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Impact of Anti Retro Viral (ART) Therapy on Clinical and Laboratory Parameters: A Longitudinal Study

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ABSTRACT

Introduction- India is among the list of countries with highest HIV prevalence. Adequate viral suppression requires strict adherence to antiretroviral therapy (ART).Telangana ranks 7th in the prevalence of HIV in India

Objectives: The research was conducted to study the prevalence poor adherence among the study group and to study the effect of poor adherence on clinical and laboratory deterioration.

Methodology-This is an observational follow up (longitudinal) study done on 142 patients which includes all newly diagnosed (diagnosed on or after 1st January 2012), sero positive, adult patients, enrolled at ART centre Nalgonda and started on treatment during the months of December 2012, January 2013, February 2013, using a pre designed, pre tested questionnaire. They were visited one year after ART initiation and their clinical and laboratory parameters were studied.

Results-After one year 129 patients remained, of which 49.61% patients had good adherence and 50.39% patients had poor adherence. Decrease in BMI, worsening of HIV grade, presence of opportunistic infections were significantly present among patients with poor adherence. Low CD4 count and severe anaemia were also significantly associated with poor adherence.

Conclusion- There is significant worsening of clinical and laboratory parameters in patients with poor adherence.

Keywords- clinical and laboratory parameters, ART

INTRODUCTION

HIV continues to be a major global public health issue. WHO estimated that 36.7 million (34.0-39.8 million) people were living with HIV at the end of 2015 globally. Sub-Saharan Africa remains the most severely affected, with an estimated prevalence of 4.4%.[1] India has the third largest HIV epidemic in the world. In 2015, the estimated prevalence of HIV in India at 0.26% translates to 2.1 million People Living with HIV (PLHIV). During the same year, there were estimated 68,000 deaths due to AIDS-related illnesses.[2]

The Government of India demonstrated its commitment to combat HIV with the launch of National AIDS Control Programme (NACP-1) in 1992.[3] The programme is currently in its fourth stage.

Highly active antiretroviral therapy (HAART) is the cornerstone for management of patients with HIV infection. Initiation of widespread use antiretroviral therapy has caused decline in the incidence of most AIDS defining conditions and mortality.[1,2] Adequate viral suppression requires strict adherence to antiretroviral therapy (ART).

Despite the effectiveness of HAART, poor adherence to treatment affects patient's quality of life

and causes a study deterioration of their health.Suboptimal adherence to medical treatment with antiretroviral agents has been associated with increased morbidity and mortality, potential transmission of drug-resistant virus, drug resistance, and failure to achieve viral suppression.[4]

Hence adherence to ART is as relevant as its initiation. This aspect has not been adequately researched in India and has never been studied in newly formed state of Telangana which ranks 7th in the prevalence of HIV in India.[5] The present study endeavours to fill this knowledge-gap by studying the prevalence poor adherence among the study group and to study the effect of poor adherence on clinical and laboratory deterioration.

OBJECTIVES

The research was undertaken to study the prevalence poor adherence among the study group and to study the effect of poor adherence on clinical and laboratory deterioration.

MATERIALS AND METHODS

A sample size of 140 was calculated based on prevalence of non-adherence as 50% (verbal communication by medical officer in charge of ARTCentre, Nalgonda), absolute precision of 10% was taken. With level of significance of 95%, and anticipated loss to follow up and case fatality rate within first year as 20% each.

This is an observational follow up (longitudinal) study done on 142 patients which included all newly diagnosed (diagnosed on or after 1st January 2012), sero positive, adult patients, enrolled at ART centre Nalgonda and started on treatment during the months of December 2012, January 2013, February 2013. Pregnant women and acutely ill patients and those unwilling to participate in the study were excluded. The figure below gives selection of study subjects and exclusion criteria.

This study was conducted at ART centre, Nalgonda which is a government-owned facility attached to the district hospital where ART drugs are provided free of charge.

