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THE CLINICAL STUDY OF PRIMARY DRUG RESISTANCE IN HIV POSITIVE PATIENTS

General Medicine

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ABSTRACT

Introduction: India has the second largest number of HIV infections in the world. Since the introduction of generic antiretrovirals (ARVs) in 2000, there has been a steep increase in the number of individuals initiating antiretroviral therapy (ART) primarily due to the reduction in cost of ART. Highly active antiretroviral therapy (HAART) has dramatically improved survival and quality of life in people living with HIV and AIDS.
Objective: Study of WHO stage, CD4 count and viral load after starting 2nd line ART.
Materials And Methods: Patients were given prophylactic treatment for OI based on NACO guidelines. Patients were closely observed and followed up for clinical failure, immunological failure and virological failure.
Results : Mean viral load in treatment failure was 231331 copies/ml and after 2nd line ART it was 697.63 copies/ml (P<0.05). 37% patients were in WHO stage I and 25% patients in stage IV who are on 1st line ART. After 2nd line ART 58% patients were in WHO stage I and 6% patients in WHO stage IV. 43 patients on 1st line ART were in between 40-49 kg. 42 patients on 2nd line ART were in between 40-49 kg weight. Mean weight of treatment failure patients was 47.17 kg while mean weight after 2nd line ART was 47.8 kg (P>0.05). Weight improvement required longer time monitoring than immunological and virological monitoring.
Conclusion : Patients, who are not responding to 1st line ART, must switch over to 2nd line ART as early as possible after ruling out adherence issue and significant drug interaction and co morbid conditions.

KEYWORDS

AIDS, ARV, Antiretroviral Therapy (ART), WHO Staging

INTRODUCTION

India has the second largest number of HIV infections in the world. Since the introduction of generic antiretrovirals (ARVs) in 2000, there has been a steep increase in the number of individuals initiating antiretroviral therapy (ART) primarily due to the reduction in cost of ART from INR 35000 a month to approximately INR 1000 a month[1].

Highly active antiretroviral therapy (HAART) has dramatically improved survival and quality of life in people living with HIV and AIDS. However, these benefits can be greatly compromised by the drug- resistant forms of the virus. As the first therapeutic regimen is probably the most important for virologic suppression, drug-resistant variants of HIV greatly challenge the efficacy of HAART in producing adequate viral suppression. In settings of incomplete viral suppression, drug-resistant mutations can easily evolve resulting in widespread drug resistance[2].

There are numerous factors that result in the development of drug-resistant strains of the virus. The high replication capacity of HIV and its error-prone transcription is a major factor contributing to the development of resistance. It has been shown that retroviral replication is a highly error- prone process with varying estimates of roughly 7 x 10^6 to 1.4 x 10^4 base- pair substitutions occurring per nucleotide per replication cycle. Another significant source of genetic variation is recombination[3]. Recombination between HIV-1 genomes has been demonstrated and probably occurs ***in vivo*** as a result of simultaneous infection of an individual by two distinct HIV-1 strains. However, the observed degree of HIV-1 genetic diversity may also be influenced by selective pressure such as the host's immune response, cell tropism of the virus and the genetic makeup of the host.[4]

Irregularity in adherence to ART is probably the most important factor contributing to the development of resistance. Patients in India commonly interrupt ART as most patients pay for ART out of their own pockets. Patients also tend to combine the HAART with drugs from alternate systems of medicine. The interactions between alternate medicines and ARV agents are unknown. As many patients access care in the private sector, they are often prescribed mono and dual therapy, as the level of knowledge about HIV and HAART among the average clinician is quite low.

Indian scenario

Despite widespread use of ARV agents, little information is available on the prevalence of HIV-1 drug resistance in- India. As treatment programs are expanded, the prevalence of HIV-1 drug resistance among ART naive patients is of paramount importance in selecting treatment regimens and planning national policies[6].

In resource limited settings like in India, drug resistant assays are virtually non-existent, for them identifying the treatment failures is equivalent to drug resistance study. so physicians are to rely on obtaining detailed ARV history, reviewing adherence data, ruling out drug interactions, drug toxicities and documentation of immunologic, clinical and virological failure before deciding on switching on to second line ART in absence of drug resistance studies.

AIMS AND OBJECTIVES

Study of WHO stage, CD4 count and viral load after starting 2nd line ART.

MATERIALS AND METHODS

This retrospective study was carried out in Department of Medicine, RNT Medical College, Udaipur on 100 patients during the year 2018.

Inclusion criteria:

1. An HIV positive patients with age>13 years who has been on HAART.
2. HIV positive patients who were 100% adhered to drug therapy while on 1st line ART.
3. HIV positive patients who are not improving by WHO stage, CD4 count or by viral load in 6 months of 1st line ART despite with strict adherence.

Exclusion criteria:

1. HIV positive patients who are on other drugs known to interact with ART interaction like with antineoplastics, immunosuppressant transplant drugs, directly acting antivirals for hepatitis C, antimalarials, corticosteroids etc.
2. HIV positive patients who have other co-morbid conditions known to interfere with natural history of HIV disease like HBsAg, HCV etc.
3. HIV positive patients on 1st line ART with improving clinical stage, CD4 count or decrease in viral load means responding to the drug therapy.

METHODS:

All HIV positive patients who were started on 2ndART and who were found to fit with inclusion criteria. The patients included in this study who gave consent and were attending the OPD of the hospital and affording to test for the limiting factors to drug therapy.

