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Prevalence of Second Line Anti Retroviral Treatment Failure among Adults at Tertiary Care Teaching Hospital in South India

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Abstract

Back ground

Human Immunodeficiency virus (HIV) has continued to be a major health problem globally. Second line antiretroviral therapy (ART) regimens are used when there is treatment failure to first line agents. It is expensive, unaffordable and not available in resource limiting settings. There is increase in the failure rate to second line ART which further narrows future options for HIV/AIDS. Hence the main aim of this study is to estimate prevalence of second line treatment failure.

Method

A retrospective study was done at ART Plus centre, Government Medical College & General Hospital (RIMS), Ongole, Andhra Pradesh, South India. Data from 2016 to 2021 was collected from case sheets in a pre – designed format. Data consists of patient demographics, baseline characteristics, treatment related and treatment failure data.

Results

A total of 1442 patients were on second line anti retroviral therapy. Treatment failures were seen in

179 patients (12.4%) non failures were 1263 (87.6%). Out of 179 second line failure patients 107 were females, 72 males. The mean ± SD age among second line failure was 42.4 ± 11.2 yrs. Mean ± SD viral load was 251902 ± 912635.4. High failure rate is seen with TDF+3TC+ATV/r (51%) followed by LPV/R+DTG (30%)

Conclusion

Higher incidence of second line failure was seen in patients with poor adherence to ART. Strict adherence to the treatment, proper counseling to patients and regular viral load estimations will improve treatment outcomes.

Key words

HIV, Second line regimen, viral load

Introduction

Human immunodeficiency virus (HIV) has been a global health problem. According to the 2019 report, there were estimated 23.48 lakh people living with HIV (PLHIV) in India [1]. The introduction of antiretroviral therapy (ART) has saved millions of lives by decreasing morbidity, mortality and number of new HIV infections [2]. Small percentage of PLHIV fails their ART regimens every year due to which there is a possibility of transmission of drug- resistant HIV [3]. Optimal adherence to ART will minimize the development of drug resistance, and it is essential to reduce viral load, and decreasing the risk of mortality [4, 5].

Denovo HIV patients begin with a standard first line regimen which consists of a combination of two nucleoside/ nucleotide reverse transcriptase inhibitors (NRTI) with one non nucleoside reverse transcriptase inhibitor (NNRTI). When ART regimen is unable to control viral replication failure of ART is considered which can be clinical, immunological or virological [2] Second line regimens are used after failure of first line regimens. The WHO 2016 consolidated guidelines [6] recommended two NRTIs plus LPV/r or ATV/r as the preferred second-line regimen for individuals for whom EFV-based or DTG-based regimens are failing; two NRTIs + DRV/r and LPV/r + RAL were recommended as alternatives because of cost constraints and the fact that DRV/r is not yet available in a heat-stable co-formulation[7]. The choice of NRTI backbone for second-line ART continued to depend on which NRTI was used in first-line ART (if ABC + 3TC or TDF + 3TC (or FTC) were used, AZT + 3TC should be used in second-line ART and vice versa) with the goal of optimizing sequencing in the context of lack of access to genotyping.

The WHO recommends viral load monitoring as the preferred approach to monitor patients on ART. In low-and middle income countries, the WHO continues to recommend the use of CD4 and clinical monitoring to diagnose treatment failure and VL testing to confirm failure in order to avoid unnecessary changes in regimen [8]. Even though improved outcomes observed in patients switched to second line regimens, there is a gradual rise in second line regimen failure. Approximately, 22%–23% of the patients on second-line ART in low-income countries experienced a virologic failure at 12 months after the start of second-line and mortality at 12 months ranges from 5.3%-10.5% [9, 10].

The need for third line ART in future is increasing with the failure of second line regimens and represents a major challenge, as it is nearly 15 times higher than that of a first-line ART regimen and over six times that of a typical second-line regimen [11]. Limited studies have been documented on the failures of second-line anti-retroviral therapy and hence the

present study has been designed to determine the prevalence of failure of second-line anti-retroviral therapy in the study area.

Methodology

A retrospective study was done at ART Plus centre, Government Medical College & General Hospital (RIMS), Ongole, Andhra Pradesh, South India. The centre follows National AIDS Control Organization (NACO) guidelines for treatment of HIV patients. Data from 2016 to 2021 was collected from case sheets in a pre – designed format. Data consists of patient demographics, baseline characteristics, treatment related and treatment failure data. Patients aged above 15years who were on second line ART for at least six months were included in the study. Patients with incomplete base line information, on alternative first line therapy, lost to follow up were excluded from the study.

