

A Study on Side Effect of Antiretroviral Therapy Among People living with HIV/AIDS

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ABSTRACT

Background: With antiretroviral therapy being the only tool against HIV/AIDS in patients suffering from the disease, research would be beneficial in identifying the side effects from ART. Thus, we conducted this study to estimate the prevalence of side effects and to find out its associated factors among people living with HIV/AIDS.

Methods: A cross-sectional study was conducted at the ART centre, Aligarh. A total of 434 people living with HIV/AIDS were approached with study tools comprising of pre-structured proforma. The current and lifetime prevalence of side effects were estimated. Data was entered in MS Excel and presented as pie chart and bar diagram.

Results: We found the self-reported prevalence of side effects in HIV positive patients to be 18.7 (81/434) at the time of interview and 91.7% (398/434) in lifetime since the start of ART. Most of the PLHA had dizziness (65.4%) while abdomen pain and nausea/vomiting were reported by 28.4% and 27.2% respectively. The side effect was found to be common among younger age group, females, lower socio-economic class and patients who were recently started on treatment. The patients taking tenofovir and efavirenz combination therapy were also found to have more side effects.

Conclusion: This study found the prevalence of ever having side effect to ART to be about cent percent while it is still considerably high in the last 30 days. A proper action and further researches are required to explore and manage side effects associated with ART.

Keywords: Adverse drug reaction, HIV/AIDS, PLHA, Side effects, ART

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INTRODUCTION

Even after more than thirty decades since the start of HIV epidemic, we have not been able to find any cure for this disease of public health importance.¹ Huge success was obtained after the discovery of Highly active antiretroviral therapy (HAART), which provided treatment and was responsible for averting millions of death due to increase in life span of HIV/AIDS patients,² but it provided no cure for the disease. With HAART, the course of HIV disease has taken a drastic turn - from an almost fatal disease to a chronic manageable one, which seemed unthinkable a decade ago.³

Out of the 2.12 million people living with HIV (PLHA) in India, around half were put on treatment.⁴ Since current test and treat guidelines advocate that each and every HIV patient to be put on antiretroviral therapy (ART), it is the need of the hour to identify

and solve problems related to side effect of ART.⁴ Currently there are a handful of regimens for the treatment of HIV/AIDS. These regimens have to be customized according to the patients profile. The HAART regimens have shown to be having a variety of short term and long term side effects.⁵ These complications have the potential to increase morbidity and mortality. In spite of these side effects, HAART is currently the only remedy available. Identifying and treating these complications has important implications for patient survival. As the data pertaining to side effects among PLHA is lean in resource limited setting, this study was conducted with the objective of: 1) to find out prevalence of side effects of ART

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among patients taking ART; and 2) to explore the factors associated with side effects of ART.

METHODS

Study design and setting

A cross-sectional study was conducted over a period of 12 months duration from January to December 2015 at ART centre, Aligarh city, India. Aligarh district being a part of North India, has lower prevalence of HIV/AIDS than the rest of India.[6] Most of the resident live in rural area who are predominantly involve in agriculture, while large share of urban population of Aligarh city indulge in lock and metal polishing industries. Incidentally, Aligarh is also an educational hub with acculturation of various populations, not from the different states but from nations.

Study Population

We aim to study HIV patients on antiretroviral therapy visiting ART centre, Aligarh. All the adult HIV patients (18 years and above) on ART, registered at this ART centre for more than 6 months were eligible for the study. The exclusion criteria were: patients on second line ART, pregnant, patients suffering from any acute medical condition during the study, or any psychiatric condition in which patient could not give a valid consent. With anticipated prevalence of 50%,[7] and non-response rate of 10%, the sample size of the study was calculated as 440 by using the formula, $n = 4p(1-p)/d^2$.

Study instruments:

A predesign pre-structured questionnaire was administered in local language to all the selected patients that studied their demographic, social profiles and clinical characteristic. Patients were asked about any history of side effect from ART, current side effects and the type of side effect they suffered in the last 30 days.

Data Management and Statistics

The data was entered in MS Excel for the analysis. Continuous variable was presented as mean and standard deviation, while categorical variables were presented as proportion and percentage. For calculation of 95% confident interval of prevalence, modified Wald method was applied.⁸

Ethics

The study was approved by an academic board of studies, and Institutional Ethics and Research Advisory Committee, JNMC, AMU, Aligarh. The study was preceded by rapport building session where the purpose of the research and its implications were discussed. The participants were ensured about the privacy and confidentiality. A written consent was taken to confirm willingness. Appropriate health education, adequate counselling and referral whenever needed, were provided to all the patients after the interview.

RESULTS

Socio-demographic and clinical characteristics

During the study period, a total of 434 patients comprising of 262 males, 170 females and 2 transgenders were interviewed. Mean age of the patients was 39.02 ± 9.82 years. Majority of them were married (65.4%), Hindu by religion (88.9%), lived in a rural area (73.7%). Majority of the participants (249/434) were asymptomatic (categorized as stage I WHO staging). Participants were taking a fixed dose combination either of tenofovir, lamivudine and efavirenz (TLE) (50.9%) or zidovudine, lamivudine and Nevirapine (ZLN) (45.2%).

