

**A COMMUNITY BASED STUDY TO ASSESS ADHERENCE
OF ANTIRETROVIRAL THERAPY AMONG PEOPLE
LIVING WITH HIV/AIDS (PLHIV) IN KOLKATA, INDIA**

Dr. Smarajit Jana (Dr. Jana S.)*

Dr. Protim Ray (Dr. Ray P.)**

Prof. Krishnangshu Roy (Prof. Roy K.)***

Dr. Debashis Mandal (Dr. Mandal D.)****

Mr. Sudhanshu Chakraborty (Mr. Chakraborty S.)*****

Dr. Shyam Sundar Jha (Dr. Jha S. S.)*****

Work was carried out by:

Sonagachi Research and Training Institute, Kolkata, India

Source of Financial Support:

This study was supported by a financial grant from the Faculty Fund of The School of Tropical Medicine, Kolkata.

Acknowledgement:

President, Secretary and all members of Mamata Network of Positive Women, Kolkata, India.

Mr. Krishna Kumar Kundu for the Statistical Analysis.

* Principal, Sonagachi Research and Training Institute, 44 Balam Dey Street, Kolkata 700006, India

** Sr. Medical Officer, Sonagachi Research and Training Institute, Kolkata, India

*** Director, Institute of Health & Family Welfare, Govt. of West Bengal, Kolkata 700091, India

**** Hon. Senior Lecturer, University of Manchester, Consultant Physician in Genitourinary Medicine, Warrington & Halton Hospitals NHS Foundation Trust. UK

***** Social Scientist, Sonagachi Research and Training Institute, Kolkata, India

***** PhD Student, Sonagachi Research and Training Institute, Kolkata, India

Abstract**Access Adherence to Antiretroviral Therapy**

A community based antiretroviral (ART) drugs adherence study was conducted in Kolkata, India beginning in January and concluding in March 2011. This study was designed to explore the level of adherence as well as factors influencing adherence to ART by those who are receiving treatment through a public health care delivery system. This health care system is implemented through the National AIDS Control Program in the state of West Bengal, India. The research findings showed a high degree of non-adherence, between 48-52%, among the ART recipients. Analysis highlights a number of key factors negatively influencing adherence including long waiting time at the ART center, distance from residence to ART Centre, travel related expenditure, and fear of being identified as HIV + to family members and neighbours. Some positive influences were identified in the data as well. If a person is a member of a positive people network there is a greater chance for adherence as well as if an individual self-identifies as positive to others. However, no single factor, rather a combination of several factors, proved to be responsible in influencing ART adherence among recipients.

Key words

HIV+ individuals, ART, Adherence, Network

Introduction

Regular intake of antiretrovirals in scheduled doses is shown to bring down the positive person's 'Viral Load' as well as boost immunity through an increase in the CD4 Count. This helps avert opportunistic diseases and other infections while improving the quality of life for people living with HIV/AIDS (PLHIV). The role of ART is to suppress the multiplication of viruses for which regular and continued treatment is essential. ART does not cure the illness but helps the incumbent individual lead a normal life as ART delays the onset of severe illness through the suppression of the virus¹. Significant reduction of viral load in a patient's circulation makes the individual noninfective. As a result HIV positive individuals taking ARTs will not be able to transmit infection to others. This helps with prevention and is commonly known as 'Treatment as Prevention' (TasP). In India, as part of the National Strategy, 'Treatment as Prevention' is considered an important element of the HIV Prevention program. However poor adherence to ART shall not protect the individual from getting opportunistic diseases and other infections.. Non-adherence to ART could be a prime reason behind the development of resistant strains. A combination of anti-retroviral drugs is the treatment of choice². To ensure success in ART regimens requires strong commitment on the part of the patient to continue with the treatment regime.

Non-adherence to ART remains a concern across the world and is recognized as the most important contributing factor behind treatment failure and the development of a resistant strain. To ensure effectiveness, patients need to take the prescribed drugs on time, with proper dosages and scheduling³. It is hard to achieve 100% medication adherence, but studies have shown that if adherence level is maintained to the tune of 70% to 90% this could bring about effective outcomes of ART intervention⁴. It has also been demonstrated that a 10% higher level of adherence results in 21% reduction in disease progression provided 'medication adherence' is good⁵.

There is no substantive information regarding percentage of treatment failure due to development of a resistant strain in India. ART delivery centres in general do not possess laboratory support systems to confirm viral suppression which is often assessed through the clinical progression of disease.. Diagnosis for treatment failure due to a mutated HIV strain often is delayed, the clinician has to rely primarily on the drop of CD4 count and deterioration of overall patient health. There is a high probability of HIV transmission from individuals, who are experiencing treatment failure⁶ as the recipients often believe that they are not going to transmit HIV infection through unprotected sex or through other possible means as they are under the treatment regime. However, one of the critical prerequisites for successful ART depends on a high level of adherence by the recipient to the prescribed medicine⁷. In absence of sophisticated laboratory support to assess adherence to ART in the country, this study was designed to measure adherence to ART using a pretested tool to collect the responses from participants.

