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CONTRACEPTIVE HORMONES AND HIV TRANSMISSION IN FEMALE FACTORY WORKERS IN ADDIS ABABA, ETHIOPIA

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Contraceptive hormones and HIV transmission in female factory workers in Addis Ababa

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Tesfalidet Debesay,(MD)

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LIST OF ABBREVIATIONS

A.A ..... Addis Ababa
AIDS ..... Acquired immune deficiency syndrome
CSWs ..... Commercial sex workers
DMPA ..... Depo Medroxy Progesterone Acetate
ELISA ..... Enzyme linked immuno sorbent assay
ENARP ..... Ethio-Netherlands AIDS Research programme
Eth.Birr..... Ethiopian Birr
FFWs ..... Female factory workers
GUD ..... Genito urinary disease
HIV ..... Human immune deficiency syndrome
IUD ..... Intra Uterine Device
MOH ..... Ministry of Health
NKA ..... Natural killer activity
mac ..... macaques
OCP ..... oral contraceptive
PBMC ..... Peripheral blood mononuclear cells
PCR ..... Polymerase chain reaction
PHA ..... Phyto hemagglutinin
RPR ..... Rapid plasma reagin test
SIV ..... Simian Immunedefciency Virus
SSA ..... SubSaharan Africa
STD ..... Sexually transmitted diseases
TCID..... Tissue culture infective dose
TPHA ..... Treponema pallidum hemagglutination assay
UNAIDS..... United nations AIDS
WHO ..... World health organization

OPERATIONAL DEFINITIONS

Hormonal contraceptives:- preparation either in the combination of oestrogen and progesterone or progestrone alone in oral or injectable forms.

Contraceptive use:- For the purpose of this study contraceptive use indicate current use of oral contraceptive pill and injectable hormones during the study.

HIV-1 negative:- negative by two ELISA tests, or one ELISA positive only, and Western Blot negative.

HIV-1 positive:- positive by two ELISA tests, or one ELISA positive only, and Western Blot positive.

ABSTRACT

A cross-sectional study was conducted from June to October 1999 in female factory workers (FFWs)in one of the factories in Addis Ababa, Ethiopia. The objective was to study the effect of contraceptive hormones on HIV-1 acquisition.

Purposive sampling was used for the study. All FFWs willing to participate and age 18-45 years were included and interviewed. Blood samples were taken from each respondent for HIV and syphilis test. Characteristics of the FFWs were compared between those using and not using contraceptive hormones. Chi-square were applied where ever appropriate. Identification of risk factors for HIV infection among FFWs was performed using univariate and multivariate analysis (logistic regression model).

A total of 350 FFWs were enrolled in the study. Their mean age was 37 years. Most of the study participants had primary level education(79% were less than grade 6) and married(77%).

Women who were taking hormonal contraceptive on average had a lower risk for HIV as majority are married ,in oral contraceptive users (88.6%) and injectable hormone users (86.2%).

In multivariate analysis, variable independently associated with protective effect against HIV infection were: Age group 35-39 years (OR=0.10, 95%CI= 0.02-0.70) and education level grade 7-12 (OR=0.23,95%CI= 0.10-0.95). Variables independently associated with an increase risk of HIV infection were : being separated (OR= 4.25, 95%CI= 1.56-11.6) and being widowed (OR=8.28, 95%CI=2.90-23.4) with reference catagory married; and having casual sex partner (OR=8.9,95%CI=1.7-47.5) compared with those having no casual partner.

There was no association between HIV sero-positivity and oral contraceptive and injectable contraceptive hormones use.

The over all HIV prevalence was remarkably high(12%)among FFWs in A.A.

Based on the results of this study strengthening interventions aimed at adolecents and youth and prospective study specially from women with long duration of hormonal contraceptive use are recommended.

Introduction

Acquired Immunodeficiency Syndrome (AIDS) has now been recognized for almost two decades. During this time it has killed millions of people and caused tremendous suffering.

Efforts to control the human immunodeficiency virus type 1(HIV-1) epidemic world wide have had limited success, and the HIV epidemic continues to grow, particularly in the developing world.
According to UNAIDS report of 1998 the HIV/AIDS epidemic has been spreading at a rate of about 16000 infections per day, the most rapid increase being observed in southern and central Africa and in south Asia. As many as 50% of all new infections were in women aged 14-24 years . UNAIDS has also estimated that at the end of 1998, 33.4 million people in the world were living with HIV/AIDS of which 22.5 million or 67% were in sub Saharan Africa, By the year 2000, according to the WHO forecasts, around 40 million new infections will have occurred and of these 90% will be in developing countries (1).

There is a wide variation in HIV/AIDS prevalence in different countries and regions through out the world. The first AIDS cases in Africa were reported from Rwanda, Zaire, and Uganda in 1983 (2) since then, there has been an alarming increase of HIV-1 prevalence

in Sub Saharan Africa. Africa itself is not uniformly affected by the epidemic. This may be probably due to differences in local migratory and behavioral patterns of the population which are the major determinants of the spread of the infection.

Most affected countries of the Subsaharan Africa are in the eastern and southern Africa. However, the trend may reverse in some countries as it has already started in Uganda, where the prevalence rate has decreased from 1 million(12%) in 1994 to 0.8 million(9%) in 1997(3,4).

Although HIV prevalence was very low in Ethiopia during the early 1980s, it has been increasing rapidly in the past few years and now the country is experiencing rapid HIV epidemic.

HIV, Probably started to spread in Ethiopia in the early 1980s. The first two seropositive cases reported in 1984 (5), and the first AIDS cases were reported in 1986 (6).

It was estimated that by 1993, adult HIV prevalence had increased to 3.2% (7). A community based sero prevalence study conducted in Addis Ababa, in 1994, revealed a prevalence of 6.0% for men and 6.9% for women (8). By 1997 it was estimated that adult prevalence had increased to 7.4%, and it is estimated to be higher in urban areas, about 21% and lower in rural areas, which is about 4.5% (9).

This implies that there were about 2.4 million HIV-1 infected adults in 1997.

In order to reduce the risk of unwanted pregnancy many women utilize contraception. However whilst protecting against pregnancy the benefit or risk of HIV transmission or acquisition may be different.

The identification of biological risk factors for HIV-1 transmission may point towards novel avenues for HIV control.
World wide , more than 65 million women use hormonal contraceptives, including oral contraceptive pills and long-acting progestin-based methods (e.g.,DMPA and Norplant [Wyeth-Ayrest], philadelphia)sub dermal implant)(10,11). Given their wide spread use by women in their sexually active years, any effect of hormonal contraceptives on risk of HIV-1 acquisition could make a major contribution to the HIV-1 epidemic. In addition, understanding the relationship between hormonal contraceptives and HIV-1 risk may yield insight in to biologic mechanisms that affect susceptibility, which could lead to new methods of prevention.

Concern about injectable contraceptives as a possible co-factor for HIV acquisition was recently heightened by a report in macaques that progesterone implants increased the risk of vaginal

transmission of the simian immunodeficiency virus (SIV)by 7.7 fold as compared with macaques treated with placebo implants(12).
In addition, the use of hormonal contraception may be associated with a reduced use of barrier contraception. A recent report has identified that almost half of previous condom users did not plan to use condoms regularly once protected from pregnancy by a hormonal implant and thus the risk of exposure to infection would change. This highlights the importance of dual protection to include protection from infection as well as pregnancy which is known as the "Double Dutch" method(13).

Epidemiological studies provide conflicting results on the effects of synthetic hormonally based contraceptives on HIV vaginal transmission. Some recent studies have found a wide range of sharp to no increase in the risk of transmission associated with the use of injectable and oral contraceptives(14).

In Ethiopia, studies linking hormonal contraceptive with HIV infection has not been conducted. This study was, therefore, conducted with the general objective of determining the association between contraceptive hormones and HIV acquisition, transmission in female factory workers in Addis Ababa, Ethiopia.

Literature review

A literature review on the association between contraceptive hormones and HIV transmission was made. The aim of which being to review the few studies which have been done previously on the risk factors, and the different behaviors associated with HIV-1 infection in women using hormonal contraceptive globally and in Ethiopia .

Human immunodeficiency virus, the cause of acquired immuno-deficiency syndrome (AIDS), is most commonly transmitted to women by sexual contact. However, little is known about the influence of hormones on HIV genital transmission in the female.

Hormonal contraception is the preparation either in the combination of oestrogen and progestogen or progestogen alone. The route of administration may be in an oral, injectable or more recently in an implant forms.

