INTRODUCTION

Out of the 40 million people living with HIV/AIDS worldwide, at the most reside in the developing countries and approximately 6 million are in immediate need of antiretroviral (ARV) therapy.1,2 Pakistan is the second largest country in South Asia that stands only a few steps behind India and Nepal in terms of HIV epidemic. Despite of many efforts, the HIV infection rate has been increased significantly over the past few years and the country has moved from a low prevalence to concentrated epidemic with HIV prevalence of more than 5% among Injecting Drug Users (IDUs), in at least eight major cities.3

Since 1987, over 4000 cases have been reported to the National AIDS Control Programme (NACP), Ministry of Health. NACP, WHO and the UN Programme on HIV/AIDS (UNAIDS) have estimated that there may be 80,000 persons living with HIV, although actual data suggested about half that number.4,5 Highly active antiretroviral therapy (HAART) has caused a dramatic decline in mortality.6,7

On the basis of data reported by Paterson, 95% adherence to therapy is widely cited as the minimum level of adherence necessary to maintain an HIV load suppression of 400 copies/ml in the majority of individuals.6

The widespread use since 1996 of highly active antiretroviral therapy (HAART) a combination of at least three drugs that includes either a protease inhibitor (PI) or a non-nucleoside-analogue reverse transcriptase inhibitor (NNRTI) and two nucleoside analogue reverse-transcriptase inhibitors (NRTIs) has significantly improved the prognosis of HIV-1 infected patients.6,8

Misconceptions, ways of life, poverty and unawareness are among the factors that could compose the greatest challenge to wide reception and adherence to ART.9-14 Since adherence is the basis of successful ART, there is

ABSTRACT

Objective: To describe the treatment outcomes in terms of adherence, outcomes and side effects of antiretroviral (ARV) agents.

Study Design: An observational study.

Place and Duration of Study: Teaching Hospital of Khyber Medical University, Institute of Medical Sciences, Kohat, from February 2007 to December 2012.

Methodology: Human Immunodeficiency Virus (HIV) positive patients, taking 1st line ARV agents for at least 6 months were included. Adherence was calculated by self report on asking the number of doses missed in last 30 days. ARVs were provided on monthly basis. Adherence data was noted over a period of 6 months. ARVs outcomes were recorded in the form of adherence, CD4 count, functional status of the patient, change in weight, further transmission of the disease, number of hospital admissions and deaths. Adverse Drug Reactions (ARDs) to ARVs were assessed clinically and by laboratory markers. Mean and standard deviation were calculated for numerical variables while frequencies and percentages were calculated for categorical variables.

Results: Total number of patients included in this study were 107. Out of them, 66.4% were males and 33.6% were females. The mean age was 39.9 ± 13.80 years. Patients taking AZT/3TC/NVP, AZT/3TC/EFZ, D4T/3TC/NVP, D4T/3TC/EFZ, TNF/3TC/NVP EFZ were 49.5%, 22.4%, 10.3%, 4.7% and 13% respectively. Most adverse affects were observed in 10 days to 90 days of initiation of therapy. Rash was observed in 71 (66.4%) patients, anaemia in 4 (3.7%) patients while only one patient (0.93%) had nausea / vomiting. Thirty (28%) patients reported no side effects. Out of 107 patients, 98 (91.5%) were alive whereas 9 (8.4%) died at the end of the study period. Twelve patients had one hospital admission (11.21%) whereas 9 (8.4%) patients had two admissions during the study period. The first mean CD4 was 325.27 cells /mL whereas mean last CD4 count was 389.86 cells/mL.

Conclusion: ARVs have very satisfactory outcomes in HIV/AIDS patients, provided they are started at proper stage of the disease. Treatment outcomes in this study are comparable with reported previously in developed countries.

Key Words: HIV. AIDS. Antiretroviral agents. Treatment outcome.
a need to evaluate the treatment outcomes of ART interventions against these factors which are considered as obstacles to mounting concerted ART programmes.9-14

The objective of this study was to describe the treatment outcomes in terms of adherence outcomes and side effects of ARVs.