Objective of the Study

In view of the lack of data surrounding ART adherence among those are receiving treatment with antiretroviral medicine. The researchers from School of Tropical Medicine jointly with DMSC developed a plan to implement a study on ART adherence among recipients in Kolkata, India. The objectives of this study were to assess adherence to ART among those who are receiving treatment, to identify factors that might affect ARTs' adherence among the recipients categorized under personal, familial, social and structural factors, and also to find out possible mechanisms and approaches that may aid in improving ART adherence.



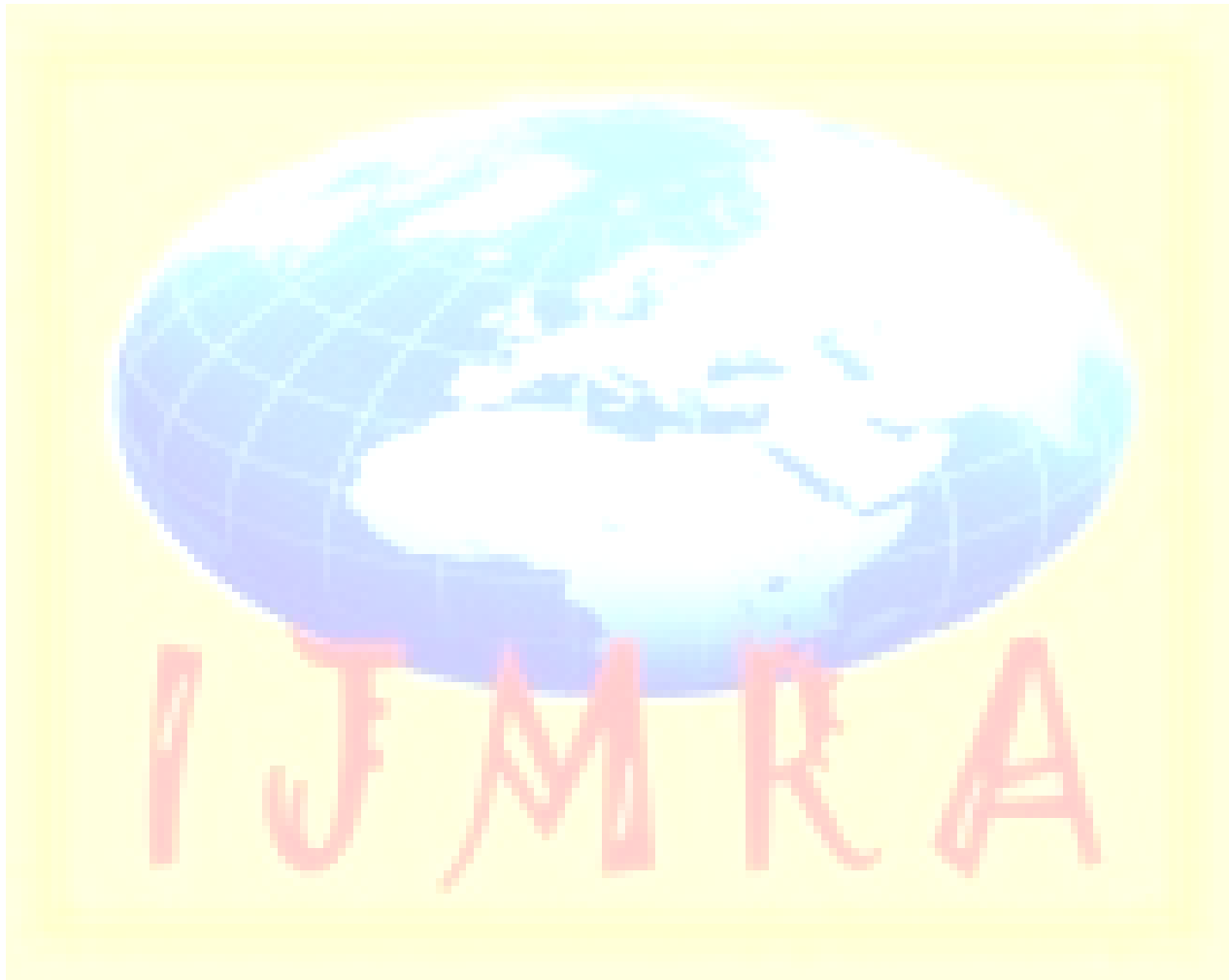
Materials and Method

The design of the study is based on the mobilization of the community through positive peoples' networks in the state of West Bengal. All samples were drawn from ART recipients who are linked to one or other positive networks but not necessarily members of the network. Information was gathered from networks to ensure reach and accessibility of the participants. The researchers decided not to involve 'service providers' of the ART centers or the staff members of the service delivery institutes to avoid any possible 'bias' and to reduce 'social desirability responses' from the participants.

Participants who agreed to take part in the study were taken as part of a valid sample for the proposed study. An Instrument was developed to collect relevant socio-demographic characteristics, health seeking behaviours including sexual behaviour and practices, state of health, knowledge and awareness on HIV and AIDS including risk perception among PLHIV who are on ART. The questionnaire was pretested among ART recipients before finalization. Information was collected on stigma and discrimination that might have affected their accessibility and utilization of ART services. Data was analyzed to look at plausible relationships between drug adherence and all other socio-structural parameters.