Hormonal cofactors may be important because progesterone, a hormone that rises in concentration during the luteal phase of the menstrual cycle and during pregnancy, induces changes in the vaginal epithelium, vaginal PH and cervical mucus of human beings. Moreover, synthetic progesterone-based (progestin) contraceptives

are in wide spread use, but the effect on HIV transmission has been difficult to document (12).

In general, very few studies examined the relationship between HIV infection and hormonal contraception. Moreover, very little data are available on injectable hormones and no published data on the implant forms.

Theoretical arguments on the association between contraceptive hormones and HIV

It has been postulated that hormonal contraception may increase susceptibility to HIV infection by increasing cervical ectopy. This has been shown to have influence on increasing the risk of chlamydia infection; thinning the genital mucosa under the influence of progestogens; inducing irregular menstrual bleeding in progestogen only pill users and increasing retrograde menstruation; or making women systematically more susceptible to infection by a direct immune suppressive effect(13).

Hormonal contraception may protect by thickening of the cervical mucus under the influence of progestogens, although this would not protect against vaginal transmission, neither by the use of

combined estrogen/progestogen combinations nor by long term injectable progestogen use(13).

Epidemiological studies regarding oral contraceptive use and HIV transmission are often confounded by the use of more than one contraceptive during the interval studied. Other differences between study groups may also confound interpretation. For example, it has been suggested that women who choose hormonal contraceptives may be less likely to use barrier methods to prevent STD infection, making studies more difficult to interpret(12).

Animal models, therefore, are uniquely valuable because they allow for controlled experimental studies when comparable data are unavailable in humans(12).

To address this question experimentally, the SIV/rhesus macaque animal model is used to test if circulating progesterone, a natural hormone, affected vaginal transmission of Simian Immunodeficiency Virus.

The SIV mac model is useful for testing potential biological co-factors because atraumatic vaginal inoculation of SIV mac results in systemic infection and AIDS in this species(15).

Various studies had previously shown that the vaginal epithelium plays a role in transmission of SIV mac. For example, the intact vaginal mucosa represents a barrier to SIV mac because about 100 to 1000 times more viral load(infective dose) is required to establish infection in most animals by this route, compared with that required to establish infection by intravenous inoculation (15-17).

A study of hysterectomized macaques with subsequent vaginal exposure to SIV mac proved that the vaginal mucosa alone is sufficient for transmission (18). A similar observation of HIV infection was made in a women with a congenital absence of the cervix (19). Therefore, the vaginal epithelium of both human beings and macaques is susceptible to infection by primate lenti viruses (15,19).

Recent in situ polymerase chain reaction (PCR) studies identified dendritic cells in the vaginal lamina propria immediately subjacent to the epithelium as the earliest target cells for SIV infection(20). Moreover, SIV-infected cells were found in the draining lymph nodes during the first week of infection. Thus, the vaginal epithelium is an initial barrier that must be traversed before the occurrence of systemic infection.

Because endogenous progesterone is known to decrease the thickness of the vaginal epithelium in women (21) and rhesus macaques (22),

the hypothesis that exogenously administered progesterone can enhance SIV vaginal transmission was tested using treatment group(n=18) and control group(n=12).

All macaques were, inoculated vaginally without trauma with one ml of virus stock containing about 640 $TCID_{50}$ (mean tissue culture infectious dose) at different phase of the menstrual cycle. SIV was subsequently isolated in only 1 of 10 placebo-treated animals as compared with 14 of 18 progesterone treated macaques at multiple time points from peripheral blood mononuclear cells (PBMCs)(12).

In the progesterone group, three macaques rapidly progressed to AIDS and were killed 38, 82 and 177 days post inoculation, respectively(12).

Based on the high virus loads and the more rapid progression to AIDS, it was concluded that progesterone treatment resulted in greater in vivo SIV replication during the early period of infection(12).

To address possible mechanisms of enhanced transmission and pathogenesis, a second experiment was performed and it appears that ample targets were present in both groups and that progesterone did

not induce observable change in the number of susceptible target cells. Collectively, these findings point to the thinning of the vaginal epithelium as being an important component for the enhanced vaginal transmission of SIV. However, other progesterone induced mechanisms can be considered. These include other changes in the cervical or vaginal epithelium that were undetected, changes in the immune system, possibly even direct enhancement of viral replication(12).

Several other potential biological mechanism may also explain the interaction between oral contraceptives and HIV.1 infection. Oral contraceptives may increase the susceptibility of the female genital tract to HIV-1 through an estrogenic effect on the genital mucosa. This can be provided by increasing the area of cervical ectopy and exposing the cervix to a greater likelihood of mucosal disruption during sexual intercourse(22,23).

Cervical ectopy is a physiologic condition defined as an extension of the endocervical columnar epithelium beyond the external os on to the vaginal surface of the cervix. It is known to be more frequent in younger women present in a large percentage of adolescent women at the onset of menarche and gradually declining through young adult hood. It is also more commonly seen in pregnant women(23,24).

The mechanism of altered susceptibility to HIV-1 with cervical ectopy are unknown. However, several possibilities have been postulated. Recent data (23,24) suggest that the Langerhans cell (dendritic cell) may be the initial target cell infected in the female genital mucosa. These cells are present in the submucosa of both columnar and squamous cervical epithelium. The columnar epithelium, characteristic of cervical ectopy may be more susceptible to trauma during sexual intercourse, leading to mucosal breaks that could facilitate viral penetration to these potential HIV-1 target cells. Another possibility is that the columnar epithelium it self could be susceptible to HIV-1 infection.

Data demonstrating the association of oral contraceptives with cervical ectopy are somewhat limited. The data have usually been provided by cross sectional studies performed at STD clinics. No prospective study has been able to clearly establish an association between oral contraceptive use and cervical ectopy. There also exists a difficulty in standardizing the classification of cervical ectopy. Several studies records the presence or absence of cervical ectopy, whereas others use a percentage term to grade the degree of ectopy(25).

There is also problem of misclassification bias when the presence of cervical ectopy is determined using visual inspection of the

cervix instead of colposcopy. The direction of such bias would be to misclassify small degree of ectopy as negative. This bias would likely be towards the null hypothesis as the effect ectopy on susceptibility is most plausibly related to the size of the area of ectopy(25).

Oral contraceptives may also act through an indirect effect by increasing the risk of chlamydia trachomatis cervicitis or possibly genital ulcers as suggested in the study by Plourde et al. (25). Chlamydia trachomatis cervicitis is known to produce an intense mononuclear cell infiltration of the cervix that could potentially lead to the presence of activated HIV-1 susceptible immuno-competent cells in the genital tract.

The postulated effect of oral contraceptives and chlamydial cervicitis on the induction of ectopy could help to explain the observed association that has been noted between these factors and HIV-1 infection(25).

Conversely, the reduced irregularity and volume of menstruation associated with combined oestrogen - progestogen contraception may protect against HIV transmission whilst the thinning of genital mucosa and menstrual irregularity associated with progestogens may increase the risk(13).

Finally, oral contraceptives may mediate steroid like immunologic change that render women more susceptible to HIV-infection.

There is also concern about the immuno modulatory effect of hormonal contraception. There are variations in the humoral responses between predominantly oestrogen, but also progesterone, where related depression of cell mediated immunity have been reported. In oral contraceptive users a significant depression in lymphocyte transformation response to phyto hemagglutinin (PHA) has been observed. Further reports suggest that the oestrogen - progestogen suppression is inversely related to the progestogenic potency. Natural killer activity(NKA) has been shown to fluctuate with the menstrual cycle and inversely related to oestradiol levels in women with endometriosis. However, NKA fluctuation is lost in oral contraceptive users, there appears to be no relation between cytotoxic activity and oestradiol concentration or significant fall in activity after 6 months of OCP use (13).

Empirical evidences on the association between contraceptive hormones and HIV

Epidemiological studies provide conflicting results on the effects of synthetic hormone based contraceptives on HIV vaginal transmission. Some recent studies have described an extreme difference in the risk of transmission associated with the use of hormonal contraceptives (14).

Simonsen et al, suggested a possible contribution to viral acquisition when they noted higher HIV prevalence among Nairobi prostitutes using oral contraception. Use of barrier methods among study participants was uncommon and hence the association between hormonal contraceptive use and HIV-Seropositivity persisted in the cross sectional study after adjustment for other covariates (26). In a cohort study of prostitutes, Plummer et al also documented that increased risk of sero-conversion was associated with the use of oral contraceptives after controlling for genito urinary disease and other factors (14).

Studies in another population in Nairobi, as well as cross-sectional studies from Uganda and Brazil have also found an independent association of HIV infection with oral contraceptive

use [25,27-29].

However, this association is not reported by all investigators. A cross-sectional case-control study at three family planning clinics in Dar-es-salaam found no association between OCP use and HIV positivity (30).