Detailed clinical history of each patient was noted with special emphasis to symptomatology and manifestations of different systems, presence and absence of Opportunistic infections.

Study includes the patients on 2nd line ART on the basis of clinical, immunological or virological failure with 100% adherence on 1st line

ART without any significant drug interactions. Past history of tuberculosis, jaundice, skin lesions, neurological symptoms, blood transfusion, intravenous drug abuse, multiple sexual partners, major surgery, drug history and occupational exposure, if any was obtained.

Detailed physical examination was carried out. Patients were given prophylactic treatment for OI based on NACO guidelines[7]. Patients were closely observed and followed up for clinical failure, immunological failure and virological failure.

RESULTS AND DISCUSSION

Table 1: Age and Gender wise distribution of patients with treatment failures

Age in years	Male	Female	Total
13-29	9	2	11
30-39	27	12	39
40-49	23	11	34
50-59	12	2	24
>60	2	0	2
Total	**73**	**27**	**100**

Maximum number of males and females were in the age group 30-39 years. Only 11 patients were in the age group of 13-29 years and only 2 were more than 60 years. Mean age of male patients were 36.41 years and female patients were 36.36 years. The mean age in present study was 36.39 years.

Table 2: Source of infection in other studies

Study Group	Heterosexual (%)	Homosexual (%)	IV Drug abuser (%)
Present Study	90	7	3
Sinha et al[9]	91.17	4.41	4.41
Mina et al[8]	89.77	5.23	5
Somneuk et al[10]	75	18	7

In present study 90% were heterosexual as compared to 91.17%, 89.77% and 75% in the study of the Sinha et al[9], Mina et al[8] and Somneuk et al[10] respectively. 18% are homosexuals and 7% are IV Drug abusers in the study of the Somneuk et al[10]. This comparison shows that the most common source of infection is heterosexual.

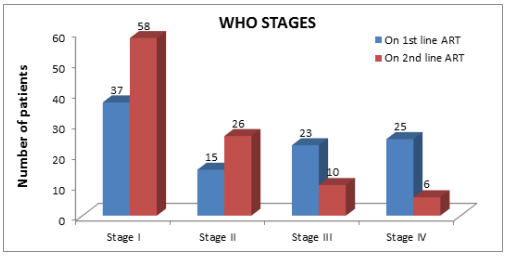
Mean duration of 1st line ART in present study was 36.3 months as compared to 32 months in study done by Sinha et al[9], 36.5 months in the study of the Mina et al[8] and 34.58 months in the study of the Somneuk et al[10]. This comparison shows that 32.26 months required for clinical or immunological manifestation of 1st line drug treatment failure to appear amongst those having virological failures.

Table 3: Comparison of viral load

Viral load (copies/ml)	On 1st line ART	On 2nd line ART
<500	0	78
500-5000	0	20
>5000	100	2
Total	**100**	**100**

Mean of viral load in treatment failure was 231331 copies/ml after 1st line ART and after 2nd line ART it was 697.63 copies/ml (P<0.05). Mean viral load of present study was 231331 copies/ml as compared to 223640 copies/ml[9], 338000 copies/ml[8] and 52374 copies/ml[10]. This shows that viral load (copies/ml) is significantly high in 1st line treatment failures which are comparable with other study groups.

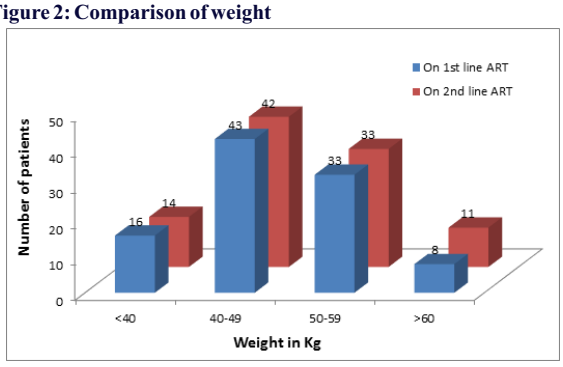
Figure 1: Comparison of WHO stages



In the present study, 37% patients were in WHO stage I and 25% patients in stage IV who are on 1st line ART. After 2nd line ART 58% patients were in WHO stage I and 6% patients in WHO stage IV.

On comparing data, number of patients increased in Stage I and decreased in stage IV after 2nd line ART but it was statistically insignificant (P>0.05). This shows that WHO staging required long time to show improvement than immunological and virological improvement.

Figure 2: Comparison of weight



43 patients on 1st line ART were in between 40-49 kg. 42 patients on 2nd line ART were in between 40-49 kg weight. Mean weight of treatment failure patients was 47.17 kg while mean weight after 2nd line ART was 47.8 kg. Mean weight in the present study is comparable with other studies[8,9,10].

On comparing data, there was increase in weight after 2nd line ART but it was not statistically significant (P>0.05). It shows that weight improvement required longer time monitoring than immunological and virological monitoring.

SUMMARY AND CONCLUSION

From this study we concluded that patients, who are not responding to 1st line ART, must switch over to 2nd line ART as early as possible after ruling out adherence issue and significant drug interaction and co morbid conditions. We also concluded, drug resistance may be the underlying cause for treatment failures, for that larger clinical study is required before applying primary drug resistance testing as a screening test in naïve drug patients.

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