Adherence to ART was recorded as taking medications as prescribed by the physician at the correct time and the correct doses during three time periods: last week, last month and the last six months. Missing of one or more doses during last month is defined as operational definition of non-adherence to treatment. Interviews were carried out in the field preceded by taking the informed consent, from the participants. All participants were given full understanding about the importance of the study and their rights not to participate and to withdraw if they decide at any point.

Four positive individuals were recruited as field investigators to carry out the study. After taking informed consent from the individuals, the investigators explained the objective of the study in detail to the interviewees prior to introduction of the questionnaire. All filled in questionnaires were checked by the field supervisor to identify gaps or inconsistencies in the responses. The data was then entered and analyzed using Epi-info package.



Results

Socio-economic background:

Out of the 113 individuals interviewed, the maximum, 23%, was between 30 to 34 years, followed by 17.7% in 35 to 39 years and 40 to 44 years (Table 1). Out of the total, 63.7% were female (Table 2) and 90.3% were married. Out of all interviewed 62.8% were literate (Table 3). Out of the 113, 52.2% were from the sex worker community while the remaining 47.8% were comprised of various employment backgrounds (Table 4).

Adherence:

Based on the operational definition used in the study, only 42.5% of the sample was found compliant to ART treatment. Reasons put forward for non-compliance to ART include side effects of medicine, distance from residence to ART Centre (Table 5), lack of social support, fear to be identified as positive followed by possible social discrimination. A large percentage of ART recipients (22.1%) shared difficulty in reaching the ART centre as the major reason for not collecting medicines regularly. Cost of travelling expenses was identified as one of the prominent demotivating factors. Out of all participants, around 62.8% of them received some kind of support from their family members whereas the remaining 37.2% did not receive supports financially, material or any other social or moral support. Of those who took part in the study, the majority of those who are (71.4%) non-compliant to ART were between the ages of 18 – 24 followed by 35 – 39 year age group (70%). It was found that people from other occupational backgrounds were more (66.7%) non-compliant to their ART regimen when compared to sex workers (49.2%). Non-compliance to ART was found to be more prevalent among those who concealed their positive identity to their family members and or to their neighbors (Table 6).

Those who had symptoms related to side effects of the medicine were less compliant (67.1%) than those (37.8%) who had not suffered from any side effects (Table 7). Those who are active members of a positive people network are more compliant than others (Table 8). Those who do not receive family support are more (59.5%) non-compliant to ART (Table 9). It was also observed that 90% of participants, who have no adequate knowledge regarding consequences of discontinuation of medicine, are more non-compliant to medicine (Table 10) as opposed to those who had adequate knowledge of discontinuation (50.5%). Out of the 113 participants, it was revealed that those who pay more than Rs. 80/-per day as travel expenses are less non-compliant (64.3%) to ART in comparison to those who paid less or nominal sum of money to attend ART Centre (36.4%)(Table 11). Waiting period at the clinic was found to also influence ART adherence. Those who had to wait shorter period of time (less than 30 minutes) at the ART Centre were more (58.8%) compliant to ART compared to those who had to wait longer than 30 minutes to collect medicine (37.5%).

Frequency of non-adherence was more prevalent among participants who are literate compared to those who are illiterate. It was encouraging to note that within the study population those who are members of positive peoples' network showed better compliance to antiretroviral drugs as compared to non members.

Multivariate analysis was done taking into account five major determinants of adherence namely long waiting time at the service outlets, expenses related to travel, attitude and practices of the health care providers (Table 12), distance from residence to ART Centre (Table 13) and those who had suffered from side effects of the medicine.

While carrying out multivariate analysis it was observed that there is no single factor which has more contribution in influencing ART adherence over the others. So it could be concluded that the poor adherence to ART can be attributed to combination of factors as mentioned above.

Discussion:

The World Health Organization (WHO) recommends that accurate assessment of adherence is necessary for effective and efficient treatment planning^{8,9}. Decisions to make change in the treatment regime, and to promote adherence depends on valid and reliable measurement of adherence and reasons behind failure to adhere. Without formal assessment, providers are unlikely to assess and identify level of adherence (and non-adherence) thereby missing the opportunity for reinforcement of the message and possible usage of constructive interventions. If adherence is below optimal levels blood levels of ART recipients would be low and HIV virus will continue to replicate¹⁰. Our study showed that adherence among the ART recipients is as low as 48%. With this level of adherence it is highly unlikely that the virus load will come down at a level that would help improvement of health status and prevention of opportunistic infection among the ART recipients and will not make him/her noninfective. HIV is highly adaptive to viral-suppressing pressures and can rapidly mutate to develop resistance^{11,12}. In some cases ART may still improve CD4 cell count despite ongoing viral replication due to development of mutant viruses which emerge less fit and less destructive than the wild-type of HIV strain¹³.