Two prospective studies did not find a significant association (31,32). In a cross sectional study of family planning clinic attendees in Nairobi no association between oral contraceptive use and HIV positivity was found (33). European data have also identified no association between oral contraceptive use and an increased risk of HIV sero conversion (34,35).

A study in Thailand reported a nonsignificant inverse association(36). A case control study of CSWs in Thailand revealed no significant association between oral pill, injectable, other contraceptives and HIV(43). Oral contraceptive use was associated with a reduction in the risk of HIV infection in a study from Italy (37). In the cross-sectional analysis of 524 heterosexual partners of seropositive clinic patients, Oral contraceptive use was also associated with a reduction in the risk of HIV infection (38).

There are only three published prospective studies addressing the

association between use of injectable contraceptives and HIV(31,39,44).

Increased risk of vaginal transmission of SIV in rhesus macaques which were given subcutaneous progesterone implants has been also been reported(12).

The crude relationship between HIV sexual transmission and contraception may be confounded by various extraneous factors(40).

Theoretical arguments applied to Analyses of the association between contraceptive use and HIV Infection

Whether steroid hormones affect transmission of HIV has been an important question that has been difficult to answer in human studies. Both estrogen and progesterone have effects on the female genital tract that may affect HIV transmission. Progesterone thins the vaginal epithelium, increases the vaginal pH, reduces the amount of cervical mucus and increases its viscosity, whereas estrogen produces the opposite effect (41).

To date studies have not distinguished between the consequences of virus exposure in the follicular and luteal phases, and designing such studies in women would be highly problematic.

The rhesus macaque model has shown that progesterone treatment of rhesus macaques results in atrophy of the vaginal epithelium and increased incidence of systemic SIV infection after intra vaginal SIV exposure. Compared with the genital tract of progesterone-treated animals, the normal female follicular-phase genital tract represents a barrier to SIV infection. Although not all potential mechanisms for the progesterone-mediated enhancement of transmission were addressed, the correlation between enhanced SIV transmission and the decreased thickness of the vaginal epithelium was striking. A thin vaginal epithelium may allow more virion to move through the epithelium, or susceptible target cells such as Langerhans dendritic cells may be more exposed in a thinner epithelium, potentiating their infection and spread of virus into the lamina propria to T cells (18).

Although the SIV/rhesus macaque model is relevant to HIV transmission and pathogenesis (15), it is not known how precisely the minimal infectious dose mimics semen-mediated transmission of HIV to women.

The finding that exogenous progesterone increased the efficiency of

vaginal SIV transmission suggests that women may be at greater risk of HIV infection from vaginal intercourse when exposed to high levels of endogenous or exogenous progesterone. However, the magnitude of this potential risk in women can not be predicted by this model(15).

Several other biological mechanisms may also explain the interaction between oral contraceptives and HIV-infection, but the overall impact remain speculative. Moreover, oral contraceptive use may be a marker for some other unidentified risk factors. Oral contraceptive use is associated with cervical ectopy, which may increase the risk of HIV acquisition and cervical chlamydial infection(14).

The immunological aspects of the association are especially unclear, steroid hormones can inhibit cell-mediated responses, but oestrogen can also boost antibody response.

In conclusion, there is only limited evidence linking especially injectable hormonal contraceptive use to HIV infection and so alterations in prescribing practices are not recommended. However, as the data suggesting a protective role of hormonal contraception are also limited an additional barrier contraceptive should also be recommended.

The scientific and public health importance of the unconfirmed association between hormonal contraceptive use and HIV infection argues to have a controlled study with comparable groups and designed specifically to examine this question with accurate measurement of oral contraceptive exposure and potential confounders to measure the association.

If some contraceptive practices interact with mechanism of human immunodeficiency virus (HIV) sexual transmission and has effect on HIV transmission, family planning campaign in this country can be slow down due to hesitation by the unconfirmed association between HIV and contraceptive use. Therefore the information generated from this study will help in giving clue in ascertaining the association between hormonal contraceptive use and HIV infection, and also points future areas of research.

Study Objectives

General objective:

To study the effect of contraceptive hormones and related risk factors on HIV-1 infection acquisition among female factory workers in one of the factories, in Addis Ababa.

Specific objectives:

1. To assess whether the different hormonal contraceptive choice affects the acquisition of HIV-1 infection.

2. To assess and compare the prevalence of HIV infection in those women using versus women not using contraceptive hormones among female factory workers in Addis Ababa.

3. To describe the socio demographic characteristics including the sexual behavior of those women using contraceptive hormones versus not using.

4. To compare the characteristics of the female factory workers by their HIV serological status.

Subjects and Methods

Study design and population

This was a cross-sectional study corresponding to the intake of ENARP cohort study, among Females aged 18-46 years who were willing to participate, in one of the factories in A.A. ENARP major focus of the scientific programme is the study of HIV infection progression in African setting. It includes all clinical and biological events from the time of infection with HIV to the development AIDS and death. Its description depends on the longitudinal follow-up of a large number of study participants over years, most HIV negative at the start. Newly HIV infected individuals are identified by regular testing of blood for HIV-1 antibodies during the follow-up. After sero conversion, HIV-infected study participants are closely monitored by the study team. Regular clinical and biological follow-up enables description of HIV infection progression, and provision of medical interventions.

The study has been conducted in Addis Ababa, the capital city of Ethiopia, from June 1999 to October 1999. Data from the ongoing cohort study by ENARP on the natural history of HIV-1 infection was selectively computed and analyzed.

Seropositive women and otherwise comparable seronegative women presenting to the factory clinic were compared with respect to their contraceptive use history and other variables selected prior to study enrollment.

Seropositive women enrolled in this fashion, therefore, represent prevalent cases.

The sampling procedure employed in this study was a purposive sampling since it was not convenient to use probability sampling techniques due to small number of eligible women.

The eligibility criteria for the on-going cohort study was being female employee of the factory and age between 18-46 years.

Even though purposive sampling was used the sample size adequacy was determined based on the formula for cross sectional study as Sample size Determination :

$$n = \frac{Z_{\alpha/2}^2 \times P(1-P)}{d^2}$$

Where:

P = the prevalence of HIV infection in the factory(12%).

d = Marginal error between the sample & the population(5%)

$Z_{\alpha/2}$ = Critical value at 95 % certainty (1.96)

Because purposive sampling instead of random sampling was used the minimum sample size found by the formula was doubled and was 320.

Variables

In order to meet the objectives of the study the following variables were used:

A. Exposure variables

There are three different groups of variables:

1. Socio-demographic: Age, residence, education, religion, ethnicity, income, marital status ,number of children.

2. Behavioral factors and sexual history: Age at first sex , number of partners, frequency of sex , Sex during menstruation.

3. History of hormonal contraceptive use

B. Out come variables

HIV-serological status (sero negativity and sero positivity).

Data collection

A structured questionnaire was prepared for the study. Questionnaires were pre-tested. Administered by nurses with experience and/or training in interviewing techniques. Data were entered by data entry clerks. Queries were sent back to the field site when inconsistencies or missing variables.

Consenting women at the clinic were interviewed to obtain information about socio-demographic characteristics, contraceptive use, sexual behavior and other health events. The interviewers were females to keep the gender match. After interview, pretest counseling was performed before blood sample was collected and transported to Ethio-Netherlands AIDS Research programme laboratory at Ethiopian Health and Research Institute (EHNRI) and analyzed there.

Ethical Consideration

Ethical clearance had already been obtained for the ongoing cohort study on the natural history of HIV-1 infection by the Ethiopian-Netherlands AIDS Research project (ENARP) from the National ethical clearance committee.

This research was also approved by the National Ethical Clearance Committee and the medical faculty of Addis Ababa.

1.Informed consent

All participants have signed an informed consent form prepared in Amharic. Prior to entry in the study explanations have been given to the potential subjects as to the aim, methods, anticipated benefits and potential hazards of the study and any discomfort it might entail. Subjects have been informed that they are at liberty to abstain from participation in the study and that they are free to withdrew consent to participate at any time.

2.Pre- and post-test counseling for HIV testing and confidentiality issues:

Pre-test counseling was offered to all study participants at the factory clinic. Post-test counseling was be left optional, for those who are willing to know their HIV-test out come.
Interviews were done in private rooms and were gender matched. Confidentiality was strict through out the study and analysis.

3.Benefit/compensation for participating in the study :

As a compensation for the effort in participating in the study, medical care was being provided free of charge to the participants and their families according to the national standards of care. Payment of fifteen Eth.birr(US dollar 2.1) was made to the study participants as compensation for the transportation and for their time lost.

