-V509 .
EXECUTE .

IF (CMCfirstbirth = 0) dur_mar_interview = V008 - V509 .
EXECUTE .

RECODE
  dur_mar_firstbrith dur_mar_interview  (SYSMIS=0)  .
EXECUTE .
```

```
COMPUTE duration_firstbirth = dur_mar_firstbrith + dur_mar_interview .
EXECUTE .
RECODE
  CMCfirstbirth
  (0=0)  (ELSE=1)  INTO  Event .
EXECUTE .
KM
  duration_firstbirth  BY HIV03  /STATUS=Event(1)
  /PRINT MEAN
  /PLOT SURVIVAL
  /TEST LOGRANK
  /COMPARE OVERALL POOLED .
```

Marriage to first birth interval- Second Sample (date of marriage is less than start of calendar)
**** To avoid repetition syntax for initial selection process is not given**

```
EXECUTE .
IF (B3$04=0) three = B3$03 .
EXECUTE .
EXECUTE .
IF (B3$03=0) two = B3$02 .
EXECUTE .
IF (B3$02=0) one = B3$01 .
EXECUTE .
COMPUTE CMCfirstbirth = four + three + two + one .
EXECUTE .
IF (CMCfirstbirth ~= 0) Dur_mar_firstbirth = CMCfirstbirth - V509 .
EXECUTE .
RECODE
  Dur_mar_firstbirth  (SYSMIS=0)  .
EXECUTE .
IF (Dur_mar_firstbirth = 0) Dur_mar_interview = V008 - V509 .
EXECUTE .
RECODE
  Dur_mar_interview  (SYSMIS=0)  .
EXECUTE .
COMPUTE Duration = Dur_mar_firstbirth + Dur_mar_interview .
EXECUTE .
RECODE
  CMCfirstbirth
  (0=0)  (ELSE=1)  INTO  Event .
EXECUTE .
RECODE
  V511
  (0 thru 18=1)  (19 thru Highest=2)  INTO  age_marriage_Gr .
EXECUTE .
KM
  currected_duration  BY HIV03  /STATUS=Event(1)
  /PRINT MEAN
  /PLOT SURVIVAL
  /TEST LOGRANK
  /COMPARE OVERALL POOLED .
```

Analysis of Interval between last two pregnancies

```
DATASET COPY HIV_Negative.
DATASET ACTIVATE HIV_Negative.
FILTER OFF.
USE ALL.
SELECT IF(HIV03=1).
DATASET ACTIVATE DataSet4.
EXECUTE .
FILTER OFF.
USE ALL.
SELECT IF(Preg_calender ~= 0).
EXECUTE .
FILTER OFF.
USE ALL.
SELECT IF(V781=0).
EXECUTE .
FILTER OFF.
USE ALL.
SELECT IF(V781=0).
EXECUTE .
FILTER OFF.
USE ALL.
SELECT IF(Preg_calend ~= 0).
EXECUTE .
FILTER OFF.
USE ALL.
SELECT IF(VAR00002 ~= 0).
EXECUTE .
RECODE
  V024
  (9=9)  (14=14)  (27=27)  (28=28)  (29=29)  (33=33)  (ELSE=0)  INTO
  state_selection .
EXECUTE .
FILTER OFF.
USE ALL.
SELECT IF(state_selection ~= 0).
EXECUTE .
ADD FILES /FILE=*
 /FILE='HIV_Negative'.
EXECUTE.
* Identify Duplicate Cases.
SORT CASES BY V013(A) V024(A) V025(A) V106(A) V190(A) HIV03(D) .
MATCH FILES /FILE = * /BY V013 V024 V025 V106 V190
 /FIRST = PrimaryFirst /LAST = PrimaryLast.
DO IF (PrimaryFirst).
COMPUTE MatchSequence = 1 - PrimaryLast.
ELSE.
COMPUTE MatchSequence = MatchSequence + 1.
END IF.
LEAVE MatchSequence.
FORMAT MatchSequence (f7).
COMPUTE InDupGrp = MatchSequence > 0.
SORT CASES InDupGrp(D).
MATCH FILES /FILE = * /DROP = PrimaryFirst InDupGrp.
VARIABLE LABELS PrimaryLast 'Indicator of each last matching case as Primary'
  MatchSequence 'Sequential count of matching cases' .
VALUE LABELS PrimaryLast 0 'Duplicate Case' 1 'Primary Case'.
VARIABLE LEVEL PrimaryLast (ORDINAL)
    /MatchSequence (SCALE).
```

