Original Research Article

Mortality and survival benefits in people living with human immunodeficiency virus initiated newly with Antiretroviral therapy irrespective of CD4 count

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ABSTRACT

Background: HIV is a global pandemic with estimated 37.9 million people living with HIV (PLHIV) worldwide in which 23.3 million (62%) PLHIV take antiretroviral therapy (ART). In 2018 UNAIDS estimated 7,70,000 people died from AIDS related illness globally. India has around 21,40,000 PLHIV and 69,110 AIDS-related deaths in 2017 according to NACO report. This study aims to know the mortality and survival benefits in PLHIV newly initiated on ART as per test and treat policy.

Methods: A prospective observational cohort study was conducted from June 2017 to June 2018, involving 100 ART-naive PLHIV attending this ART Centre at Hospitals attached to BMCRI, Bangalore, India. Survival analysis was done by Kaplan Meier estimates. Spectrum of opportunistic infections and their role in cause of mortality was studied.

Results: The overall survival rate was 92% at 6 months and 91% at one year after ART initiation. The mortality rate at the end of one year was 9%, out of which Pulmonary Tuberculosis is the most common cause of mortality. There was a significant increase in the CD4 count during follow up, the mean increase in the CD4 T-cell count at the end of 6 months and 12 months was 157 cells and 286 cells per cubic millimeter respectively above the baseline value.

Conclusions: In this study early initiation of ART is found to be beneficial in clinical and immunological recovery with increase in CD4 counts and reduction in opportunistic infections in PLHIV. Pulmonary Tuberculosis remains the grave risk factor for mortality among PLHIV/AIDS patients on ART.

Keywords: Acquired immunodeficiency syndrome, Antiretroviral therapy, Mortality, Pulmonary tuberculosis, Survival

INTRODUCTION

India has the third largest HIV epidemic in the world with prevalence of 0.22% (ages 15 to 49). HIV infection is scourge to mankind which downregulate the immune system, leaving the victim vulnerable to various opportunistic infections, systemic disorders and unusual malignancies. The first case of HIV was documented in India in 1986 among female sex workers in Chennai by Sellappan Nirmala. The ART programme has impacted great changes in HIV related deaths. There were around 69,110 PLHIV deaths in 2017 due to AIDS related causes nationwide. India’s HIV epidemic is declining between 2010 and 2017, new infections reduced by 27% and AIDS related deaths declined by 56%. UNAIDS data provided information that in 2018, 79% of PLHIV were aware of their status of whom 62% were on ART.

The 2016 WHO guidelines recommended early ART initiation to all PLHIV irrespective of CD4 count based...
on studies showing increased risk of AIDS related deaths associated with delay in treatment. The Government of India launched the “Test and Treat Policy for HIV patients” in April 2017, according to which all PLHIV are to be treated with ART regardless of CD4 count, clinical stage, age or population. The benefits of early ART in PLHIV regarding survival and mortality with clinical improvement, immunological recovery by increase in CD4 count, viral load suppression has been studied in developed world but there are fewer studies in India. This study aims to know the mortality and survival benefits in PLHIV naïve initiated early on ART. The immunological recovery, spectrum of opportunistic infections (OIs) and reduction of OIs was also noted.

Aim of the study was to calculate the six-month, one year mortality and survival benefits in PLHIV newly initiated with ART. It also aimed to determine the immunological recovery and to see opportunistic infections as a significant contribution for mortality.

METHODS

A prospective observational cohort study was conducted from June 2017 to June 2018, involving 100 ART-naïve PLHIV attending this ART Centre at Hospitals attached to BMCRI, Bangalore, India. This study was approved by the Ethical Committee of the institution.

Inclusion criteria

- Subjects diagnosed to be HIV positive.
- Age more than 18 years.
- Patients who are willing to participate in the study by giving informed written consent.

Exclusion criteria

- Patients on prior ART.
- Patients who are lost to follow up.

Follow-up

All PLHIV naïve during the study period in their hospital visit as per test and treat policy was enrolled for initiating ART, before initiating a thorough clinical examination and all relevant baseline investigations including the CD4 counts done. After initiation of ART, these patients were regularly followed for one year on monthly basis and CD4 counts done at the end of 6 months and 1 year, during this study period if any OIs were noted.

Statistical analysis

A database entry, including patient demographics, clinical diagnoses at each visit and ART for each cohort attending this ART centres was documented. Survival after the initiation of ART was estimated using the method of Kaplan and Meier. The role of OIs in mortality was analysed. All statistical analyses were performed using SPSS software (version 16.0, SPSS, Chicago, USA). All statistical tests were two-sided and p≤0.05 was considered statistically significant.

RESULTS

In this study cohort of 100 ART naïve PLHIV, 46 (46.0%) were males and 54 (54.0%) were females. Most of the patients were in the age group of 20-40 years as shown in (Table 1).

Table 1: Age and sex distribution of subjects in the study.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
<th>Column N%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;30 years</td>
<td>30</td>
<td>30.3 %</td>
</tr>
<tr>
<td>31 - 40 years</td>
<td>39</td>
<td>39.4 %</td>
</tr>
<tr>
<td>41 - 50 years</td>
<td>20</td>
<td>20.2 %</td>
</tr>
<tr>
<td>&gt;50 years</td>
<td>10</td>
<td>10.1 %</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>54</td>
<td>54.0 %</td>
</tr>
<tr>
<td>Male</td>
<td>46</td>
<td>46.0 %</td>
</tr>
</tbody>
</table>

The box and whisker plot depicted in the (Figure 1) shows the distribution, median value and variability of CD4 count of subjects at baseline, at follow up period of 6 months and 12 months.