4. Preventive and curative services such as, information and education about HIV/AIDS transmission and its prevention was provided to the study participants during pre-and post-test counseling. Medical care provided free of charge to the study participants according to the national standards of care. Early diagnosis and treatment of STDs, treatment and prophylaxis of opportunistic infection and tuberculosis are available in ENARP factory clinic. Condoms are available free of charge for participants who wish to use them.

Laboratory Methods

From each study participant 2 tubes of 10 ml each blood was collected using vacutainer tubes at the ENARP factory clinic and transported to ENARP laboratory daily. All specimen were processed in the laboratory of ENARP at Ethiopian Health and Nutrition Research Institute (EHNRI). At the ENARP laboratory plasma and

cells were isolated and frozen. HIV and syphilis serology were performed on plasma. The HIV test was performed using HIVSPOT test kit(Genelabs, Singapore) and ELISA(Organon Murex HIV 1+2 UK, virnostika HIV Uni-form II,France). Initially, all antibody reactive samples by ELISA were analysed by a second ELISA(Wellcozyme) test for confirmation. If the results were indeterminate they were confirmed by Western Blot(HIV-BLOT2.2, Genelabs, Singapore) test. Sero conversion was defined as the development of positive ELISA and western blot.

For syphilis serology test, Trepanoma Pallidum hemagglutination assay(TPHA, Fujirebio, Japan)and Rapid Plasma Reagin(RPR,Bio Merieux) were used on the same sample. All TPHA reactive samples were confirmed by RPR. Samples reactive only by TPHA were considered as treated and cured. Syphilis Samples reactive by both TPHA and RPR were interpreted as recent and active syphilis. Syphilis results were returned within short time to the ENARP factory clinic matched to the participants name using their registry, and treatment for patients diagnosed with syphilis was given based on the protocol of the MOH. A data set was created which contained the code number of each participant, the interview and laboratory results. No name or individual address was included in the data set so that it was not possible to link any laboratory result with individuals.

All individuals participating in the study were informed that the blood would be used in part for HIV testing and related research. HIV results were returned to the ENARP factory clinic for counseling service. Post test counseling was left optional for those interested to know their HIV status.

Data entry and analysis

A register of all case report forms (raw data) received regularly were updated. Data were then entered in to computer where it was verified and validated using standard software programme.

Statistical analysis were performed using STATA-software programme. Univariate analysis were initially performed on selected variables to determine which factors to include in multivariate Analysis. Odds ratio(OR) with 95% Confidence interval(95%CI) was used to estimate the effect of a risk factor on HIV acquisition and Comparison on proportions was done using chi-square on different variables (contraceptive use and HIV) when appropriate. Multi variate analysis was done using logistic regression.

Results

1. Socio-demographic characteristics of the study participants

From all 561 Akaki factory female workers a total of 350 women age 18-46 years, were enrolled in the study.

Their socio-demographic characteristic is summarized in table 1. The ages of the study subjects ranged between 20 and 46 years (mean, 36.9 ± 6.6 years) and 42.3% of them were in the age group 24-34 years. Majority of the study participants had little education (79.4% were grade 6 or less) and are married (77.3%), and (90.1%) had at least one child. The majority of the study participants identified themselves with Amhara (47.7%) and Oromo ethnic group (38.2%).

Majority were residents of Akaki area (95%) and those with duration of stay in the residency area for 17 years or less were 23%.

Majority of study participants had household sizes ranging between 4 and 6 (53%).

Monthly income of the majority of the study participants 218(62.6%)

is greater or equal to 200 Eth.Birr.

2. History of contraceptive use

Out of the total 350 study participants 163(46.6%) women were using any method of contraception during the time of the study. From these 163 women 87 (53.4%) were oral contraceptive users, 64(39.3%) were injectable hormones users 6(3.7%) were norplant users, and only 5(3.1%) used other methods.

Almost all women (96.4%) were getting their contraceptives from the factory clinic.

Comparison of socio-demographic variables between all method contraceptive hormone users & non users is summarized in Table 3.

The mean age of all hormonal contraceptive users was 35.7 ± 6.5 years ranging between 24 and 46 years and majority 126(77.3%) had education level grade 6 or less and are married 143(87.7%).

Women who were taking hormonal contraceptive on average have a lower risk for HIV as the majority are married as compared to the non users.

Among all contraceptive users, those having monthly income of 200 and more Eth.birr were 96(59%).

The socio-demographic characteristic of oral contraceptive pill users is summarized in Tables 4.

The mean age of oral contraceptive users was 34.5 ± 6.5 range between 24 and 46 years, and most 66(75%) had education less than grade 6 and are married 78(88.6%).

Monthly income of 41(46.6%) of the oral contraceptive users was less than 200 Eth.birr.

The socio-demographic characteristic of injectable contraceptive hormone users is summarized in Tables 5.

The mean age of injectable contraceptive users was 37.1 ± 6.6 years ranging between 24 and 46 years and majority 54(83.1%) had education level of grade 6 or less, and are married 56(86.2%).

Among injectable contraceptive users, those having monthly income of 200 and more Eth.birr were 39(60%).

The socio-demographic characteristic of all contraceptive hormone users is summarized in Tables 6.

3.Sexual behaviors

The mean age at first sex was 16.35 ± 13.4 years(range:10-30 years)(table 1).

Females having casual sex partners were 6 (1.8%) and those having no casual sex partners are 342 (98.2)(table 1).

From the 350 study participants 319(91.9) were having no sex during menstruation.

Syphilis serology with TPHA and RPR were positive in 81(23.3%) and 23(6.6%) respectively in the study participants.

4. HIV Prevalence and related factors

From the 350 females studied, HIV-1 test result was obtained or available from 348 (two test results were not available at the time of Data analysis).

The association between HIV infection and socio demographic characteristics among the FFWs is available in table 1.

The HIV prevalence among these female factory workers of Addis

Ababa was 42/348 (12%);[95% CI = 8.6-15.5%].

The HIV sero prevalence was 17.6%, 17.2% and 18.1% among women in the age group 20-24, 25-29 and 30-34 years respectively. Where as in the age group 35-39 and 40-46 years it is lower that is 6 and 8.3% respectively(table 1). HIV prevalence tended to decrease with age ($p<0.02$; test for trend).

The prevalence of HIV among the widowed was 40% as compared to the married ones 8.5%. Being widowed was associated with HIV infection as compared to the married ones (OR=9.77, 95%CI= 2.87-33.24) in multivariate analysis(table 1).

HIV-1 sero-prevalence was also high among-females who were single and separated with prevalence of 20% and 18.2% respectively, as compared to those who were married and living with their spouse(8.5%). Being separated was associated with HIV infection as compared to the married ones (OR=4.52, 95%CI= 1.46-14.04) in multivariate analysis.

Although monthly low income ($\leq$ 199 Eth. Birr) as opposed to higher income ($\geq$ 200 Eth. Birr) was associated with HIV infection in univariate analysis (OR =3.55, 95% CI= 1.81-6.96), the association disappeared after inclusion of the variables contained in

multivariate model (OR=1.88, 95%CI= 0.7-5.07).

House hold size 7-9 in the family was also associated with HIV infection only in univariate analysis (OR= 0.34, 95%CI= 0.12-0.95) as compared to those (table 1). The prevalence of HIV-1 tended to decrease as the house hold size increases (test for trend p<0.03).

Number of children in the family was not associated HIV infection(table 1).

The association between selected sexual behavior and HIV serological status among the FFWs is available in table 2.

Only six women out of 348 admitted having casual sex partner was significantly associated with HIV-1 infection(OR= 8.5, 95% CI= 1.5-47.6)in the multivariate analysis(table 1). In addition Prevalence rate of HIV-1 infection also tended to increase as the number of casual partner increased (test for trend, p<0.02).

Sex during menstruation was not associated with HIV infection in univariate as well as in multivariate analysis.

Positive syphilis serology (TPHA) was significantly associated with HIV infection(OR=2.6, 95%CI= 1.3-5.0)in univariate analysis.

Similarly Positive syphilis serology (RPR) was significantly associated with HIV infection(OR=3.6, 95%CI= 1.4-9.4)in univariate analysis.

History of abnormal vaginal discharge was not associated with HIV infection (OR= 1.63, 95% CI= 0.75-3.52). Similarly genital ulcer was not associated with HIV infection(OR= 2.14,95% CI=0.67-6.83),even though history of abnormal vaginal discharge and genital ulcer was very rare in the study participants (not shown in tables).

Prevalence rate of HIV-1 among all contraceptive users was 12.4% and among non users was 11.8% where the difference was not significant.

HIV-1 prevalence in oral pill uses is 14.9%, and in injectable hormone users is 10.9% where the difference was also not significant.