Prevalence and associated factors

In the last 30 days, about one-fifth of the patients had side effects due to antiretroviral therapy. It was reported in 18.7% (95% CI: 15.2 – 21.6%) (81/434) of patients. This self-reported history of having side effects increased to 91.7% (95% CI: 88.7 – 93.8%)

(398/434) on asking life time history of side effects associated with ART after starting the treatment. Among those who were having side effects, about two-third reported dizziness (65.4%), and about one-fourth had abdomen pain and nausea/vomiting (28.4% and 27.2% respectively).

It was seen that patients who were younger, reported presence of side effect more in comparison to older age groups. Similarly, females and patients who were recently started on treatment had more side effects when compared to males and patients with long history of ART intake. The patients taking tenofovir and efavirenz combination therapy reported more side effects.

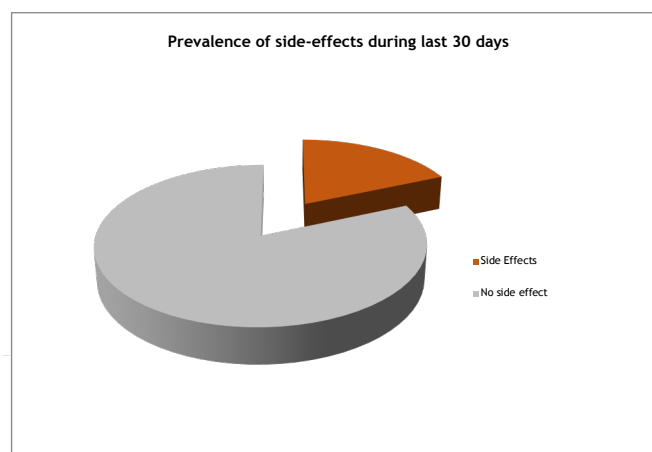


Figure 1: Prevalence of side effects among patients taking ART in last 30 days

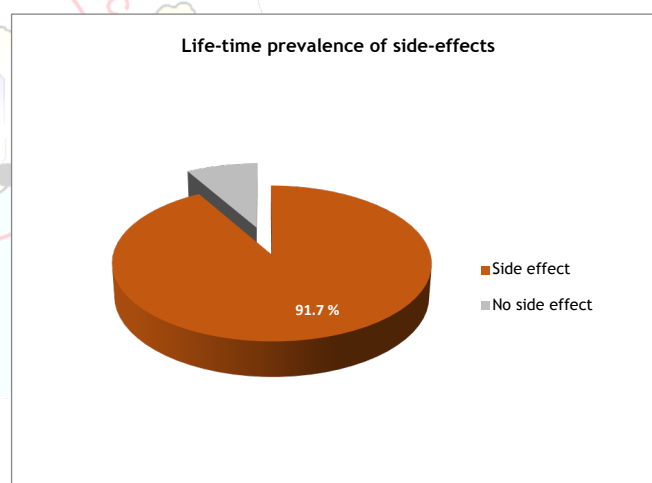


Figure 2: Life-time prevalence of side effects among patients taking ART.

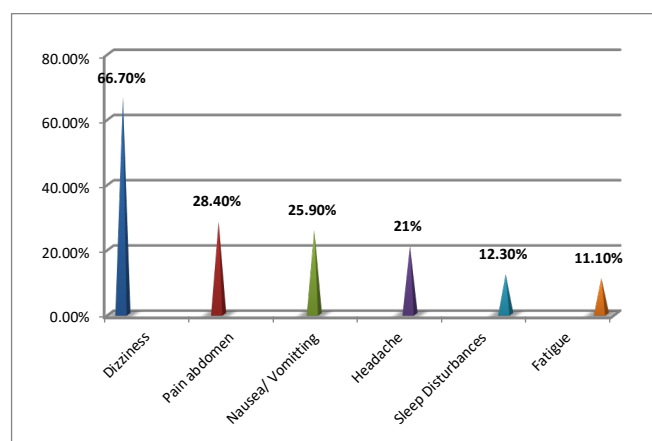


Figure 3: Type of side effects among patients taking ART during last 30 days

Table 1: Distribution of side effects among study population

| Variable | | Total | Side effect in last 30 days | |
|----------------------|-------------|-------|-----------------------------|---------|
| | | | Absent | Present |
| Gender | Male | 262 | 225 | 37 |
| | Female | 170 | 126 | 44 |
| | Transgender | 2 | 2 | 0 |
| Age group | <35 years | 131 | 95 | 36 |
| | >35 years | 303 | 258 | 45 |
| Residence | Rural | 320 | 261 | 59 |
| | Urban | 114 | 92 | 22 |
| Socio economic | Upper | 71 | 67 | 4 |
| | Lower | 363 | 286 | 77 |
| Time since treatment | <5 years | 321 | 253 | 68 |
| | > 5 years | 113 | 100 | 13 |
| WHO Stage | I | 249 | 210 | 39 |
| | II | 153 | 122 | 31 |
| | III | 29 | 18 | 11 |
| | IV | 3 | 3 | 0 |
| Drug regimen | TLE | 221 | 163 | 58 |
| | ZLE | 16 | 12 | 4 |
| | ZLN | 197 | 178 | 19 |
| Total | | 434 | 353 | 81 |