A pilot study was conducted from 1st to 15th of October on 30 patients to assess feasibility of the research project, refine questionnaire and establish content validity. First interview & clinical examination was conducted from 1st December 2012 to 28th February 2013. Follow up interview and clinical examination was conducted from 1st December 2013 to 28th February 2014. (One year following the first interview). A pre designed questionnaire was used. Data was collected after acquiring written informed consent from the patient. The research study was approved by the Institution Ethics Committee of Kamineni institute of medical sciences, Nalgonda. Permission to conduct the study was also obtained from the Medical Superintendent ofdistrict hospital, Nalgonda and the District Coordinator of hospital services (DCHS).

Adherence**:** Study subjects who had taken > 90% of the prescribed doses were considered as adherent. This level was selected as a minimum of 90% adherence has been recommended for good viral suppression.[6] Currently this is calculated at the ART centre by pharmacy refill tracking method. In this method, patients collecting their medications regularly on due dates are assumed to be adhering to treatment. Number of days delayed is taken as number of doses missed.

Interview and examination were conducted during the OPD hours of ART centre after their examination by medical officerand dispatch of their drugs. The interview and examination were conducted in complete privacy with the help of ART counsellors. Patient's ART number, residential address and phone number were recorded on their individual pro forma in order to approach them during follow-up.

The ART centre was visited again from 1st December 2013 (one year following the commencement of study) to 28th February 2014. The study group was interviewed soon upon completion of 1 year of being on ART when came for monthly supply of drugs and clinical examination.Their adherence was calculated for one year based on records at ART centre. Effect of adherence on clinical and laboratory parameters was studied.

Among the LFU cases who could be reached at their homes, only clinical examination for opportunistic infections, BMI, reasons for disengaging from care could be recorded. Laboratory tests like CD4 count and haemoglobin could not performed in the field due to logistic difficulty.

Data obtained was analysed and presented using appropriate tests.The data was entered in excel sheet and analysed for proportions. Mean and standard deviations were calculated. Influence of socio demographic factors on adherence was estimated using odds ratio & 95% confidence intervals using SPSS software. Chi square test was performed to assess statistical significance ($p<0.05\%$).

RESULTS

In the present study majority of the subjects were males (64.8%) and followed by females (35.2%). The mean age was 39.33 ± 10.29 SD and the range is 18 to 70.Mortality at the end of one year was

9.15% (13 patients). Loss to follow up(LFU) which included 25 patients (17.6%) and death cases together constituted 26.76%. All the calculations for adherence below exclude the dead patients. Thus at the end of one year 129 patients remained. Of this a total of 64 patients (49.61%) had good adherence and 65 patients (50.39%) had poor adherence. 25 patients became loss to follow up (LFU) of which 10 cases could not reached at the address provided by them. At least three home visits were undertaken before indicating that a patient was not available. Surrogate interviews were not permitted, however house hold members assisted the patient in recalling information. All LFU cases were taken to have poor adherence.

Table 1- Association between poor adherence and clinical deterioration (n=119)**

Variable	Adherence		Total (n=129) n (%)	OR (95% CI)
	Poor (n=65) (%)	Good (n=64) (%)		
Opportunistic infections				
Present	41 (34.46)	2 (1.68)	43 (36.14)	90.79* (19.6-420.62)
Absent	14 (11.77)	62 (52.1)	76 (63.86)	
Worsening of HIV clinical stage				
Yes	35 (29.41)	0	35 (29.41)	4.200* (2.865-6.157)
No	20 (16.8)	64 (53.78)	84 (70.59)	
BMI				
Undernourished	39 (32.78)	20 (16.8)	59 (49.58)	5.363*(2.443-11.770)
Well nourished	16 (13.44)	44 (36.97)	60 (50.42)	

*p=<0.05, **Excludes dead cases and those LFU cases who could not be reached at their homes for follow up examination

Table 2- Association between poor adherence and deterioration in laboratory indicators (n=104)**