Hormonal contraceptive use was higher in the age group 20-24 years compared to others and higher in married women compared to non-married in multivariate analysis(table 3).

There was no significant difference in sexual behaviors between

contraceptive hormone users and non users.

Education level grade 1-6 was significantly associated with HIV infection among oral pill users(OR=0.14, 95%CI=0.03-0.7) in univariate analysis(see table 4).

Monthly low income was also significantly associated with HIV infection among oral pill users (OR=8.1 95%CI=1.7-39.0)(table 4). No association between socio-demographic characteristics and HIV infection was observed among the injectable contraceptive hormone users both in univariate and multivariable analysis (table 5). History of ulcer was associated with HIV infection among injectable hormone users (P=0.018)(not shown in tables).

Being widowed was associated with HIV infection among all hormonal contraceptives users as compared to married ones (OR=13.7, 95CI = 1.10-172.5) in multivariate analysis(table 6).

Monthly low income was associated with HIV infection among all hormonal contraceptive users as compared to those having higher income (OR=3.87 95%CI=1.40-10.70) in univariate analysis but disappeared in multivariate analysis(table 6).

Positive syphilis serology (TPHA) was associated with HIV

infection among all hormonal contraceptives users as compared to those having negative serology (OR=3.5, 95% CI=1.2-9.8) in univariate analysis but disappeared in multivariate analysis (see table 7)

No association between hormonal contraceptives use and HIV infection was observed among the study participants(table 8).

The variables independently associated with HIV infection in multivariate analysis are available in table 9.

In the multivariate analysis those independently associated with an increased risk of HIV were: being separated, widowed and having casual sex partner, and those independently associated with protective effect were being in the age group 35-39 years and having educational level grade 7-12.

TABLE 1. Association of socio-demographic characteristics and and HIV serological status among females in one of the factories, A.A, Ethiopia, October 1999.

Variable	N=348 n (%)	HIV-1 + n (%)	OR(95%CI) Univariate	OR(95%CI) Multivariate
Age(years)				
20-24	17(4.9)	3(17.6)	1.0	1.0
25-29	64(18.4)	11(17.2)	0.96(0.24,3.95)	0.55(0.10,3.07)
30-34	83(23.9)	15(18.1)	1.02(0.26,4.04)	0.31(0.05,1.92)
35-39	100(28.7)	6(6.0)	0.3(0.1,1.3)	0.05(0.01,0.42)*
40-46	84(24.1)	7(8.3)	0.42(0.1,1.8)	0.06(0.01,0.57)*
Education				
Read and write	115(33.1)	18(15.6)	1.0	1.0
grade 1-6	161(46.3)	19(11.8)	0.72(0.36,1.44)	0.50(0.20,1.24)
grade 7-12	54(15.5)	4(7.4)	0.43(0.14,1.34)	0.18(0.04,0.81)*
12 complete	8(2.3)	0(0.0)	-------	------
> grade 12	10(2.8)	1(10.0)	0.59(0.1,5.02)	0.40(0.02,6.58)
Marital status				
Married	269(77.3)	22(8.2)	1.0	1.0
Separated	40(11.5)	8(20.0)	2.84(1.17,6.91)*	4.52(1.46,14.04)*
Single	11(3.7)	2(18.2)	2.53(0.51,12.4)	2.56(0.28,23.1)
Widowed	25(7.2)	10(40.0)	7.57(3.04,18.84)*	9.77(2.87,33.24)*
Religion				
Other	26(7.5)	1(3.8)	1.0	1.0
Orthodox	322(92.5)	41(2.7)	3.65(0.48,27.68)	2.92(0.29,29.82)
Monthly income (Eth.Birr)				
200-999	218(62.6)	15(6.9)	1.0	1.0
≤ 199	130(37.4)	27(20.8)	3.55(1.81,6.96)*	1.88(0.7,5.07)

Table 1 continued

Variable	N=348 n (%)	HIV-1+ n (%)	OR(95%CI) Univariate	OR(95%CI) Multivariate
Number of children				
No	33(9.9)	6(14.2)	1.0	1.0
1-5	274(78.7)	31(73.7)	0.57(0.22,1.50)	0.59(0.17,2.09)
≥ 5	41(11.4)	5(11.9)	0.63(0.17,2.26)	1.42(0.21,9.51)
Ethinicity				
Amhara	166(47.7)	13(30.9)	1.0	1.0
Oromo	133(38.2)	25(59.5)	2.72(1.33,5.56)*	2.23(0.96,5.19)
Tigrian	15(4.3)	2(4.8)	1.81(0.37,8.9)	1.07(0.15,7.75)
Gurage	17(4.9)	1(2.4)	0.74(0.09,5.99)	0.57(0.05,6.59)
Other	5( )	0(0.0)	------	------
Mixed	12( )	1(2.4)	1.07(0.13,8.9)	1.6(0.13,20.18)
Duration of stay in residency area				
<17	81(23.3)	15(35.7)	1.0	1.0
18-24	96(27.7)	10(23.8)	0.51(0.22,1.21)	1.48(0.51,4.33)
25-30	105(30.3)	7(16.7)	0.31(0.12,0.81)*	0.84(0.25,2.75)
31-45	65(18.7)	10(23.8)	0.80(0.33,1.92)	4.04(1.03,15.94)*
Household size				
1-3	69(19.8)	13(30.9)	1.0	1.0
4-6	184(52.9)	22(52.4)	0.58(0.28,1.24)	1.19(0.45, 3.15)
7-9	72(23.6(	6(14.3)	0.34(0.12, 0.95)*	0.98(0.23, 4.14)
10-12	13(3.7)	1(2.4)	0.36(0.04, 3.01)	0.73(0.05, 10.03)

* $p<0.05$

TABLE 2. Association between selected sexual behaviour & HIV serological status Among female workers in one of the factories in A.A, Ethiopia, October 1999

Variable	N=348 n (%)	N=42 HIV-1 + n (%)	OR(95%CI) Univariate	OR(95%CI) Multivariate
SEXUAL BEHAVIOUR				
Age at first sex				
10-15	153(45.7)	21(13.7)	1.0	1.0
16-17	66(19.7)	8(12.1)	0.87(0.36,2.07)	0.9(0.4,2.5)
18-25	107(31.9)	12(11.2)	0.79(0.37,1.69)	1.0(0.5,2.3)
>25	9(2.7)	1(11.1)	0.79(0.09,6.6)	1.1(0.1,10.6
Mean	16.35 $\pm$ 13.4			
casual sex partner				
No	342(98.2)	39(11.4)	1.0	1.0
Yes	6(1.8)	3(50.0)	7.7(1.52,39.8)*	8.5(1.5,47.6)*
Sex during mensus				
No	319(91.9)	36(11.3)	1.0	1.0
Yes	28(8.1)	6(21.4)	2.14(0.8,5.6)	1.7(O.6,5.0)
Syphilis (TPHA)				
Negative	267(76.7)	25(9.36)	1.0	1.0
Positive	81(23.3)	17(20.9)	2.6(1.3,5.0)*	1.7(0.7,4.0)
RPR				
Negative	325(93.4)	35(10.8)	1.0	1.0
Positive	23(6.6)	7(30.4)	3.6(1.4,9.4)*	2.7(0.8,8.9)

* $p<0.05$

TABLE 3. Comparison of Socio-demographic variables between contraceptive hormone users and non users among females in one of the factories in A.A, October 1999.

Variables	All women(N=348) Users=163 n (%)	Non users=187 n (%)	OR(95%CI)
Age(years)			
20-24	13(7.9)	4(2.1)	1.0
25-29	33(20.3)	32(17.1)	0.31(0.09,1.08)
30-34	43(26.4)	40(21.4)	0.33(0.09,1.09)
35-39	45(27.6)	55(29.4)	0.25(0.07,0.83)*
40-46	29(17.8)	56(30.0)	0.16(0.05,0.53)*
Mean	35.7 ± 6.5	37.9 ± 6.4	
Education			
Read and write	47(28.8)	68(36.4)	1.0
grade 1-6	79(48.5)	84(44.9)	1.36(0.84,2.20)
grade 7-12	31(19.0)	23(12.3)	1.95(1.01,3.75)
12 complete	3(1.8)	5(2.7)	0.87(0.19,3.81)
>grade 12	3(1.8)	7(3.7)	0.62(0.15,2.52)
Marital Status			
Married	143(87.7)	128(68.5)	1.0
Separated	13(8.0)	27(14.4)	0.43(0.21,0.87)*
Single	1(0.6)	10(5.4)	0.09(0.11,0.70)*
Widowed	4(2.5)	21(11.2)	0.17(0.57,0.51)
Religion			
Others	10(6.2)	16(8.6)	1.0
Orthodox	153(93.9)	171(91.4)	1.43(0.63,3.25)
Monthly income(Eth.Birr)			
200-999	96(59.0)	63(33.7)	1.0
<= 199	67(41.0)	124(66.2)	1.37(0.89,2.12)

* $p<0.05$

TABLE 4. Association between socio-demographic characteristics and HIV infection among oral contraceptive hormones users among females in one of the factories in A.A, Ethiopia, October 1999.

