Abstract

Introduction: Targeted intervention (TI) project aimed to interrupt HIV transmission among highly vulnerable population and their clients. Aims and Objectives: To compare survival among HIV-positive versus survival among HIV-negative women. Subjects and Methods: Study Design: Prospective cohort with retrospective comparison. Study Setting: Two drop-in center clinics. Study Tool and Process of Data Collection: Data were collected for 5 years from 2009 to 2014. Pretested semi-structured questionnaire was used for data collection. Results: The mean age of high-risk women was 32.48 ± 4.67 years. The mean survival among HIV-negative women was 110.62 ± 0.6 months and mean survival among HIV-positive women was 91.09 ± 7.67 months. The mean interval to death among women with sexually transmitted diseases (STDs) was 113.50 ± 1.30, whereas the mean interval to death among women with no STDs was 105.65 ± 0.76. P = 0.00 by log-rank test. Conclusion: Status of high-risk women according to HIV, STDs, typology, category and partner wise were found to have a significant difference in survival experience, whereas PRR positivity for syphilis, literacy, alcohol intake do not have a significant difference.

Keywords: High-risk women, Kaplan–Meier curves, time to HIV positivity, targeted interventions

INTRODUCTION

One of the most important components of the National AIDS Control Programme is the targeted intervention (TI) project that aims to interrupt HIV transmission among highly vulnerable population (female sex worker [FSW], men who have sex with men, intravenous drug user, and migrant) and clients of sex workers or bridge populations.[1]

The Community Medicine Department is working with high-risk women (FSWs) since 1997. The department was undertaking the prevention and control activities for STIs and HIV under this TI project in the red light area of city. The project was receiving funds from the Department for International Development, UK, later on from the National AIDS Control Organization (NACO) since 2000, and managed by the State AIDS Control Society (SACS).

The project provides beneficiary services for quarterly medical checkups, rapid plasma reagin (RPR) testing and integrated counseling and testing center (ICTC) testing, STIs detection (syndrome wise) and treatment through drop-in center (DIC) clinics or urban health centers, linkages and referral services with ICTC centers, antiretroviral therapy and directly observed treatment, short-course therapy, etc.

Many research projects have been carried out among these women from time to time.[2] Records of project beneficiaries such as women who got HIV infections and died over a period of time etc., are being maintained.

Few studies on FSWs have focused on assessing survival among them based on risk factors like RPR positivity, sexually transmitted disease (STD) positive status, intake of alcohol, their educational status, typology, category and partner status. Comparison of time to HIV positivity (seroconversion rate) among them according to their RPR positive and STD status was also novel objective of this study.

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With this background, the aim of the study was to compare survival among HIV-positive versus survival among HIV-negative women.

The primary objectives of the study were to compare survival among, RPR-positive versus RPR-negative women, STD-positive versus STD-negative women, survival among them according to intake of alcohol, educational status, typology, category, and their partner status. The secondary objective was “comparison of time to HIV positivity among RPR-positive versus RPR-negative women and STD-positive versus STD-negative women”.

**Subjects and Methods**

It was a mix of primary and secondary data analysis carried out among high-risk women (FSWs). Participant’s data who were enrolled during the financial year 2009–2010 and stayed in the project getting TI services till 2013–2014 were collected. Data were collected for 5 years from 2009 to 2014, prospectively for 2013–2014, and retrospectively from records for 2009–2012. Each year/2 yearly participant’s registration was updated and confirmed. Cohort was followed up from 2009 onward till April 2014. The selected women were beneficiaries of TI project implemented by the Community Medicine Department, Government Medical College under SACS.

**Study design**

Prospective cohort with retrospective comparison. Prospective cohort study with comparison to existing program data.

**Study setting and sample size**

Two thousand one hundred and ninety-three registered women availing services through two different DIC clinics and project field area of city were taken.