METHODOLOGY

Patients taking ARVs from February 2007 to December 2012 were included in a retrospective observational study. Adherence was calculated by self report on asking the number of doses missed in last 30 days and was assumed as ARVs taking habit for whole period since start till filling of proforma for adherence. Provision of ARVs and follow-up of patients were done on monthly basis. Collection of adherence data was started in July 2012 and completed in 6 months. A total of 107 patients, who were taking 1st line ARVs for at least 6 months, were included in the study. Data was analyzed using Statistical Package for Social Sciences (SPSS) version 14. Mean and standard deviation were calculated for numerical variables while frequencies and percentages were calculated for categorical variables. Adherence was calculated according to following formula:

\[
\text{Adherence} = \frac{\text{Total number of doses to be taken} - \text{Number of doses missed}}{\text{Total doses}} \times 100
\]

ARVs outcomes in the form of adherence, CD4 count, functional status of the patient, change in weight, further transmission of disease, number of hospital admissions and deaths were calculated. Adverse Drug Reactions (ADRs) to ARVs were assessed clinically and by laboratory markers.

Patients with positive rapid test were advised enzyme-linked immunosorbent assay (ELISA) for HIV antibodies. Those having positive ELISA test were registered in the ARVs centre. After that, patient were counselled, clinically evaluated and then subjected to laboratory investigations. Booking of registered patients for CD4 count were done at Pakistan Institute of Medical Sciences (PIMS), Islamabad. If patients were found clinically eligible (i.e. clinical stage 4 irrespective of CD4 count, or clinical stage 3 or CD4 count < 350 cells/mL) and agreed to adhere to treatment, then one of the following first-line regimens was started including Zidovudine (ZDV) (300 mg) + Lamivudine (3TC) (150 mg) + Nevirapine (NVP) (200 mg) or Efavirenz (EFV) (600 mg) or Stavudine (D4T) (30 mg) / Tenofrivir TFN + 3TC (150 mg) + NVP (200 mg) or EFV (600 mg).

ARV agents were provided free of cost to the patients along with treatment of opportunistic infections (OIs). Vaccination against Hepatitis B virus (HBV) and pneumococcal pneumonia was also provided free of charge. Voluntary counselling and testing services were also provided to the families of HIV positive patients. This study was approved by the ethical committee of the institute.

RESULTS

Total number of patients included in this study were 107. Out of them, 71 (66.4%) were males and 36 (33.6%) were females. All patients were on antiretroviral first-line agent regimen and remained on it until the last visit to ARVs centre for refilling. Among them, 27 (25.23%) males and 15 (14%) females were treatment naive patients whereas 52 (48.6%) males and 13 (12.15%) females were referred from another HIV treatment centre and they were already taking ARVs.

Patients taking AZT/3TC/NVP, AZT/3TC/EFZ, D4T/3TC/NVP, D4T/3TC/EFZ, TNF/3TC/NVP or EFZ were 49.5%, 22.4%, 10.3%, 4.7% and 13% respectively (Table I).

Patients with age group from 21 - 30 were 21 (19.6%), 31 - 40 were 32 (29.9%), 41-50 were 25 (23.4%), 51 - 60 were 19 (17.8%), age less than 20 years were 7 (6.5%) and more than 60 years were 3 (2.8%). The mean age of patients registered for treatment was 39.90 ± 13.80 years.

Most adverse affects were observed in 10 days to 90 days of initiation of the therapy. Rash was observed in 71 patients (66.4%) taking Nevirapine, 4 patients (3.7%) presented with anaemia taking Zidovudine while only one patient (0.93%) presented with severe nausea/vomiting. Thirty patients (28%) reported no side effects.

During the 6 years treatment period, 19.6% of patients (21/107) had one or more hospital admissions for opportunistic infections (OIs). The frequency of OIs was highest in the initial months of treatment. Tuberculosis (TB) was the most common OI, found in 10 patients (9.63%).

In this study, 27 (25.5%) patients were on ARVs for 1 year, 26 (24.3%) were for 3 - 6 years, 24 (22.4%) were for 1 - 3 years, 13 (12.14%) were with 6 months duration, 10 (9.3%) were with 6 years duration and 7 (6.5%) patients were with 9 months duration. Weight and CD4 counts of the patients improved during the treatment period. The mean weight gain was 57.54 ± 1.45 kg in 6 months treatment period. Mean weight at start of treatment was 56.51 ± 14.47 kg and mean weight after 6 months taking ARVs were 58.57 ± 14.62 kg.

Out of 107 patients, 98 (91.5%) were alive whereas 9 (8.4%) died during the study period. Out of 98 patients who were alive, 72 (73.47%) were working whereas 26 (26.53%) were non-working but they were not bedridden.
Table I: Demographic data.