Variable	N=87 n(%)	N=42 (%)HIV-1 +	OR(95%CI) Univariate	OR(95%CI) Multivariate
Age(years)				
20-24	9(10.3)	22.2	1.0	1.0
25-29	22(25.3)	13.6	0.6(0.1,4.0)	0.4 (0.04 ,4.7)
30-34	21(24.1)	28.6	1.4(0.2,8.8)	0.9(0.1,10.8)
35-39	24(27.6)	4.2	0.2(0.01,1.9)	0.4(0.01,10.4)
40-46	11(12.6)	9.1	0.4(0.02,4.6)	0.7(0.01,43.5)
Education				
Read and write	28(32.2)	28.3	1.0	1.0
grade 1-6	37(42.5)	5.4	0.14(0.03,0.74)*	0.14(0.01,1.1)
grade 7-12	19(21.8)	15.8	0.5(0.1,2.1)	0.36(0.04,2.9)
12 complete	2(2.3)	0.0	----	----
> grade 12	1(1.2)	0.0	----	----
Marital status				
Married	77(88.8)	13.0	1.0	1.0
Separated	5(5.8)	40.0	4.5(0.7,30.6)	6.3 (0.5,75.3)
Single	1(1.2)	0.0	----	----
Widowed	3(3.5)	33.3	3.4(0.3,41.0)	7.3(0.1,502.3)
Religion				
Other	5(5.7)	20.0	1.0	1.0
Orthodox	82(94.3)	14.6	0.7(0.1,6.7)	0.3(0.02,4.8)
Monthly income (Eth.Birr)				
200-999	46(52.9)	4.4	1.0	1.0
≤ 199	41(47.1)	26.8	8.1(1.7,39.0)*	7.0(0.57,85.5)

* $p<0.05$

TABLE 5. Association between socio-demographic characteristics and HIV infection among injectable contraceptive hormone users among females in one of the factories in A.A, Ethiopia, October 1999.

Variable	N=64 n(%)	N=42 (%)HIV-1 +	OR(95%CI) Univariate	OR(95%CI) Multivariate
Age(years)				
20-24	4(6.3)	0.0	----	-----
25-29	9(14.1)	22.2	1.0	1.0
30-34	17(26.6)	11.8	0.7(0.1,6.0)	1.02(0.14,7.44)
35-39	19(29.7)	5.3	0.3(0.02,3.8)	0.25(0.02,3.20)
40-46	15(23.4)	13.3	0.8(0.1,7.0)	0.47(0.03,6.90)
Education				
Read and write	18(28.1)	11.1	1.0	1.0
grade 1-6	35(54.7)	14.3	1.3(0.23,7.7)	0.38(0.11,1.30)
grade 7-12	11(17.2)	0.0	----	-----
Marital status				
Married	55(85.9)	9.1	1.0	1.0
Separated	7(10.9)	14.3	1.7(0.17,17.1)	2.97 (0.63,13.90)
Widowed	1(1.6)	100.0	----	-----
Religion				
Other	4(6.2)	0.0	----	----
Orthodox	60(93.8)	11.7	----	----
Monthly income (Eth.Birr)				
200-999	38(59.4)	10.5	1.0	1.0
<= 199	26(40.6)	11.5	1.1(0.2,5.4)	0.7(0.06,8.5)

TABLE 6. Association between socio-demographic characteristics and HIV infection among all contraceptive hormones users among females in one of the factories in A.A, Ethiopia, October, 1999.

Variable	N=161 n(%)	HIV-1 + n(%)	OR(95%CI) Univariate	OR(95%CI) Multivariate
Age(years)				
20-24	13(8.1)	2(15.4)	1.0	1.0
25-29	32(19.9)	5(15.6)	1.02(0.17,6.10)	0.85(0.13,5.60)
30-34	43(26.7)	8(18.6)	1.26(0.23,6.80)	1.02(0.14,7.44)
35-39	45(27.9)	2(4.4)	0.25(0.32,2.00)	0.25(0.02,3.20)
40-46	28(17.4)	3(10.7)	0.66(0.09,4.52)	0.47(0.03,6.90)
Education				
Read and Write	47(29.2)	10(21.3)	1.0	1.0
grade 1-6	77(47.8)	7(9.1)	0.37(0.13,1.05)	0.38(0.11,1.30)
grade 7-12	31(19.2)	3(9.7)	0.40(0.10,1.60)	0.30(0.06,1.60)
12 complete	3(1.9)	0(0.0)	----	-----
> grade 12	3(1.9)	0(0.0)	----	-----
Marital status				
Married	141(87.6)	15(10.6)	1.0	1.0
Separated	13(8.1)	3(23.1)	2.60(0.63,10.30)	2.97 (0.63,13.90)
Single	1(0.6)	0(0.0)	-----	-----
Widowed	4(2.5)	2(50.0)	8.50(1.11,65.10)*	13.70(1.10,172.5)*
Religion				
Other	10(6.2)	1(10.0)	1.0	1.0
Orthodox	151(93.8)	19(12.6)	1.29(0.15,10.8)	1.44(0.15,12.90)
Monthly income (Eth.Birr)				
200-999	94(58.4)	6(6.4)	1.0	1.0
≤ 199	67(41.6)	14(20.9)	3.87(1.40,10.70)*	2.60(0.60,10.90)

* $p<0.05$

TABLE 7. Association between selected sexual behaviour and HIV infection among hormonal contraceptive users in FFWs in one of the factories, A.A, Ethiopia 1999

Variable	N=161 n (%)	HIV-1 + n (%)	OR(95%CI) Univariate	OR(95%CI) Multivariate
SEXUAL BEHAVIOR				
Age at first sex				
10-15	57(35.8)	8(14.1)	1.0	1.0
16-17	41(25.8)	4(9.8)	0.66(0.18,2.34)	0.7(0.1,7.5)
18-25	57(35.8)	8(14.1)	1.0(0.35,2.88)	0.9(0.3,3.2)
>25	4(2.5)	0(0.0)	-------	------
Mean age	16.74 ± 3.22			
casual sex partner				
No	156(96.9)	18(11.5)	1.0	1.0
Yes	5(3.1)	2(40.0)	5.1(0.8,32.7)	5.3(0.5,52.2)
Sex during mensus				
No	149(92.6)	19(12.6)	1.0	1.0
Yes	12(7.5)	1(8.3)	0.6(0.1,5.1)	0.7(0.1,6.6)
Syphilis (TPHA)				
Negative	135(83.9)	13(9.36)	1.0	1.0
Positive	26(16.1)	7(26.9)	3.5(1.2,9.8)*	4.2(1.1,16.6)
RPR				
Negative	154(95.7)	18(11.7)	1.0	1.0
Positive	23(6.6)	2(28.6)	3.0(0.5,16.7)	0.8(0.1,7.5)

* $p<0.05$

TABLE 8. Association between hormonal contraceptive use and HIV serological status among females in one of the factories, A.A, Ethiopia, October 1999

Contraceptive use	n(%)	HIV-1+ n (%)	OR (95%CI)
Oral contraceptive			
No	191(68.7)	22(11.5)	1.0
Yes	87(31.3)	13(14.9)	1.35(0.6,2.99)
Injectable contraceptive			
No	191(74.9)	22(11.5)	1.0
Yes	64(25.1)	7(10.9)	0.94(0.35,2.49)
Norplant			
No	191(96.9)	22(11.5)	
Yes	6(3.1)	0(0.0)	

Table 9. Variables independently associated with HIV-infection among FFWS,in one of the factories A.A, October 1999.

Variables	OR	95 % CI
Age 35-39 years	0.10	0.02-0.70
Education grade 7-12	0.23	0.10-0.95
Separated	4.25	1.56-11.6
Widowed	8.28	2.90-23.40
Casual sex partner	7.70	1.52-39.80

Discussion

The present study analyzed the socio-demographic characteristics, history of contraceptive use, sexual behavior and other factors associated with HIV-1 infection among female factory workers. The findings indicate an overall high sero prevalence of 12% among a population of mostly married female factory workers in Addis Ababa. This indicates an alarming progression of the infection since the HIV prevalence rate was 6.0% and 6.9% for men and women respectively, in a community based sero prevalence study conducted in Addis Ababa in 1994 (8).

