Chapter-7

Conclusion and Limitations

7.1: Conclusion

In general, the mortality rate was very high within first three to six months of ART initiation and reached to stabilize later. Moreover, the results of the multivariable proportional hazards Cox regression model showed that lower CD4 count at the start of ART, lower bodyweight, higher clinical stage, older age and being of bedridden or ambulatory functional status are associated with higher risk of mortality. Therefore, healthcare personals and other ART clinic staff should plan for more frequent contacts with patients during the early phase of treatment in order to prevent the many deaths that occur during the early weeks of ART. Therefore, patients should be informed about the need for early diagnosis of HIV infection and starting treatment early is very important. Moreover, treatment of opportunistic infection parallel to the ART programme may reduce the risk of mortality. The results of this study suggest that the existing care options for PLHIV did not appear to fully address this issue. Further research should be conducted why lower bodyweight and old age patients associated with increased rate of mortality.

In our findings, the follow-up time was long enough to estimate survival and its associated factors. This study used the routine treatment program data, which is cost effective and the findings would probably give a crucial insight to develop an effective and efficient HIV care treatment, support program and carved a sustainable way to respond HIV epidemic in Andhra Pradesh.

The analysis includes the death risk with more than one year observational period. This enabled us to include variations in death risks during the first two years and to reduce the effect of the high mortality peak often observed during the first 12 months after patients have started ART.
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A separate treatment programme for drug user patients is important and careful monitoring of drug adherence should be made available, as the effect of the treatment is highly dependent on adherence. Finally, health workers and peer educators and data clerks, working with patients under HAART, should be given special training to improve the quality of the data records of patients. Moreover, attempt should be made to investigate the causes of deaths that occurred out of hospitals, and mechanisms should be devised to trace patients lost to follow up. This study demonstrates that HIV patients live longer with early start of antiretroviral treatment, highlights the effect of scale-up in ART services and factors responsible for their survival.

Our results have shown that individuals highly adherent to ART regimes had a significantly lower risk of death than similar individuals who were not as adherent to ART. Therefore, underscoring the importance of high ART adherence level in the clinical management of HIV-infected individuals may have played an important role in addition to decreasing HIV disease progression and HIV transmission.

This research describes and evaluates a range of existing statistical measures for validating prognostic models for independent survival outcomes. In one part of this research, the practical uses of some of the validation measures for standard survival models have been presented. In other parts, this research extended the C-index, D statistic and K statistic, for use with models for survival outcomes. The use of these measures when making predictions in validation dataset that includes either the same to those in the development data is also discussed. An important point to note is that one needs to investigate the characteristics of the validation data before choosing the validation measures.

Numeral areas have been identified where further research is possible. Further investigation could be conducted based on other survival models such as accelerated failure time (AFT) models and non-parametric models to assess whether the measures perform well for these models. Based on the simulation results one could recommend
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whether these measures are generalisable to all of these survival models. In addition, further investigation may be required to see whether the measures are sensitive to model mis-specification that means fitting of a wrong model.

7.2: Limitations

The improvement in survival from the first period of HAART is undeniable and should be commended. However, results should be viewed in light of some study limitations:

1. As in any analysis of large secondary datasets, there is a trade-off between the increased comprehensiveness of patient data under analysis and the deficiencies in terms of coverage and quality of databases. With this sense, the missing information identified in the current study constitutes serious limitations, not only in terms of the resulting analyses, but also from the broader perspective of monitoring and policymaking.

2. This study has no specific information on the causes of death. Moreover, the mortality outcome of loss to follow-up patients in this study was unknown. Lost to follow-up patients might be at higher risk of death.

3. Although patients were not randomly selected from all patients enrolled over the country. The results may be generalized with focus on biological explanatory variables rather than socioeconomic explanatory variables.

4. Residual confounding does remain since we did not have information on some factors which were found by some studies to be good prognostic factors such as co-infection status, HIV viral load, drug adherence and active injection-drug use.

5. Some of the patients were transferred out within or outside the state, withdrawn from treatment and loss to follow-up from the HIV care. Since further information on patients was not collected in these groups. It is possible that those who transferred out, withdraw or are lost to follow-up are terminally ill. Therefore, these factors are unlikely to produce bias our results.

6. The present study includes only baseline values of the clinical variables i.e. CD4 cell counts, clinical stages, bodyweight and functional status. However, some
other factors such as treatment adherence over time, treatment switches or substitution, number of missed appointments, which are associated to mortality of AIDS patients, are not included in the study.

7. The study used CD4 cell count as indirect surrogate indicator instead of viral load. The study has also used weight, which might be affected by height, instead of BMI.

8. The retrospective cohort study design limited our ability to gather data about factors that may influence the risk of mortality, for instance factors such as lack of social supports networks, disclosure of infection status and depression. Data was collected from those who were attending ART centers mostly through self-reporting and hence may have reporting and recall bias.

9. The adherence value is calculated by pill count method in the ART programme and we used it as an exposure variable. However, this concern might be alleviated by the fact that the relationships between the participants and their interviewers have been built on trust and respect over many years.

7.3: Recommendations

The present study has indentified the following recommendations to HIV control programme in India;

1. Though survival at one year is promising, long-term sustainability and survivability which would show the great benefit of ART in developing countries are unknown. Further study is desired to find the answer for the most devastating disease in this area.

2. Probability of survival at one year after initiation of the therapy is lower than survival of patients in developed countries. This would be explained by more advanced HIV diseases in the study. More effort should be done to enrolled patients with early HIV-diseases and strengthen opportunistic infections prophylaxis, diagnosis and treatment.
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3. NACO needs to start more focus in data management part as lots of missing values in clinical and programme variables were observed in the ART dataset. Comprehensive training, direct data into software and regular monitoring may be helpful in making complete dataset.

4. The proportion of lost to follow-up (LFUs) patients was very high among those who started treatment within six month. Major efforts are required to trace these LFUs when they missed their monthly dose and come back to national programme.

5. Nutritional support should form a fundamental part of the response to HIV and AIDS in India, including more efforts toward providing nutritional counseling, support, and encouragement to clients.

6. There is a need at ICTC centers to council the HIV positive individuals to early enrollment to the HIV care to avoid delay in initiation of treatment. A special emphasis is required to asymptotic, separated and HRG cases.

7. There are HIV positive patients after getting their reports from ICTC centers at higher risk for delayed presentation to ART center. An appropriate system should be developed to trace these cases and bring them back to the HIV care.

8. Special counseling session may be helpful for the PLHIVs with CD4 count > 350 as they are more likely to be defaulter.

9. Regular updating of patients contact details including phone numbers needs to be done at the ART centre. Active tracing with the help of District Level Network of PLHIV and analyzing the individual reasons leading to lost to follow up will greatly help the programme.

10. External validation in prognostic modeling process is essential. Therefore, future research is required to identify the best approach to validate a model's predictive performance through an external validation exercise where the validation data include a number of new clusters.
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7.4: Future Implications

1. Larger longitudinal cohort studies with non-HIV control groups in controlled conditions to be planned for preparation of the life-table for HIV/AIDS patients in India.

2. Till date, time-to-event outcomes and longitudinal clinical predictors (e.g.; CD4, viral loads, staging, BMI, Hb etc.) are assessed separately. However, studies with joint modeling approach should be planned to find the joint effects.