Loss of antiviral efficacy to the present regimen is the treatment failure which can be identified by clinical or immunological or virological criteria. Clinical failure for adults is defined as a new or recurrent clinical event indicating severe immunodeficiency (WHO clinical stage 4 condition and certain WHO clinical stage 3 conditions (pulmonary TB and severe bacterial infections) after 6 months of effective treatment. Patients with CD4 count at or below 250 cells/mm3 following clinical failure or persistent CD4 levels below 100 cells/ mm3 (three consecutive CD4 cell count in a row in one month interval between three values is less than100 cells/mm3) is immunological failure while virological failure is Plasma viral load above 1000 viral copies/ ml [12].

Statistical Analysis

Data collected was entered in Microsoft Excel version 2010. Data expressed in percentages, tables, bar diagrams & pie charts.

Results

A total of 1442 patients were on second line anti retroviral therapy. Out of which 732 were females, 726 were males and 4 transgender. Out of 1442 patients, second line treatment failures were seen in 179 patients (12.4%) non failures were 1263 (87.6%) (fig:1). Out of 179 second line failure patients 107 were females, 72 males (fig :2).

The mean ± SD age among second line failure was 42.4 ± 11.2 yrs with highest frequency in the age group of 31 – 60 yrs. Fig:3 shows age wise & gender wise distribution of second line treatment failures. Viral load was estimated at the time of State AIDS Clinical Expert Panel (SACEP) assessment baseline. Mean ± SD viral load was 251902 ± 912635.4. Highest failures were seen after 2years (24 months) of follow up (50.8%) in 2019 followed by 26.8% in 2020 (table 1). High failure rate is seen with TDF+3TC+ATV/r (51%) followed by LPV/R+DTG (30%) Fig:4

Discussion

The main aim of this study is to identify the prevalence of second line failures. In the present study the prevalence of failure of second line regimen was 12.4%. This is lower compared with that of study in Northern Ethiopia[13]. More than half (59.77%) of the subjects were females. This is similar with that of study in Northern Ethiopia [13] and in contrast with that of in Amhara [14] and North West Ethiopia[15]. The mean age was 42.4 years which was near to the study in Mumbai [16] and Northern Ethiopia[13].

Higher incidence of treatment failure was seen in patients between 35 to 45years. This finding is similar to the study conducted in Asia[17] but in contrast to the study in Brazil [18] younger age (<30years) have

been associated with second line treatment failure. This difference might be due to socio demographic differences.

In our ART plus centre viral load was done every six months to assess treatment outcome. The mean baseline viral load at second line failure was found to be 251902 ± 912635.4. In India, viral load monitoring is not available in public sector. Regular viral load monitoring is an important tool to identify ART failure at an early stage. Hence every effort should be made to provide viral load testing and to prevent delay in recognizing treatment failures.

The key role in the success of ART is strict adherence to the treatment. Higher incidence of treatment failure was seen in patients with poor adherence which is similar to the studies in South Africa [10], Vietnam [19] and Amhara [14] regions. One of the main reasons for poor adherence was the high cost of second line regimen.