```
EXECUTE.
COMPUTE one = MatchSequence=1 .
EXECUTE .
COMPUTE two = MatchSequence=3 .
EXECUTE .
COMPUTE three = MatchSequence=5 .
EXECUTE .
COMPUTE four = MatchSequence=7 .
EXECUTE .
COMPUTE five = MatchSequence=9 .
EXECUTE .
COMPUTE cases = one + two + three + four + five .
EXECUTE .
FILTER OFF.
USE ALL.
SELECT IF(cases = 1).
EXECUTE .
IF (Births = 1) Start_B1 = B3$01 .
EXECUTE .
IF (Births ~= 1) Start_B2 = B3$02 .
EXECUTE .
COMPUTE Satrt_Dur = Start_B1 + Start_B2 .
EXECUTE .
RECODE
  Satrt_Dur
  (0=0)  (ELSE=1)  INTO  Outcome .
EXECUTE .
IF (moths_aftercal ~= 0) CMC_start_termination = V017 + moths_aftercal .
EXECUTE .

COMPUTE Start_CMC = CMC_start_termination + Satrt_Dur_B .
EXECUTE .


IF (sustract_interview ~= 0) end_one = V008 - sustract_interview .
EXECUTE .
IF (Event=2) end_two = B3$01-9 .
EXECUTE .
IF (Event=0) end_three = V008 .
EXECUTE .

COMPUTE End_CMC = end_one + end_two + end_three .
EXECUTE .

IF (Months_marrg ~= 0) End_Nonmarried = V017 + Months_marrg .
EXECUTE .
COMPUTE Final_end_CMC = End_CMC + End_Nonmarried .
EXECUTE .
RECODE
  Event
  (0=0)  (ELSE=1)  INTO  eventCox .
EXECUTE .
COMPUTE DurationCox = Final_end_CMC - Start_CMC .
EXECUTE .
COMPUTE Age_start = (Start_CMC - V011) / 12 .
EXECUTE .
IF (Births=1 and Termination=0) amon_one = M7$1 .
EXECUTE .
IF (Births  > 1 and moths_aftercal = 0) amon_two = M7$2 .
EXECUTE .
```

```
COMPUTE Dur_amon = amon_one + amon_two .
EXECUTE .
IF (Births=1 and Termination=0) BF_one = M5$1 .
EXECUTE .
IF (Births  > 1 and moths_aftercal = 0) BF_two = M5$2 .
EXECUTE .
COMPUTE Dur_BF = BF_one + BF_two .
EXECUTE .
RECODE
  Age_start
  (15 thru 19=1)  (20 thru 24=2)  (25 thru Highest=3)  INTO  AgeStart_gr .
EXECUTE .

COXREG
  DurationCox  /STATUS=eventCox(1)
  /METHOD=ENTER Dur_BF Dur_amon HIV03 contraception
  /CRITERIA=PIN(.05) POUT(.10) ITERATE(20) .
COXREG
  DurationCox  /STATUS=eventCox(1)
  /PATTERN BY HIV03
  /CONTRAST (HIV03)=Indicator  /CONTRAST (contraception)=Indicator
  /METHOD=ENTER Dur_BF Dur_amon HIV03 contraception
  /PLOT SURVIVAL
  /PRINT=CI(95)
  /CRITERIA=PIN(.05) POUT(.10) ITERATE(20) .
```