Figure 1: Box and whisker plot of Pre ART CD4, Post ART CD4 A at 6 months and Post ART CD4 B at 12 months.

The mean increase in the CD4 T-cell count at six months was 157 cells per cubic millimeter (401 to 558 per cubic millimeter). The CD4 T-cell count at six months was greater than the baseline value in 86 of 92 patients (93.47 percent) and decreased from baseline in 6(6.5percent). The mean increase in the CD4 T-cell count at 12 months was 286 cells per cubic millimeter (401 to 687 per cubic millimeter). Mean baseline CD4 count was 401 and follow up CD4 at 6 month and 1 year were 558 and 687 respectively as shown in (Table 2).

The CD4 count increment was seen in 85 % of the subjects in the study while decrement in CD4 count was...
seen in 6% of the subjects and 9% of patients died following ART initiation as shown in (Table 3).

**Table 2: Baseline and follow up CD4 count after ART initiation.**

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>SD</th>
<th>Median</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRE ART CD4 (PLHIV naïve)</td>
<td>401.05</td>
<td>290.95</td>
<td>365.0</td>
<td></td>
</tr>
<tr>
<td>POST ART CD4 count at 6 months</td>
<td>558.89</td>
<td>317.79</td>
<td>473.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>POST ART CD4 count at 12 months</td>
<td>687.93</td>
<td>331.45</td>
<td>654</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Table 3: Outcome of CD4 T-cell count among subjects.**

<table>
<thead>
<tr>
<th>Outcome of CD4 cell count</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increment</td>
<td>85(85.0%)</td>
</tr>
<tr>
<td>Decrement</td>
<td>6(6.0%)</td>
</tr>
<tr>
<td>Expired</td>
<td>9(9.0%)</td>
</tr>
</tbody>
</table>

**Figure 2: Overall survival during the course of follow-up of one year.**

The spectrum of OIs in this patient showed candidiasis as the most common opportunistic infection followed by tuberculosis as shown in (Table 4).

**Table 4: Spectrum of opportunistic infections in study subjects.**

<table>
<thead>
<tr>
<th>Opportunistic Infections</th>
<th>Number of PLHIV</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Candidiasis</td>
<td>8</td>
<td>8.0%</td>
</tr>
<tr>
<td>Extra pulmonary TB</td>
<td>7</td>
<td>7.0%</td>
</tr>
<tr>
<td>Pulmonary TB</td>
<td>6</td>
<td>6.0%</td>
</tr>
<tr>
<td>Nil</td>
<td>79</td>
<td>79.0%</td>
</tr>
</tbody>
</table>

Of the 100 patients started on ART, the mortality rate at the end of one year was 9% (nine deaths). Out of nine deaths occurred, five deaths were due to pulmonary TB while four deaths were due to extra pulmonary TB. The overall survival rate was 92% at the end of 6 months on ART and 91% at the end of one year of ART (Figure 2) illustrates the survival function using Kaplan Meier analysis during the course of study.

**DISCUSSION**

There were 9 deaths during this study which all were attributed to Tuberculosis which shows the role of opportunistic infections as a grave causal of mortality. In 2017 WHO reported TB as the leading cause of death among PLHIV, accounting for 32% of deaths in PLHIV attributing to TB.7 India with the highest burden of TB in the world had an incidence of 2.79 million cases of TB in 2016 out of which 87,000 of TB infection was seen in PLHIV.8 Authors have shown in this study tuberculosis is the grave risk factor for mortality in PLHIV. Majority of deaths in this study occurred within 3 months of starting ART, as also observed in previous studies.9,10 HIV infection increases the risk of progression of latent TB infection to active TB disease thus increasing risk of death if not timely treated for both TB and HIV.

A study from North-Eastern India by Bhattacharjya C et al, showed that Tuberculosis was the leading cause of death among PLHIV accounting for about 28% of the total deaths.12 In a study from South India, Rajagopal et al, concluded that TB at first admission(OR=4.86) was significant risk factor for mortality and also negatively impacted survival (p=0.002).13 A study from Ghana, Africa by Lartley M et al, showed that Tuberculosis was the commonest cause of AIDS related deaths accounting for 57.7% of all deaths.14

There was a mean increase in the CD4 T cell count of 157 cells/cumm at 6 months and 286 cells/cumm at 12 months above the baseline values after the initiation of ART. Various studies in India have shown significant increase in CD4 counts in PLHIV after initiation of ART.15,17

The survival rate in this study at the end of six months was 92% and at the end of one year was 91% after initiation of ART. Ram Bajpai, et al concluded a similar survival probabilities of 94.8% and 92% at 6 months and 1 year respectively.9 Good survival benefits in PLHIV after ART initiation has been reported in other studies from the developing world.18,19 The beneficial effects of ART among PLHIV in reduction in the incidence of various Opportunistic infections has been seen.20

Screening efforts are essential in early detection and management of opportunistic infections in PLHIV to improve survival rates and reduce the mortality. This study has shown the efficacy of early initiation of ART irrespective of CD4 count in PLHIV naïve in clinical and immunological recovery.
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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

References


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