Figure 1: Second line failures of ART

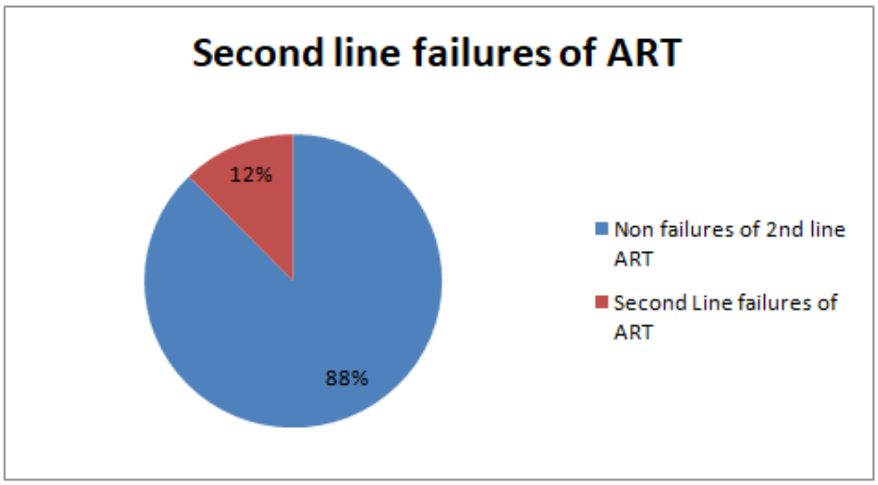

Figure 2: Gender wise distribution of second line failures

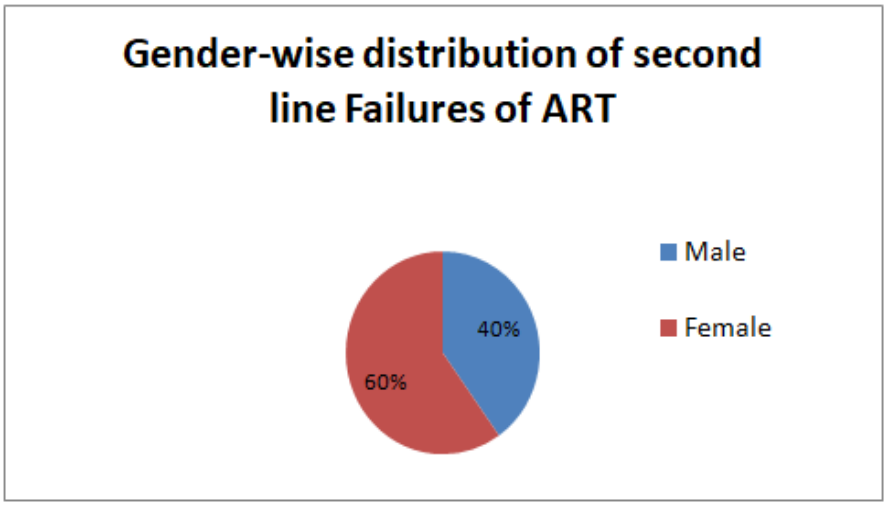

Figure 3: Age wise distribution of second line failures

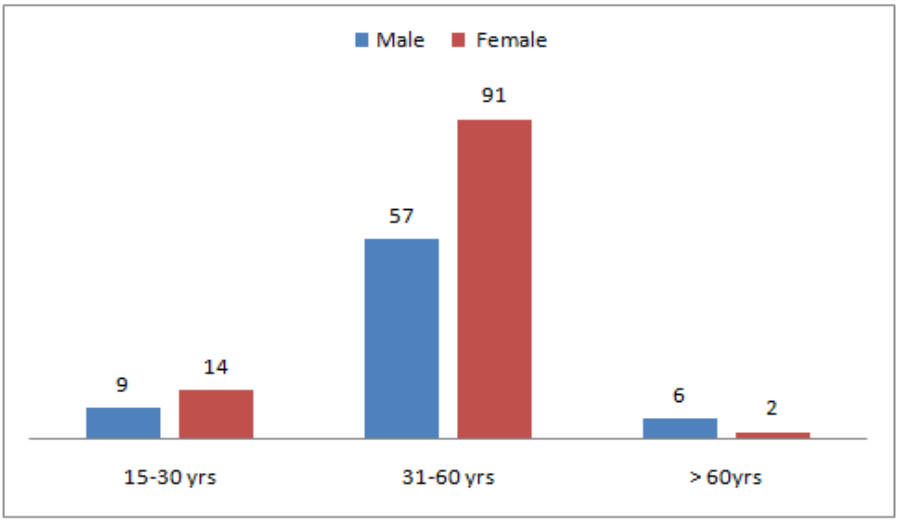

Figure 4: Failure rate among second line regimens

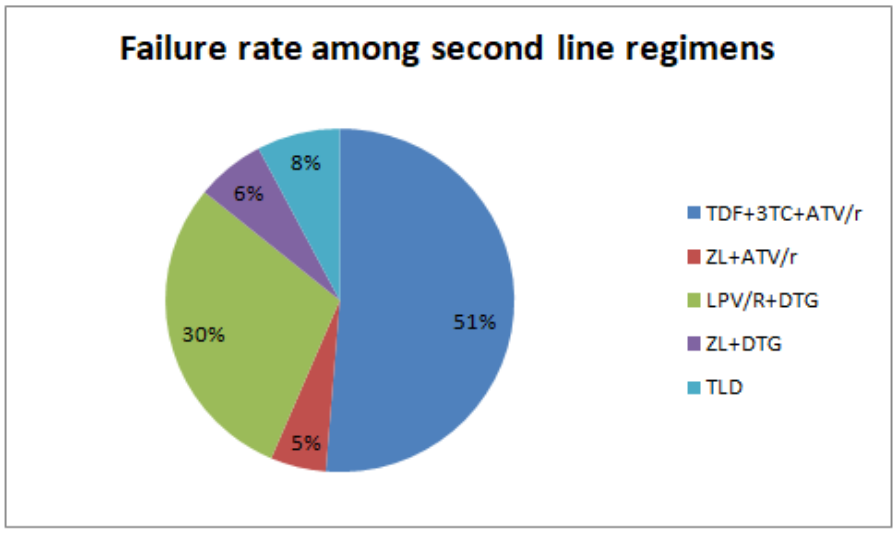

Table 1: Year wise distribution of second line failures

Year	Number	(%)
2018	19	10.6
2019	91	50.8
2020	48	26.8
2021	21	11.7

Conclusion

Higher incidence of second line failure was seen in patients with poor adherence to ART and after 2years of follow up of treatment. Strict adherence to the treatment, proper counseling to patients regarding treatment failures, drug resistant infections, co-morbidities and regular viral load estimations will improve treatment outcomes which further reduces the switch to unaffordable third line regimen.

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