**Data collection and questionnaire**

Pretested semi-structured questionnaire was used for data collection. Complete/incomplete data in data records were gathered through visits at DIC clinics and completed with staff and participant interviewing and cooperation. As participants were enrolled under this TI project and getting services since long time. Data available in crude form at DIC clinic were validated and collected as per designed questionnaire and variables. The study was approved by Gujarat State AIIDS Control Society. Data collection was done by researcher herself as researcher was also working as coinvestigator under this project. Variables in the questionnaire were sociodemographic profile (age, marital status, education, alcohol consumption at baseline), typology (home based, street based, others), category wise distribution (category A/B/C or others), STDs, (RPR testing for syphilis and its positivity), and integrated counseling and testing and its status.

As per TI guidelines, screening for STDs was done at every 3 months along with recovery management checkup testing or whenever the participant is symptomatic. Whenever a participants turn up positive, they were treated for STD as per syndromic management guidelines.

**Definitions used**

**Category of high-risk women (FSWs)**

As per NACO guidelines for TIs FSWs has to be categorized into one of the category A/B/C based on 7 parameters for risk assessment.[3]

**Subtypology of high-risk women**

As per NACO guidelines they can be categorized broadly into three types of subtypes homebased or “secret,” Street based sex workers and others.[1]

**Data entry and validation**

Data entry from different records, data cleaning, and merging different variables of both DIC clinics were done with the help of excel software. Information was collected separately for both clinics and later compiled into a single sheet for each year from 2009 onward. Combined sheet was used for further analysis. Validation of data during field, DIC clinic visits, and in the data entry sheet was done.

**Statistical analysis**

It was done with the help of SPSS software (version 20) (Veer Narmad South Gujarat University, Surat, Gujarat, India). Descriptive statistics were calculated for the demographic data. Kaplan–Meier curves were plotted to compare survival and time to HIV positivity among different categories of variables.

Statistical significance was seen using Breslow (Generalized Wilcoxon), log-rank (Mantle-Cox), and Tatone ware test.

**Ethical considerations**

Confidentiality was maintained at every stage of study. Permission from SACS and institutional ethical committee was obtained.

**Results**

The mean age of high-risk women was 32.48 ± 4.67 years. Out of 2193 women, 1924 (87.73%) were married, whereas 269 (12.27%) were unmarried, widowed, divorced, and separated. 1370 (62.47%) women were literate, whereas 823 (37.53%) were literate. Two hundred and twenty-eight (10.4%) women were having habit of alcohol consumption, whereas majority 1965 (89.6%) did not drink alcohol.

Typology wise 1129 (51.50%) women were home based, 619 (28.20%) were street based, whereas 445 (20.30%) belonged to category other than home or street based. One thousand one hundred and sixty-six (53.2%) women belonged to category A, whereas 800 (36.5%) belonged to category B and 227 (10.4%) belonged to category C. 2124 (96.9%) women had regular partner, whereas few 69 (3.1%) did not have regular partner.
Thirty-two women were identified HIV positive over a period of time. Two hundred and twelve (9.67%) women had STDs. Ten women were having RPR positivity for syphilis.

Survival and seroconversion (time to HIV positivity) over a period of time was compared among high-risk women.

There was significant difference in survival function among HIV-positive versus HIV-negative women. Breslow test (Generalized Wilcoxon) showed statistically significant difference with $P = 0.02$.

The mean survival among HIV-negative women ($n = 2161$) was $110.62 \pm 0.6$ months and mean survival among HIV-positive women ($n = 32$) was $91.09 \pm 7.67$ months. In the beginning, HIV-negative women were having higher survival, whereas in the late stage survival was more or less similar among HIV-positive and HIV-negative women [Graph 1].

The mean interval to death among women with STDs ($n = 212$) was $113.50 \pm 1.30$, whereas the mean interval to death among women with no STDs ($n = 1981$) was $105.65 \pm 0.76$, $P = 0.00$ by log-rank test.