Variable	Adherence		Total (n=104) (%)	OR (95% CI)
	Poor (n=40) (%)	Good (n=64) (%)		
CD4 count (cells/mm^3)				
</=200	13 (12.5)	6 (5.77)	19 (18.27)	4.654* (1.597-13.565)
>200	27 (25.97)	58 (55.77)	85 (81.73)	
Anemia				
No anemia	0	3 (2.89)	3 (2.89)	1.000
Mild	4 (3.85)	2 (1.92)	6 (5.77)	3 (0.97-9.3)
Moderate	1 (0.96)	11 (10.58)	12 (11.54)	1.09 (0.92-1.3)
Severe	35 (33.65)	48 (46.15)	83 (79.8)	1.729* (1.439-2.08)

*p=<0.05, **Excludes dead cases and those LFU cases who could not be reached at their homes for follow up examination

The present study found that poor adherence was significantly associated with presence of opportunistic infections. It was found that poor adherence was significantly associated with fall in WHO staging (from the patients grade 1 year ago). OR found was to be 4.2. It was also found that poor adherence was significantly associated with undernourishment. (OR=5.36).

Our study found that CD 4 count in those who were not adherent to ART were at a 4-5 times greater risk of having lower CD4 counts that those who had good adherence. Our study showed a statistically significant relationship between poor adherence and development of severe anaemia. (OR=1.729).

DISCUSSION

At the end of one year 129 patients remained. Of this a total of 64 patients (49.61%) had good adherence and 65 patients (50.39%) had poor adherence.LFU cases were taken to have poor adherence. A cross sectional study done by Cauldbeck et al [7] found the rate of adherence to be 60%, Study by Golin CE et al [8] found a 71% rate of adherence after 4 weeks study period and a cross sectional study done by Gordillo V et al,[9] in their study found a 57.7% rate of adherence.

poor adherence was significantly associated with presence of opportunistic infections. This was consistent with findings of other studies. A randomised control trial done by Zolopa A et al [10] found that early ART arm had fewer opportunistic infections than ART deferred receiving arm. This association was found to be statistically significant.

It was found that poor adherence was significantly associated with fall in WHO staging (from the patients grade 1 year ago). A randomised control trial done by Zolopa A et al [10] found that early ART arm had fewer AIDS progression/deaths (OR = 0.51; 95% CI = 0.27-0.94) and a longer time to AIDS progression/death than ART deferred receiving arm. This be borne in mind and effectively communicated to the patients during counselling sessions.

We found that poor adherence was significantly associated with undernourishment. Our study findings are in agreement with the study done by Surendra K Sharma et al [11] where the body mass index increased from a median of 19.2 at baseline to 21.6 among adherent patients at the end of follow up period. Therefore, the National HIV programme must incorporate nutritional counselling sessions and emphasise the importance of adherence as it has a direct bearing on the patient quality of life.

Our study found that CD 4 count in those who were not adherent to ART were at a 4-5 times greater risk of having lower CD4 counts that those who had good adherence.

Study by Sarna et al,[12] Adane et al [13] also showed similar kind of results. Study by Kumarasamy et al[14]reported association of adherence with current CD4 count, study reported higher CD4 count in adherent PLHA.

Our study showed a statistically significant relationship between poor adherence and development of severe anemia. Study by Adane et al [13] found that patient hemoglobin showed significant improvement after ART initiation. Their study showed that from a prevalence of 52.6% anaemia before ART initiation, the prevalence was decreased to 37.4% after ART initiation. This was found to be statistically significant. Similar results were found in study done by Berhane et al.[15]

Absence of viral load data is a limitation in this study because viral load has a more proximal association with adherence than does CD4.

CONCLUSION

There is significant worsening of clinical and laboratory parameters in patients with poor adherence. This must be borne in mind to educate the patient about need for good adherence and information regarding the same must be incorporated in counselling sessions.

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