<table>
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<th>Demography</th>
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<tr>
<td>WHO staging</td>
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<tr>
<td>Stage I/II</td>
<td>79</td>
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<tr>
<td>Stage III A</td>
<td>25</td>
<td>23.4</td>
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<td>Stage IV</td>
<td>1</td>
<td>0.9</td>
</tr>
<tr>
<td>Treatment</td>
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</tr>
<tr>
<td>AZT / 3TC / NVP</td>
<td>53</td>
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</tr>
<tr>
<td>AZT / 3TC / EFZ</td>
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Base line CD4 count was available in 74 patients. Last CD4 count was available in 45 patients. The mean of first CD4 is 325.27 cells / mcL whereas mean of last CD4 count was 389.86 cells / mcL.

Hundred percent adherence is observed in 88 (82.2%) patients, 34% adherence in 4 patients (3.7%), 12 (11.2%) patients were not taking ARVs, 67% adherence was observed in 2 (1.9%) patients and 93% adherence was observed in 1 (0.9%) patient.

DISCUSSION

Analysis of demographic profile of the patients showed that majority of those most at the risk of HIV/AIDS are youth but the proportion of males in the treatment group was almost double of females. This is unlike the results reported by Ngwai et al.15 ARVs initiations in the patients were done according to WHO guidelines for developing countries. A large number of patients presented very late to treatment facility, with poor baseline parameters like low CD4 count, associated OIs, hepatitis B or C infection and low body weight but treatment outcomes remained satisfactory.

This study revealed that first line regimen is effective, provided good adherence is reassured. The survival rate in 6 years period of these patients was 91.6% whereas death was 8.4%. The causes of death in majority of patients are non-adherence, irregularity in ARVs use at some time of their treatment period, co-infections like hepatitis B, C disease and injection drug use. Two female patients died because of poor adherence due to associated depression. Whereas out of 7 male patients, 3 injection drug users were suffering from chronic hepatitis B or C infection as well. But co-infection by then had not resulted in chronic liver disease. Therefore, it may be assumed that compliance may increase survival. Associated interesting finding in this study was that patients who were indulged in injection drug use were suffering more from hepatitis B, C co-infections. Other factors which had resulted death of patients were low initial CD4 count on initiation of ARVs because one male was having 8 CD4 count on commencement of therapy and pulmonary tuberculosis as well. In this study non-adherence, injection drugs use, and OIs are the major risk factors for poor treatment outcomes. Among OIs tuberculosis is major killer in patients with low CD4 count. Adherence to medication and lifestyle changes is a key factor to positive treatment outcomes in the therapy of HIV/AIDS.

In comparable studies conducted in developed countries, rates of adherence by self report ranged from 40% to 70%, whereas in this study, rate of adherence was better i.e, 100% in 88.3% patients. The reason may be regular counselling on every visit, and good working relationship of the healthcare providers with the patients. Ninety three percent adherence was observed in 1 patient because he could not manage to reach the treatment center in time. Otherwise he had 100% adherence since he started medication till his second last visit. Among 4 patients with 37% adherence, one female became severely anemic and she missed doses for some days. Three patients were IDUs, who were very irregular in taking medications. It is believed that free of cost and easily approachable treatment is an important factor for enhancing retention in antiretroviral treatment and continued long-term immuno-virological response which had been illustrated by the situation in Brazil, where a free national programme had wide coverage with satisfactory outcomes.

Since Adverse Drug Reactions (ADRs) are the most common reason for reduced adherence to treatment, identifying risk factors for the occurrence of ADRs is of fundamental importance to optimize the initial choice of ARVs regimen before initiating therapy and to adapt the swiftness of supervision to each unique situation. However, in this study, only few patients dropped medications due to side effects.

In this study, most of the side effects were observed in first 3 months of initiation of ARVs, except in 2 patients; one became anaemic after 3 years of initiation of AZT and the other experienced psychotic symptoms after 4 years of EFZ. This call for the need to intensify long-term ADRs monitoring in patients on ARVs.

Rash was observed in 66.4% of patients and anaemia in 3.7% of patients and occurred exclusively in patients on AZT. This is similar to other studies conducted in Nigeria, Côte d'Ivoire, Haiti and India that observed anaemia rates of 3% - 12%. Skin toxicity results are quite high in this study as compared to18% in other reports. One
patient died due to grade 4 rash in this study. In this study, patients receiving ART revealed significant increase in CD4-cell count, improvement in activity status and weight gain that is comparable to other studies.24

CONCLUSION

ARVs have very satisfactory outcomes in HIV/AIDS patients, if started at proper stage of the disease. Treatment outcomes in this study are comparable to that reported in the developed countries.

REFERENCES


2. The WHO and UNAIDS Global Initiative to provide antiretroviral therapy to 3 million people with HIV/AIDS in developing countries by the end of 2005 [Internet]. Available from: http://www.unaids.org