The mean interval to death among RPR-positive women ($n = 10$) was $107.17 \pm 12.22$ months, whereas the mean interval to death among RPR-negative women was ($n = 2183$) $110.66 \pm 0.62$, $P = 0.97$ by log-rank test.

In the early stage, interval to death was lesser among literate women in comparison to illiterate women but the difference disappears in the later period.

The mean interval to death among women with alcohol consumption ($n = 228$) was $112.48 \pm 1.86$ months, whereas the mean interval to death among women with no alcohol consumption ($n = 1965$) was $98.86 \pm 0.85$.

The survival among home based high-risk women was lower as compared to street based counterparts. The mean interval to death among high-risk women from home based typology ($n = 1129$) was $95.01 \pm 1.12$ months, whereas the mean interval to death among street based high-risk women ($n = 619$) was $108.70 \pm 1.10$ and the mean interval to death among women from typology other than ($n = 445$) home based and street based was $101.92 \pm 2.06$, $P = 0.00$ by log-rank test [Graph 2].

The mean interval to death among women from risk category ($n = 1166$), vulnerable category ($n = 800$) and other category ($n = 227$) was $92.74 \pm 1.19$ months, $108.25 \pm 1.05$ and $110.88 \pm 2.04$ respectively with $P = 0.00$ by log-rank test [Graph 3].

The mean interval to death among women with regular partners ($n = 2124$) was $101.69 \pm 0.78$ months, whereas the mean interval to death among women with nonregular partners ($n = 69$) was $56.81 \pm 4.27$ months, $P = 0.00$ by log-rank test [Graph 4].

The mean interval for HIV positivity among RPR-negative women ($n = 2183$) was $109.90 \pm 0.64$ months, whereas the mean interval among RPR-positive women ($n = 10$) was $105.67 \pm 9.64$ months. Log-rank test shows Chi-square statistic of 0.79 with a $P = 0.37$. 

Graph 1: Kaplan–Meir curves for survival among HIV-positive and HIV-negative female sex workers

Graph 2: Kaplan–Meir curves for survival among high-risk women according to their typology

Graph 3: Kaplan–Meir curves for survival among high-risk women according to their category (risk/vulnerable/others)
The mean interval to HIV positivity among women with no STDs ($n = 1981$) was $110.31 \pm 0.69$ months, whereas the mean interval to HIV positivity among women with STDs ($n = 212$) was $111.74 \pm 1.42$ months and the difference was not found to be statistically significant.

**DISCUSSION**

As per information published in Global AIDS update, high-risk women are at 13 times more risk of acquiring HIV compared with the general population, due to an increased likelihood of being economically vulnerable, unable to negotiate consistent condom use, and experiencing violence, criminalization, and marginalization.\(^{(4)}\) Beginning in 2003, large scale, targeted HIV prevention programs, including the Avahan program funded by the Bill and Melinda Gates Foundation, were implemented among high-risk women and other key populations in high prevalence states, and resulted in significant increases in the uptake of HIV prevention services and safer sexual behaviors, and reductions in the number of STIs/STDs.\(^{(5,6)}\) According to an UNAIDS report, by the year 2010, India saw a drop of 56% in the incidence of new HIV infections.\(^{(7)}\) Despite these important gains in HIV prevention, HIV prevalence continues to be relatively high among them in India at about 4.9%.\(^{(8)}\) In some Southern states, up to 15% of high-risk women are reported to be living with HIV. Further gains in prevention are likely to depend on a more nuanced understanding of the factors contributing to the persistence of high levels of risk among them.\(^{(9)}\)

In our study in the first phase of 100 months, survival among HIV-positive women was clearly lesser than those who were HIV negative, but the survival experience in both the groups became comparable after the period of 100 months. Probability of event is proportionally higher at early time points than in later period in HIV-positive group. Breslow test gives more weightage to deaths at early time points, it does not require a consistent hazard and hence we can report the $P$ value on the basis of this test.