Complete viral suppression is defined as less than 40 HIV copies/ml of blood¹⁴. Failure to sustain complete viral suppression is a precursor for the development of HIV mutation followed by treatment failure¹⁵ leading to progression of the disease. Moreover, development of resistance against the first line of treatment reduces physician choices leaving behind only the more costly options to start with second or third line of ART treatment. Transmission of HIV including the mutated strain through exchange of body fluid will create major public health problems in addition to increase the burden for heightened expenditure.

Studies have established that up to 95% adherence is necessary for HIV viral

suppression^{16,17}. Studies have linked the relationship between adherence and viral load (VL), as adherence decreased¹⁸ VLs increase sharply in a dose-response effect and it is possible to conclude that greater adherence levels are associated with greater reduction in VLs^{19,20}. Accurate and reliable measures of adherence and better understanding of both barriers and facilitators of adherence is needed to help clinicians identify patients who need additional assistance with their pill taking, to design and evaluate effective interventions to enhance adherence, and to interpret the role of adherence in evaluating clinical outcomes and making treatment decisions^{21,22}. Our research shows that major barriers to ART adherence are long waiting time, distance from house to ART Centre, burden of travelling expense and fear of discrimination and behaviour of staff at the ART centres.

In order to identify adherence related issues and challenges (irrespective of which class of ART patients are on) and to develop appropriate interventions, adherence measurement is fundamental and tools need to be developed to assess adherence^{23,24,25}. In India, at present there are more than 500,000 cases registered under ART having no mechanism in place for systematic collection of data or analysis of ART uptake and adherence there is an urgent need to probe into these issues with an objective to find out possible gaps and challenges. Our findings suggest that reasons behind non-compliance to ART are many and multiple in nature as observed in other studies^{26,27}. Various familial, social and structural factors affect regular intake of ART at individual level. It is of paramount importance to address those underlying factors so as to improve the quality of life of positive people through influencing their ART adherence behavior and practices^{28,29,30,31}.

Conclusion

It is assumed that multiple stakeholders at various levels influence ART adherence. Without undermining the role of service providers in improving ART adherence one needs to look into a gamut of socioeconomic and cultural factors as observed in our findings^{32,33,34}. In India ARTs are made available and accessible to all those who need it and is provided free of cost. However poor compliance to ART is likely to diminish the effectiveness of any national program on care and treatment³⁵. The outcome of this study can help in designing a better framework of service delivery program to improve ART adherence, which in turn would help improve the quality of life for positive peoples while preventing the occurrence of a resistance strain. Ensuring adherence would also help prevention programs as the infected individuals who are receiving ART regularly will be noninfective and unable to transmit infection..

The efficacies of the current antiretroviral drugs are extremely good. Therefore, the most important factor for virological control depends on high degree of adherence. From the public health point of view the significance of transmission of HIV from the infected individual to others would be nil or significantly less, provided the infected individual is adhered to ART. These could be a huge waste of national resources provided the objective of ART failed to bring about desired outcome in the life of the individuals due to poor adherence leading to development of a resistant strain. This would force the physician to prescribe more costly 'second' or 'third' lines of ART regimen.

The following recommendations have emerged from the study. There is a need to develop an effective mechanism to monitor ART adherence at each ART Centres followed by analysis and interpretation of data. This would help providing requisite feedback to physician and to develop system to improve adherence to ART. A system should be in place to support of HIV positive patients through linking them with HIV support groups and networks. More social

and clinical support services have to be organized closer to the residences of the positive HIV people. This could be made possible through routing delivery of services through community based organizations and positive people networks. Early identification of side effects and a user-friendly system of management needs to be developed and delivered at the earliest opportunity. The ART centers should review their patient flow system and bring down the waiting time for patients who attend clinics.

ART adherence is a big challenge, there is no shortcut procedure to improve adherence among the ART recipients. It requires effective communication with the patients, aided with adequate social support, and encouragement to the positives. All other factors identified in the study linked stigma and discrimination. This has to be address through an introduction of a system for reporting cases of discrimination, followed by counseling and training of the service providers with provisions for compensation to those discriminated against.

Tables

Table 1: ART Compliance among people of different age group

| ART Compliance | | Age Group | | | | | | | Total |
|----------------|-------------------------------|-----------|---------|---------|---------|---------|---------|--------------|-------|
| | | 18 – 24 | 25 – 29 | 30 – 34 | 35 – 39 | 40 – 44 | 45 – 49 | 50 and above | |
| No | Count | 5 | 8 | 10 | 14 | 12 | 9 | 7 | 65 |
| | % within age group (in years) | 71.4 | 53.3 | 38.5 | 70.0 | 60.0 | 64.3 | 63.6 | 57.5 |
| Yes | Count | 2 | 7 | 16 | 6 | 8 | 5 | 4 | 48 |
| | % within age group (in years) | 28.6 | 46.7 | 61.5 | 30.0 | 40.0 | 35.7 | 36.4 | 42.5 |
| Total | Count | 7 | 15 | 26 | 20 | 20 | 14 | 11 | 113 |
| | % within age group (in years) | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |

Out of the 113 interviewees, the maximum (71.4%) non-compliant found was in the age group of 18 – 24 years followed by those in the age group of 35 – 39 years.