HIV-prevalence was higher among the age group 20-24 years(17.6%) whereas in the age group 35-39 years the prevalence lower(6.0%). This association was statistically significant in multivariate model(OR=0.10, 95%CI= 0.02-0.7). This might be related to their low risk sexual behavior as most could be married as well as faithful to their partner as their age increases.

These data indicate that interventions aimed at adolescents are critical to prevent the increased prevalence that occurs in early adulthood.

HIV-prevalence tended to decrease with age($p<0.02$; test for

trend).

As opposed to HIV prevalence syphilis prevalence tended to increase with age (test for trend, p , 0.01), as may be expected for a non-fatal disease which has been there for many decades, and whose serology remains positive even after treatment.

Higher HIV prevalence was observed among the widowed(40%) and separated(20%) women, while sero positivity was lower(8.1%) among married women. This association was statistically significant in both univariate and multivariate models. This might be related to risky sexual behavior(having multiple sexual partner) in these groups compared to the married ones. Having casual sex partner was also significantly associated with HIV infection in multivariate model for the same reason given above for the widowed and separated.

HIV positivity decreased with increasing educational status. High prevalence was observed among those with educational level less than grade 1 (15.6%) as compared to those grade 7-12 which is lower(7.4%). This might be related to the better information about safer sexual practices in those with higher education as compared to those with lower education.

The key objectives of this study was to assess the association between the use of hormonal contraceptives and HIV infection.

In this study no association between HIV sero positivity and use of oral contraceptives was shown. This can be due to lower risk groups of our study participants i.e. the majority are married particularly the oral contraceptive pill user. Studies which found an association between contraceptive hormones and HIV were mostly studies done on commercial sex workers and STD clinic attendants with higher risk for HIV(mostly not married and having multiple sexual partners(14,26), which was not the case in this study.

Epidemiological studies regarding oral contraceptive use and HIV transmission are often confounded by the use of more than one contraceptive during the interval studied and other differences between study groups may also confounded interpretation. For example, it has been suggested that women who choose hormonal contraceptives may be less likely to use barrier contraceptives to prevent STD infection making studies difficult to interpret(12).

To control for confounders multivariate analysis using logistic regression was done in this study.

The association between HIV and oral contraceptive use has been assessed by few published prospective studies. One study reported a significantly increased risk of HIV, among contraceptive users in sex workers from Nairobi(14). However, the validity of these results were questioned because of statistical methodology employed using Odds Ratio(OR), but Relative Risk(RR) may have been the more appropriate statistic for these data which were collected prospectively, and because selection bias may have occurred (fully half of the oral contraceptive users were lost to follow up).

Three other prospective studies did not find a significant association (30-32). In addition a cross-sectional study of family planning clinic attendees in Nairobi showed no association between oral contraceptive use and HIV-positivity(33). European data have also identified no association between oral contraceptive use and an increased risk of HIV sero conversion (34,35) and these results were similar to our study. In addition, a study in Thailand reported a non significant inverse association (36), and Italian study found a significant protective association (37).

In the present study injectable contraceptive use was also not associated with HIV infection. Recently, similar findings among

commercial sex workers in Addis Ababa was also found (42).

There are three published prospective studies addressing the association between use of injectable contraceptives and HIV. In a study involving commercial sex workers in Thailand the risk of HIV among injectable contraceptive users was 3.83 (31). Among the possible explanations given was the thinning of vaginal epithelium following the use of such hormones. In addition, it was also assumed that since these hormones lead to amenorrhea they may allow more frequent sexual activity by the sex workers (31). In another study involving 1150 women visiting prenatal clinics in Rwanda, a weak association between HIV and hormonal contraceptives (mainly injected medroxy progesterone acetate) was observed (39). In the third Kenyan study done among CSWs attending municipal STD clinic, association between HIV and DMPA. Trend for an association between use of high dose OCP and HIV was also found(44).

A number of possible mechanisms could explain the observed association between injectable contraceptives(mostly DMPA) and HIV-1. Residual confounding by sexual exposure, despite controlling for exposure variables, could account for the observed association. Measurement of sexual exposure was based on self-reported behavior, and under reporting of sexual exposure

may take place.

Recently, a 7.7-fold increased risk of vaginal transmission of SIV in rhesus macaques given subcutaneous progesterone implants has been reported (10), possibly due to thinning of the vaginal epithelium. But this animal study can not be extrapolated to human as women differ from macaques and progesterone may interact in a complex manner with the immune system, depressing cellular immunity, and enhancing humoral immunity. Several mechanisms are expected to interact to modify susceptibility of women to HIV infection (local immunity, STDs, vaginal pH, lacto bacilli cervical ectopy, mucus thickness, epithelium thickness etc.), and the situation cannot be summarized to a number of epithelial cells.

Sexual intercourse during menstruation and post coital genital bleeding were also factors mentioned as being associated HIV sero positivity(30). In this study HIV sero prevalence was not associated with having sex during menstruation. This could be due to the small number of the participants who had sex during mensus as they were married and the study became low powered to see significant association.

Strength and limitations of the study

There are no similar studies in Ethiopia, hence it gives a clue about the association between HIV infection and hormonal contraceptive use and points area of research, and also the scientific precautions taken to keep the validity of the study can be sited as strength. In addition multivariate analysis using logistic regression model was performed to control for possible confounding effect of all other variables.

The major drawback with this design is that it is virtually impossible to determine the time of HIV-1 sero-conversion. Therefore, determining exposure status to any particular variable at the time of HIV-1 infection is equally difficult. Hence, in a cross-sectional study, it is impossible to definitely establish whether or not oral contraceptives were used at the time of HIV-1 infection. This type of misclassification will decrease the ability of the study to demonstrate a significant association between a particular variable and HIV infection but the ongoing prospective study by ENARP will eventually solve this problem.

In addition, the other limitation of this study is that specific information on the type of oral contraceptive (low, high dose) or duration used was not collected. However, all women obtained

there contraception from the factory clinic that mostly provide combined estrogen/progesterone.

Measurement of sexual exposure was based on self reported behavior, and under reporting of sexual exposure may take place as sensitive behavioral issues (e.g. Life time partner).

Lastly, this study also needs careful interpretations and cautious generalization to all the urban female population. It must be remembered that the study was done in female factory workers and majority were married women and may not be representative of all women of reproductive age in Addis Ababa. Therefore the generalizability should be limited to similar population only.

Conclusions and Recommendations

1. HIV prevalence was high among the FFWs of Addis Ababa.

2. In multivariate analysis,variables independently associated with increased risk of HIV infection were: being separeted, widowed and having casual sex partner were. Variables independently associated with decreased risk of HIV infection were: Being in the age group 35-39 and having education level grade 7-12.

3. No association between oral injectable contraceptive hormones and HIV was found in this study.

4. The study population were lower risk groups majority were married, having low number of life time partners, and to be TPHA negative as compared to others.

5. Based on our findings and those of other investigators, we conclude that there is no evidence to suggest that the use of oral and injectable contraceptives is associated with increased risk of HIV-infection.

Based on the results of this study the following recommendations were given:

1. Hormonal contraceptives use in this group of women did not increse risk of HIV infection, therefore hormonal contraception should continue as before, but use of an additional barrier (e.g condom) method is also recommended among hormonal contraceptive users at risk for HIV/STDs.

2. Interventions like intensive health education aimed at adolescents and youth are critical to prevent the increased prevalence that occurs in early adulthood.

3. A community based sero prevalence surveillance is necessary to monitor the magnitude of the problem.

4. Further prospective study among users of oral contraceptive pills and injectable hormones, especially among women with long duration of use is recommended.

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Annex 1

Questionnaire on Contraceptive Use and HIV Infection

Among Female Factory workers, Addis Ababa

1. Participant's code number: _____
2. Date of interview: _____
3. Interviewer's name: _____
4. Factory: 01.
   02.
   03.