Differences in survival among women with STDs and without STDs may be there that the treatment-seeking behavior of STD-positive women was more as compared to those not suffering from STDs. No statistically significant difference in survival among RPR-positive versus RPR-negative women indicates that the mean interval to death is not different among two groups.

Mortality density in our study was 3.65 per 1000 person years. In a study done by Ryavanki Sridhar et al. among HIV patients in Surat, mortality density was 10.8 per 1000 person years. In their study, marital status as a social factor does not significantly contribute to survival.\(^{(10)}\) In our study also, marital status does not have contribution toward survival among women.

In a Karnataka based study by Javalkar et al., of the total people living with HIV registered with the program, about 9% died within the 5-years of program period with an overall death rate of 38 per 1000 person-years. The mortality rate was higher among males, aged 18 and above, among illitertates, and those residing in rural areas.\(^{(11)}\) Age wise differences in survival was not found in our study.

Based on differences in interval to death among literate and illiterate women education does not have a significant influence on interval to death as evident from the $P > 0.05$ in log-rank test.

In the early stage, interval to death was greater among those not taking alcohol in comparison to alcoholic group but the difference disappears in the later period. Difference observed in the survival experience of alcoholic and nonalcoholic women is due to chance only with $P = 0.05$ by log-rank test.

Lower survival among home based high-risk women as compared to street based women may be because of more domestic violence and secrecy observed among home based women. The survival among women from vulnerable and other category was more compared to women from risk group in the early stage but survival becomes similar in three groups in the later period. Vulnerable group is having less susceptibility as compared to risk group in all stages, hence log-rank test is appropriate test of significance. Survival among women having regular partners was more at all periods as compared to those having nonregular partners. In a study among high-risk women (FSWs) in northern Karnataka by Becker et al., overall mortality rate of 2.44 per 100 person-years, and an HIV-related mortality rate of 2.11 deaths per 100 person years of women was observed. Their study revealed that almost 90% of deaths among women in the cohort were attributable to HIV. Older age and lack of a regular partner were associated with mortality. Lack of a regular partner may indicate lack of social and financial support, resulting in increased need for more active engagement in sex work.\(^{(12)}\)

Time to HIV positivity among RPR-positive women was less as compared to HIV positivity among RPR-negative women, but this difference was not statistically significant. This indicates the difference between two groups was due to
chance. There is no difference in time to HIV positivity among those who were STD positive versus those who were STD negative. In a seroconversion study among high-risk women in Thailand (1998), the incidence of HIV-1 seroconversion in the 1st year of follow-up was 20.3 per 100 person-years among 126 brothel-based commercial sex workers (CSWs) and 0.7 per 100 person-years among 159 other CSWs. In a multivariable proportional hazards model applied by Kilmarx et al., seroconversion was significantly associated ($P < 0.05$) with brothel-based sex work (adjusted risk ratio, 7.3) and Chlamydia trachomatis cervical infection (adjusted risk ratio, 3.3).\textsuperscript{13,14}

**Conclusion**

In this study, survival curves of the HIV-positive and HIV-negative high-risk women were compared by Kaplan–Meier method. Breslow (Generalized Wilcoxon), log-rank (Mante-Cox), and Tatone were test used to test whether there is a significant difference in the survival experience. $P < 0.05$ was considered as significant difference.

Status of high-risk women according to HIV, STDs, typology, category and partner wise were found to have a significant difference in survival experience, whereas PRR positivity for syphilis, literacy, alcohol intake do not have a significant difference in the survival experience of high-risk women.

PRR positivity for syphilis and STDs does not have any significant influence on time to HIV positivity (seroconversion) among them.

**Limitations**

Being secondary data collection collected information has to be relied on. Slight changes in the modifications of TI definitions and reporting formats for updating as standardized by higher authorities from time to time were accepted and taken into consideration.

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**Conflicts of interest**

There are no conflicts of interest.

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