Table 2: ART Compliance among genders

| Gender | Compliant | Non-compliant |
|--------|------------|---------------|
| Male | 11 (26.8%) | 30 (73.2%) |
| Female | 37 (51.4%) | 35 (48.6%) |

Out of the 113 interviewees, it was found that males were more (73.2%) non-compliant to ART compared to females (48.6%)

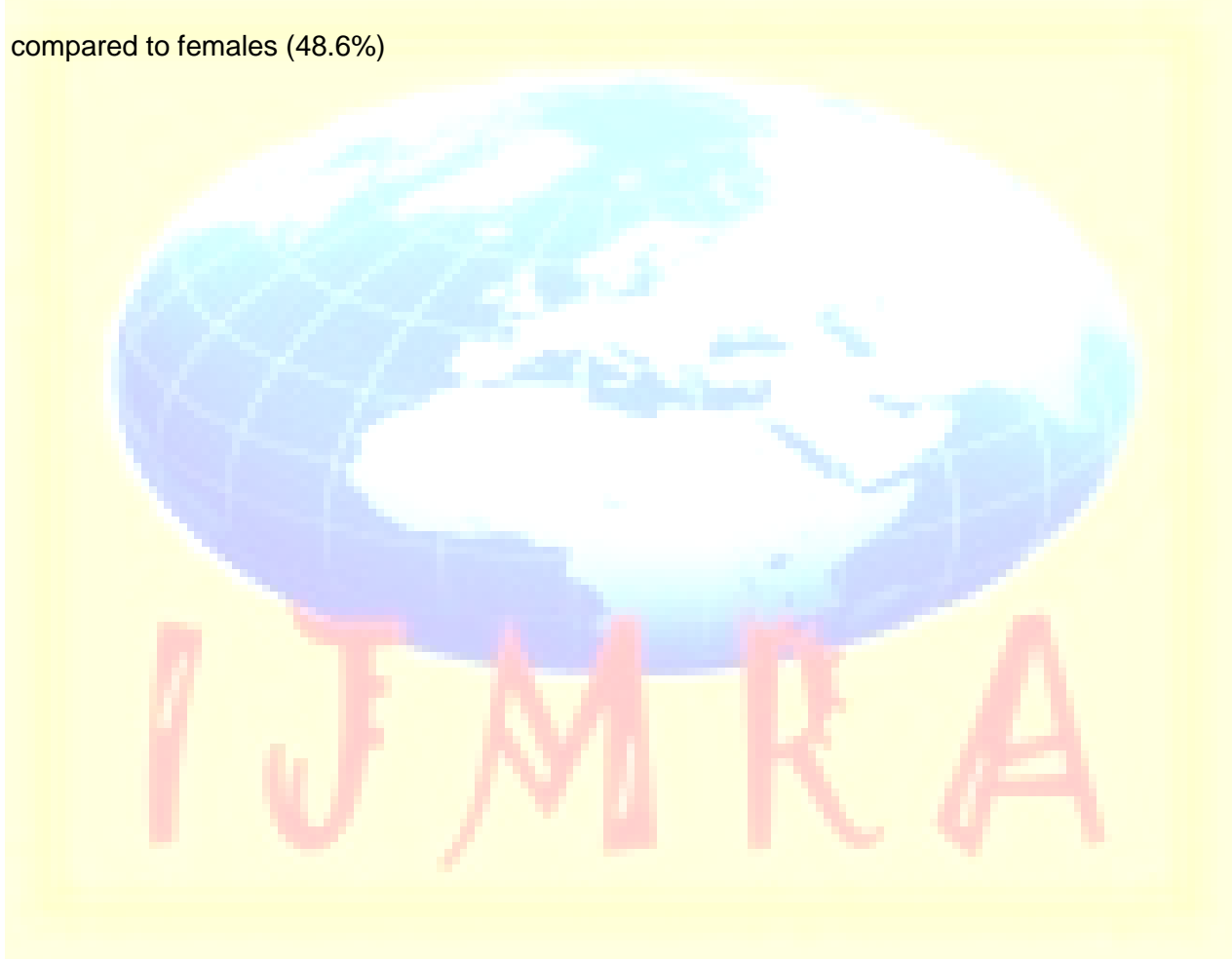


Table 3: ART Compliance among people of different educational status

| ART Compliance | | Educational Status | | Total |
|----------------|-----------------------------|--------------------|----------|-------|
| | | Illiterate | Literate | |
| No | Count | 18 | 47 | 65 |
| | % within Educational status | 42.9 | 66.2 | 57.5 |
| Yes | Count | 24 | 24 | 48 |
| | % within Educational status | 57.1 | 33.8 | 42.5 |
| Total | Count | 42 | 71 | 113 |
| | % within Educational status | 100 | 100 | 100 |

Out of the 113 interviewees, it was found that educated individuals are more (66.2%) non-compliant to ART compared to illiterates (42.9%)

Table 4: ART Compliance among people of different occupation

| ART Compliance | | Occupation | | Total |
|----------------|---------------------|---|------------|-------|
| | | All other occupation in combination | Sex Worker | |
| No | Count | 36 | 29 | 65 |
| | % within occupation | 66.7 | 49.2 | 57.5 |
| Yes | Count | 18 | 30 | 48 |
| | % within occupation | 33.3 | 50.8 | 42.5 |
| Total | Count | 54 | 59 | 113 |
| | % within occupation | 100 | 100 | 100 |