Explain the purpose of the questionnaire:

. evaluation of hormonal contraceptive use and HIV status

. evaluation of the risk of HIV/ AIDS epidemics for the community by assessing individuals' behaviours

STRESS THAT ALL INFORMATION IS KEPT STRICTLY CONFIDENTIAL, AND THAT A CODE NUMBER IS USED TO PRESERVE ANONYMITY OF THE QUESTIONNAIRE

DEMOGRAPHICS

1. What is your curret residence?

1. Akaki
2. Kaliti
3. Addis Ababa
4. other
5. unknown

2. To which occupational category do you belong?

01. field worker
02. administrative/office
03. factory worker
04. maintenance/garage
05. medical
06. housewife
07. students
08. suppottive personnel(driver, cleaner..)
88. other
99. unknown

3. How old are you? _____years

77. refuse to answer
99. unknown

4. What is your ethnic group?

01. Amhara

02. Oromo

03. Tigray

04. Gurage

05. other

06. mixed

77. refuses to answer

5. What is your religion?

1. Orhodox christian

2. Muslim

3. Protestant

4. Roman Catholic

5. other

6. non-religious

7. refuses to answer

9. unknown

6. Which level of education did you acheive?

1. less than grade 1

2. grade 1-6

3. grade 7-12

4. grade 12 completed, without further education

5. education after grade 12

7. refuses to answer

9. unknown

7. How many people live permanently in your house?

_____number of peple

99. unknown

8. What is your monthly personal income?

1. <100 Birr

2. 100-199 Birr

3. 200-299 Birr

4. 300-399 Birr

5. 400-999 Birr

6. >1000 Birr

7. refuses to answer

8. unknown

9. What is your other household income?

1. <100 Birr

2. 100-199 Birr

3. 200-299 Birr

4. 300-399 Birr

5. 400-999 Birr

6. >1000 Birr

7. refuses to answer

9. unknown

GEOGRAPHIC STABILITY

10. For how many years have you been resident of your current residntial place (spending more than six months every year in your resdent area)?

_____years

99. unknown

11. For how many years have you worked in your current working place?

_____years

88. not applicable (does not work)

99. unknown

RISK BEHAVIOUR AND HEALTH STATUS

Remind the study subject that the following information will be kept strictly confidential

12. What is your current marital status?

1. single, never married
2. married and living together
3. married, but temporarily not living together
4. married, but separated or divorced
5. widowed
9. unknown

13. How old is your spouse (If married and living together)? Or

how old would be your spouse (If married not living together, divorce or widowed)?

_____years

88. not applicable (single never married)

99. unknown

14. What is the occupation of your spouse?

01. field worker

02. administrative/office

03. production worker

04. maintenance/garage

05. medical

07. students

08. suppottive personnel(driver, cleaner..)

09. other

10. unemployed

88. not applicable (single never married)

99. unknown

15. What educational level does he has?

1. less than grade 1

2. grade 1-6

3. grade 7-12

4. grade 12 completed, without further education

5. education after grade 12

7. refuses to answer

8. not applicable

9. unknown

16. What ethnic group does he belong to?

01. Amhara

02. Oromo

03. Tigray

04. Gurage

05. other

06. mixed

77. refuses to answer

17. At what age did you first marry?

_____years

88. not applicable (single never married)

99. unknown

18. How many times have you been married?

_____ number of times

8. not applicable (single never married)

9. unknown

19. For your only or recent marriage, for how many years have you been married?

_____ number of times

88. not applicable (single never married)

99. unknown

20. How many children do you have?

_____number of children

7. 7 or more

8. not applicable

9. unknown

21. Do you Have abnormal vaginal discharge from your genitalia currently

1. yes

2. no

7. refuses to answer

9. unknown

22. Do you Have an ulcer around your genitalia currently?

1. yes

2. no

7. refuses to answer

9. unknown

23. How many individual injections have you had in the past 12 months?

1. 0

2. 1 to 10

3. 11 to 49

4. 50 or more

9. unknown

24. Are you currently using any of these contracetive methods?

01. oral pill

02. injections (Depropovera)

03. IUD

04. tubal ligation

05. hormonal implant (Norplant)

06. traditional medicine

07. diaphram

08. spermicide

09. condoms

10. diaphram + spermicide

11. condoms + spermicide

12. no contraception

77. refuses to answer

88. not applicable

99. unknown

25. Do you use oral pill currently?

1. yes

2. no

7. refuses to answer

8. not applicable

9. unknown

26. Do you use injectable hormones currently?

1. yes

2. no

7. refuses to answer

8. not applicable

9. unknown

27. Do you use IUD currently?

1. yes

2. no

7. refuses to answer

8. not applicable

9. unknown

28. Do you use any other contraceptive method currently?

1. yes

2. no

7. refuses to answer

8. not applicable

9. unknown

29. If yes, please mention which one?

1. tubal ligation

2. hormonal implant (Norplant)

3. traditional medicine

4. diaphram

5. spermicide

6. condoms

7. calender method

8. not applicable (not used)

9. unknown

30. From where do/did you get your contraceptive hormones?

1. factory clinic

2. health centre

3. health station

4. private clinic

5. private pharmacy

6. other

Stress again to the study subject that the following information will be kept strictly confidential

31. At what age did you have sexual intercourse for the first time? _____ years

77. refuses to answer

88. never /not applicable

99. unknown

32. If not currently married, do you currently have a steady sexual partner (someone with whom you have been having sex with for atleast three months?

1. yes

2. no

7. refuses to answer

8. not applicable/married

9. unknown

33. How often do you use condoms with your spouse or your steady partner?

1. never
2. less tha once per month
3. more than once per month, less than once per week
4. more than once per week, less than once per day
5. every day
7. refuses to answer
8. not applicable/no spouse or regular partner
9. unknown

34. In your last sexual intercourse with your spouse or your steady partner were condoms used?

1. yes
2. no
8. not applicable/no spouse or regular partner
9. unknown

35. Have you already had sexual intercourse while you had your menstrual periods? 1. yes
2. no
7. refuses to answer
9. unknown

36. What is the total number of partners you have had sexual intercourse with during your lifetime (including current spouse and stedy partner)?

01. 0

02. 1

03. 2-4

04. 5-9

05. 10-19

06. 20-49

07. 50 or more

77. Refuses to answer

99. unknown

Annex 2

Informed consent form for the ongoing cohort study

we are conducting a long-term study on the health status of the population working at the Akaki Fibre factory.

The information we are collecting concerns the socio-demographic charactersistics and the health status of the factory workers. We are intending to follow study participants for a period of at least eight years. You will visite the study team twice a year. At each visit, we will ask you to answer a questinnaire, and to provide samples for laboratory anaysis (blood, stool, and eventually urine). At the first visit, you will have in addition a skin test to detect past exposure to common infectious including tuberculosis. The samples will be collected by experienced tecnicians using sterile equipment. There is no harm attached to the study procedures.

These samples will be used to diagnose infections such as sexually transmitted diseases and intestinal parasities. As the study will also look at the impact of HIV infectionon the community, part of the bllod sample will be used for HIV testing. Also, in the the questinnaire, some questions will address will behaviours which may be risk factors for acquring sexually transmitted diseases. However, the questionnaires and the tubes for blood test will be coded so that all these information will be kept confidential. HIV testing will be performed at the Ethiopian Health Nutrition Research Institute (EHNRI)

in Addis Ababa. No one except you, the project counsellors, and the medical doctor in charge will have access to the results of the HIV test. Both the counsellor and the medical will keep it strictly confidential.

If you ask for the result of the HIV test, we will communicate it to you through a post-test counselling visit. Post-test counselling will be routinely done at the ENARP study clinic, but may be available at the Texitle Factory Labour Union for those who would prefer it for confedintiality purpose. If you do not want to know your HIV test result, we will not tell you. The results from all other labouratory tests will be communicated to you. You will be treated free of charde, according to the national standared of care, for any infection diagnosed during the routin visites of the follow-up.

During the study period, you and your close relatives living in the same household (parents, spouse, brothers, sisters, and childern) will be provided free medical care according to the national standareds of care. Mecical care will be provided at the fibre factory for you and at the Textile Factory Labout Union Clinic for your family. If the study were to end prematurely, this privilege would be lost with the termination of the study. If you decide to withdraw from the study, you and your family would also loose this privilege, At each visit scheduled by the study team (twice a year), you will be paid 15Eth. Birr for transportation and time lost.

The information of the study will be used for reaserch purpose only and for assessing the health status of the community, which would be for the benefit of the community. Information collected will be kept in strict confidence. If you have any question concerning the study procedures, you have the right to ask one of the investigators. You are entirely free to participate in the study, and there will be no consequences to you if you refuse to participate, whether it concerns your working situation or your future medical management. You are also free to withdraw consent to participate at any time, without any prejudice except loosing the benefit of free medical care for you and your family.

Do you agree to take in the study?

Yes_____

If yes please sign here_____

No_____

Date_____

DECLARATION

I, the undersigned, declare that this thesis is my original work and all sources or materials used for this thesis have been duly acknowledged

Name Tesfalidet Debesay

Signature Dir Te. Fantalidet

Place Addis Ababa

Date of submission December, 1999

This thesis has been submitted for examinationwith my approvalas university advisor.

Dr. Misganaw Fantahun