DISCUSSION

With this study we attempted to determine two things; the estimate of side effects due to antiretroviral therapy among the patients of HIV/AIDS and the factors associated with it. The prevalence of side effect in last 30 days was 18.7% at the time of interview and 91.7% any time since start of therapy. The side effect was commoner among younger age group, females, lower socio-economic class, patients started on treatment recently and patients on tenofovir- efavirenz combination therapy.

As far as prevalence of side effect is concerned, NACO reports that about 60-80% people who initiate on ART, experience side effects during initial period.⁵ Studies done in various parts of the world also have varied prevalence of side effects ranging from 11.3 – 94%.⁹⁻¹² Our findings on prevalence of side effect during lifetime and in last 30 days are in coherent with these studies. With the advancement of HAART, side effects have significantly decreased in PLHA. Newer drugs are not only effective but also safer. Still some categories of side effects are common in these drugs, but its severity has decreased as compared to drugs used initially. This is an important public health issue. In fact side effect is one of the foremost cause of treatment default in HIV patients leading to non-adherence.¹³⁻¹⁴ Non-adherence may lead to emergence of resistance, treatment failure and switching to 2nd line ART.³ Moreover we need to strengthen the pharmacovigilance for receiving the drug adverse effect data of ART.

The most common side effect among our study population was dizziness following ingestion of medication, which was reported in

two-third of patients with side effects. Many HIV/AIDS drugs have been reported to have CNS disturbances including dizziness.⁵ Most common side effects due to efavirenz – the most common drug consumed by our study participants – are central nervous system disorders. About one-fourth of the patients did complained of gastrointestinal disorder including abdomen pain and nausea/vomiting, which is also common in HIV medication. NACO currently advocates that all the HIV patients should be put on ART irrespective of their clinical profile.⁴ The first line of treatment for HIV patients prescribed by NACO is a combination of tenofovir+lamivudine+efavirenz (TLE), because of lesser serious adverse effects, inspite of common mild side effects.⁵ Among socio-demographic profiles, we found side effects to be higher among females and younger patients. Similar findings have been reported in various parts of the world.¹⁵⁻¹⁷ The reasons for these differences could be because of differences in pharmacodynamic of drugs in either sexes, due to differences in body mass index, fat composition, hormones, or genetic constitution. We found patients belonging to higher socio-economic class to be have lesser complains of side effects. Higher economic status is often associated with good nutrition, healthy life style, good diet and as a result good immunity, which might be the reason behind our findings.

Among clinical factors, we found side effect to be associated with fixed dose combination of tenofovir, lamivudine and efavirenz (TLE) as well as ZLE (Zido-vudine + Lamivudine + Efavirenz) more when compared to those who were on ZLN (Zido-vudine + Lamivudine + Nevirapine). Efavirenz is said to be strongly associated with neuro-toxicity, although they are usually not serious and subside with time.^{9,18} Efavirenz is also documented to be associated with neuropsychiatric side effects including depression.¹⁸⁻²⁰ Interestingly, patients who had taken ART for more than five years, reported to have lesser side effects, which goes along with notion that side effects of Efavirenz decline with time. This leads us to the conclusion that, patients become used to drugs kinetics after being on treatment for long duration and its side effects diminishes.

With more than 90% of side effect from ART anytime since the start of the treatment, and one-fifth of patients on ART currently having it, we need to take necessary measure to control the side effects. New drug research along with development of newer treatment guidelines for antiretroviral therapy would be helpful.

We had some limitation in our study. The choice of study centre was based on convenience. As this was a centre based study, finding may not replicate the prevalence in a community, preventing its generalizability. With the stigma attached with PLHA, it would difficult to do this study in a community. Furthermore, most of the HIV patients in India are registered at these ART centre. A larger and multicentre study with the involvement of community based network would be beneficial.

CONCLUSION

Result from this study lends evidence of high prevalence of side effects of ART in resource limited settings. The study highlights the importance of drug selection for ART and the monitoring of side effects. In this study, few important factors were discovered including socio demographic and clinical determinants. These study findings should prompt HIV programs to now pay greater attention to accessing the patient's profile and drug regimen before starting on ART. A stronger pharmacovigilance collaboration with NACO along with a regular screening of patients for toxicity and presence of side effect the is need the hour.

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