Out of the 113 interviewees, it was found that people from all other occupation in combination are more (66.7%) non-compliant to ART compared to sex workers (49.2%)

Table 5: ART Compliance among people who has difficulty in reaching centre

| ART Compliance | | Difficult to reach centre | | Total |
|----------------|------------------------------------|---------------------------|------|-------|
| | | No | Yes | |
| No | Count | 52 | 13 | 65 |
| | % within difficult to reach centre | 59.1 | 52.0 | 57.5 |
| Yes | Count | 36 | 12 | 48 |
| | % within difficult to reach centre | 40.9 | 48.0 | 42.5 |
| Total | Count | 88 | 25 | 113 |
| | % within difficult to reach centre | 100 | 100 | 100 |

Out of the 113 interviewees, who finds difficulty in reaching to the centre are in fact less (52.0%) non-compliant to ART compared to those who do not find it difficult to reach to the ART Centre (59.1%)

Table 6: ART Compliance among people whose neighbor knows the result

| ART Compliance | | Neighbor knows your positive status | | Total |
|----------------|---|--|------|-------|
| | | No | Yes | |
| No | Count | 49 | 16 | 65 |
| | % within neighbor knows your positive status | 57.6 | 57.1 | 57.5 |
| Yes | Count | 36 | 12 | 48 |
| | % within neighbor knows your positive status | 42.4 | 42.9 | 42.5 |
| Total | Count | 85 | 28 | 113 |
| | % within neighbor knows your positive status | 100 | 100 | 100 |

Out of the 113 interviewees, it was found that non-compliance was more than 50% whether their positive status was known to the neighbor or not

Table 7: ART Compliance among people who feels side effects to take medicine

| ART Compliance | | Feel any side effects to take medicine | | Total |
|----------------|---|---|------|-------|
| | | No | Yes | |
| No | Count | 14 | 51 | 65 |
| | % who has not suffered from any side effects to take medicine | 37.8 | 67.1 | 57.5 |
| Yes | Count | 23 | 25 | 48 |
| | % who has not suffered from any side effects to take medicine | 62.2 | 32.9 | 42.5 |
| Total | Count | 37 | 76 | 113 |
| | % who has not suffered from any side effects to take medicine | 100 | 100 | 100 |

Out of the 113 interviewees, it was found that those who had suffered from any side effects were more non-compliant (67.1%) to ART compared to 37.8% of them who were having no side effects

Table 8: ART Compliance among people who are member of various networks

| ART Compliance | | Member of | | | | Total |
|----------------|--------------------|-----------|-------------------|-------------------------|---------------------|-------|
| | | None | Mamata Network | Krishnanagar Network | Ranaghat Network | |
| No | Count | 14 | 32 | 10 | 9 | 65 |
| | % within member of | 63.6 | 52.5 | 83.3 | 50.0 | 57.5 |
| Yes | Count | 8 | 29 | 2 | 9 | 48 |
| | % within member of | 36.4 | 47.5 | 16.7 | 50.0 | 42.5 |
| Total | Count | 22 | 61 | 12 | 18 | 113 |
| | % within member of | 100.0 | 100.0 | 100.0 | 100.0 | 100 |

Out of the 113 interviewees, it was found that those who were members of Ranaghat Network (50.0%) and Mamata Network (52.5%) were less non-compliant

Table 9: ART Compliance among people who receive family support

| ART Compliance | | Receive family support | | Total |
|----------------|---------------------------------|------------------------|------|-------|
| | | No | Yes | |
| No | Count | 25 | 40 | 65 |
| | % within receive family support | 59.5 | 56.3 | 57.5 |
| Yes | Count | 17 | 31 | 48 |
| | % within receive family support | 40.5 | 43.7 | 42.5 |
| Total | Count | 42 | 71 | 113 |
| | % within receive family support | 100 | 100 | 100 |

Out of the 113 interviewees, it was found that those who do not receive family support were more (59.5%) non-compliant to ART compared to those who received support (56.3%)

Table 10: ART Compliance among people who has knowledge about effect of discontinuation of medicine

| ART Compliance | | Knowledge about effect of discontinuation of medicine | | Total |
|----------------|---|---|------|-------|
| | | No | Yes | |
| No | Count | 18 | 47 | 65 |
| | % has knowledge about effect of discontinuation of medicine | 90.0 | 50.5 | 57.5 |
| Yes | Count | 2 | 46 | 48 |
| | % has knowledge about effect of discontinuation of medicine | 10.0 | 49.5 | 42.5 |
| Total | Count | 20 | 93 | 113 |
| | % has knowledge about effect of discontinuation of medicine | 100 | 100 | 100 |

Out of the 113 interviewees, it was found that those who had no knowledge about effect of discontinuation of medicine were more (90.0%) non-compliant to ART compared to those who had knowledge about effect of discontinuation (50.5%)

Table 11: ART Compliance among people whose travel cost to reach ART Centre is expensive

| ART Compliance | | Travelling Expense | | Total |
|----------------|-----------------------------|--------------------|------|-------|
| | | No | Yes | |
| No | Count | 4 | 9 | 13 |
| | % within Travelling Expense | 36.4 | 64.3 | 52.0 |
| Yes | Count | 7 | 5 | 12 |
| | % within Travelling Expense | 63.6 | 35.7 | 48.0 |
| Total | Count | 11 | 14 | 25 |
| | % within Travelling Expense | 100 | 100 | 100 |

Out of the 113 interviewees, it was found that those whose travelling expense was more were more (64.3%) non-compliant to ART compared to those whose travelling expense was less (36.4%)

Table 12: ART Compliance among people which depended on behavior of health staff

| ART Compliance | | Behavior of health staff | | Total |
|----------------|-----------------------------------|--------------------------|-------|-------|
| | | No | Yes | |
| No | Count | 13 | | 13 |
| | % within Behavior of health staff | 54.2 | | 52.0 |
| Yes | Count | 11 | 1 | 12 |
| | % within Behavior of health staff | 45.8 | 100.0 | 48.0 |
| Total | Count | 24 | 1 | 25 |
| | % within Behavior of health staff | 100 | 100 | 100 |

Out of the interviewees, it was found that behavior of staffs did not have any effect on compliance

Table 13: ART Compliance among people whose house is far from ART Centre

| ART Compliance | | Far from the house | | Total |
|----------------|----------------------|--------------------|------|-------|
| | | No | Yes | |
| No | Count | 3 | 10 | 13 |
| | % far from the house | 42.9 | 55.6 | 52.0 |
| Yes | Count | 4 | 8 | 12 |
| | % far from the house | 57.1 | 44.4 | 48.0 |
| Total | Count | 7 | 18 | 25 |
| | % far from the house | 100 | 100 | 100 |

Out of the 113 interviewees, it was found that those whose house was further away from the ART Centre were more (55.6%) non-compliant to ART compared to those whose house were nearby (42.9%)

Bibliography

- ¹ Sethi AK, Celentano DD, Gange SJ, Moore RD, Gallant JE: Association between adherence to antiretroviral therapy and human immunodeficiency virus drug resistance. *Clin Infect Dis* 2003, 37(8):1112-8.
- ² Porco TC, Martin JN, Page-Shafer KA, et al. Decline in HIV infectivity following the introduction of highly active antiretroviral therapy. *AIDS* 2004;18:81-88
- ³ Hoffmann C, Mulcahy F: Goals and Principles of Therapy – Eradication, Cost, Prevention, Adherence. [<http://www.hivmedicine.com/textbook/haart/goals2.htm>] website.
- ⁴ Turner BJ: Adherence to antiretroviral therapy by HIV-infected patients. *Journal of Infectious Disease* 2002, 185(S2):S143-51.
- ⁵ Fogarty L, Roter D, Larson S, Burke J, Gillespie J, Levy R: Patient adherence to HIV medication regimens: a review of published and abstract reports. *Patient Educ Couns* 2002, 46(2):93-108.
- ⁶ Castilla J, del Romero J, Hernando V, Marincovich B, Garcia S, Rodriguez C. Effectiveness of highly active antiretroviral therapy in reducing heterosexual transmission of HIV. *JAIDS* 2005;40:96-101.
- ⁷ Haynes RB. *Determinants of compliance: the disease and the mechanics of treatment*. In: Haynes RB, Sackett DL, editors. *Compliance in health care*. Baltimore: Johns Hopkins University Press; 1979. p. 49-62.
- ⁸ Arnsten, JH., Demas, PA., Farzadegan, H., Grant, RW., Gourevitch, MN., Chang, CJ., Schoenbaum, EE. (2001). Antiretroviral Therapy Adherence and viral suppression in HIV-Infected drug users: Comparison of self-report and electronic monitoring. *Clin Infect Dis.*, 33(8), 1417-1423.
- ⁹ Bangsberg, D.R., et al., (2001). Non-adherence to highly active antiretroviral therapy predicts progression to AIDS. *AIDS*, 15(9), 1181-1183.

- ¹⁰ Gulick, R. M. (2006). Adherence to antiretroviral therapy: how much is enough? *Clin Infect Dis*, 43(7), 942-944.
- ¹¹ Simoni JM, Pearson, C., Pantalone, D., & et al. (2006). Efficacy of interventions in improving highly active antiretroviral therapy adherence and HIV-1 RNA viral load: A meta-analytic review of randomized controlled trials. *JAIDS*, 43:(S1), S23-S35.
- ¹² Walsh, J. C., Pozniak, A. L., Nelson, M. R., Mandalia, S., & Gazzard, B. G. Virologic rebound on HAART in the context of low treatment adherence is associated with a low prevalence of antiretroviral drug resistance. *J Acquir Immune Defic Syndr*. 2002 Jul 1;30(3):278-87.
- ¹³ Wood, E., et al., *The impact of adherence on CD4 cell count responses among HIV-infected patients*. *J Acquir Immune Defic Syndr*. 2004 Mar 1;35(3):261-8.
- ¹⁴ Bangsberg DR, Hecht FM, Charlebois ED, et al. *Adherence to protease inhibitors, HIV-1 viral load, and development of drug resistance in an indigent population*. *AIDS* 2000; 14:357-66.
- ¹⁵ Paasche-Orlow MK, Cheng DM, Palepu A, Meli S, Faber V, Samet JH: Health literacy, antiretroviral adherence, and HIV-RNA suppression: a longitudinal perspective. *J Gen Intern Med* 2006, 21(8):835-40.
- ¹⁶ Bangsberg DR, H. F., Charlebois ED, et al. (2000). Adherence to protease inhibitors, HIV-1 viral load, and development of drug resistance in an indigent population. *AIDS*, 14, 357-366.
- ¹⁷ Bangsberg, D. R. (2006). Less than 95% adherence to no nucleoside reverse-transcriptase inhibitor therapy can lead to viral suppression. *Clin Infect Dis*, 43(7), 939-941.

- ¹⁸ Maggiolo F, A.M., Kleinlog HD, et al., (2007). Effect of adherence to HAART on virologic outcome and on the selection of resistance-conferring mutations in NNRTI- or PI-treated patients. *HIV Clin Trials*, 8, 282-292.
- ¹⁹ Mills EJ, N. J., Bangsberg, et al., (2006). Adherence to HAART: a systematic review of developed and developing patient-reported barriers and facilitators. *Plos Med*, 3, e438.
- ²⁰ Mills EJ, N.J., Buchan I, Orbinski J, Attaran A, et al., (2006). Adherence to antiretroviral therapy in sub-Saharan Africa and North America: a meta-analysis. *JAMA*, 296, 679-690.
- ²¹ Parienti JJ, Massari V, Descamps D, Vabret A, Bouvet E, Larouzé B, & Verdon R. (2004). Predictors of virologic failure and resistance in HIV-infected patients treated with nevirapine- or efavirenz-based antiretroviral therapy. *Clin Infect Dis.*, 38(9),1311-1316.
- ²² Paterson, D.L., et al., (2000) Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. *Ann Intern Med.* 133(1), 21-30.
- ²³ Battaglioli-DeNero, A. M. (2007). Strategies for improving patient adherence to therapy and long-term patient outcomes. *J Assoc Nurses AIDS Care*, 18(1 Suppl), S17-22.
- ²⁴ Bangsberg., D. (2008). Preventing HIV antiretroviral resistance through better monitoring of treatment adherence. *The Journal of Infectious Diseases*, 197, S272-278.
- ²⁵ Mannheimer, S., et al., (2008). A randomized comparison of two instruments for measuring self-reported antiretroviral adherence. *AIDS Care*, 20(2): p. 161-9.
- ²⁶ Gardner, EM., Sharma, S., Peng, G., Hullsiek, K., Burman, WJ., MacArthur, RD., Mannheimer, SB. 2008). Differential adherence to combination antiretroviral therapy is associated with virological failure with resistance. *AIDS*, 22, 75-82.
- ²⁷ Johnson, M.O., et al., (2005). Perceived adverse effects of antiretroviral therapy. *J Pain Symptom Manage.* 29(2):193-205.

- ²⁸ Malta M, Strathdee SA, Magnanini MM, & Bastos, F. (2008). Adherence to antiretroviral therapy for human immune deficiency syndrome among drug users: a systematic review. *Addiction*, 103, 1242-1257.
- ²⁹ Erickson, S.R., et al., (1998). Use of a paging system to improve medication self-management in patients with asthma. *J Am Pharm Assoc.* 38(6):767-769.
- ³⁰ Chakrapani, V., Newman, P. A., Shunmugam, M., Kurian, A. K., & Dubrow, R. (2009). Barriers to Free Antiretroviral Treatment Access for Female Sex Workers in Chennai, India. *Aids Patient Care and Stds*, 23(11), 973-980.
- ³¹ Gross, R., et al., (2002). *Provider inaccuracy in assessing adherence and outcomes with newly initiated antiretroviral therapy.* *AIDS.* 16(13):1835-7.
- ³² Bangsberg, D. R., Charlebois, E. D., Grant, R. M., Holodniy, M., Deeks, S. G., Perry, S., et al. (2003). High levels of adherence do not prevent accumulation of HIV drug resistance mutations. *AIDS.* 17(13), 1925-1932.
- ³³ Montaner, J. S., Reiss, P., Cooper, D., Vella, S., Harris, M., Conway, B., et al. (1998). A randomized, double-blind trial comparing combinations of nevirapine, didanosine, and zidovudine for HIV-infected patients: the INCAS Trial. Italy, the Netherlands, Canada and Australia Study. *JAMA*, 279(12):930-7.
- ³⁴ Ware NC, Wyatt MA, & T, T. (2006). Social relationships, stigma and adherence to antiretroviral therapy for HIV/AIDS. *AIDS Care*, 18(8):, 904-910
- ³⁵ Rueda S, Park-Wyllie LY, Bayoumi A, & et al. (2006). Patient support and education for promoting adherence to highly active antiretroviral therapy for HIV/AIDS (Review).