

Original Research Article

Treatment outcome of antiretroviral treatment naive HIV infected patients initiated on antiretroviral therapy in a tertiary care hospital in South India

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ABSTRACT

Background: About 2.1 million people are infected with HIV in India. Clinical profile of patients has evolved over a period of time in the Antiretroviral treatment (ART) era. This study was done to document the clinical presentation of patients in a tertiary care in Mysuru in Karnataka. The aim of the study was to follow the patients who were initiated on ART over a period of time and to know its effect on the clinical outcome and overall morbidity and mortality of the patients.

Methods: A prospective study of HIV positive patients who were initiated on ART was done regarding clinical profile and outcome over a period of one and a half to two years depending on when they were initiated on ART.

Results: Totally 183 patients were registered during the period, out of which 114 patients (62.29%) were males and the rest were females (37.70%). The commonest route of transmission was heterosexual route seen in 97.3% (178). Most (56.8%) of the patients were asymptomatic. The mean basal CD4 count was 162.70. The mean age of patients was 39.07. The mean BMI was 20.29. A 23.5% (43) had one or other side effects. Anemia (44.2%) was the most common side effects seen. There were 18 deaths (12.2%). A 39.34% (72) patients had opportunistic infections (OI), the commonest being tuberculosis 45(%)

Conclusions: It was concluded that patients with low CD4 count, low BMI were more prone for Opportunistic infections and death. Early initiation of ART can prevent such incidences and improve the quality of life of HIV positive patients.

Keywords: Anemia, CD4 count, HIV infections, Opportunistic infections and tuberculosis

INTRODUCTION

HIV infection is a global problem. According to UNAIDS 2017 data, there were approximately 36.7 million people worldwide living with HIV/AIDS at the end of 2016.¹ An estimated 1.8 million individuals worldwide became newly infected with HIV in 2016-about 5,000 new infections per day. As of July 2017, 20.9 million people living with HIV were accessing antiretroviral therapy (ART) globally. The vast majority

of people living with HIV are in low- and middle-income countries.

It is estimated that 90% of HIV infected persons live in the developing countries with Indian estimates being 2.1 million.^{2,3} Overall, the average prevalence rate of HIV among adults in India is about 0.9% and it accounts for 10% of global HIV burden and 65% of that in south and south-east Asia.⁴

Early diagnosis of the disease and initiation of antiretroviral therapy and treatment of opportunistic infections are important for the control of HIV replication, disease progression and ultimately control of the transmission of the disease.⁵

METHODS

We did a prospective study of patients who came to the HIV clinic of the medicine department on clinical profile, progression of the disease, opportunistic infections and side effects of medications over a period of one and a half to two years depending on when they were initiated on ART till December 2015.

The present study was conducted at JSS Medical college and Hospital, Mysuru in Karnataka. HIV positive patients above the age of 18 and who were treatment naïve at the time of recruitment were considered for the study. All these patients attended the infectious disease clinic of the medicine department Patients who were already on ART were not considered. Pregnant women were also not considered for the study.

The study was approved by the ethical committee of the institution. A written consent was taken for the study. History and physical examination was done and recorded on a pre-designed schedule which included the socio-demographic profile of the patients, mode of transmission, presenting symptoms, opportunistic infections etc.

Patients whose CD4 was less than 350 cells/ml were started on Cotrimoxazole prophylaxis and its adherence was tested. All patients and their care takers were counseled regarding the importance of adherence to treatment. Once it was convinced that the adherence was good, patients were initiated on ART. The cutoff for initiating ART was 350 cells/ml.

Statistical analysis

The data was entered into an excel sheet. Categorical variables were described using relative frequencies, whereas the standard deviation and mean were used for continuous variables. Paired t-test analysis was carried out to identify statistical differences between the two groups. All analyses were carried out using SPSS software version 21.0. A p-value <0.05 was considered statistically significant.

RESULTS

Totally 183 patients were registered during the period, out of which 114 patients (62.29%) were males and the remainder were females (37.70%). There was no transgender. When age was considered, 37.7% were in the age group of 31 to 40 years, 25.7% in the age group of 41 to 50. 23% were less than 30 years and 13.7% were more than 50 years.

Regarding education, 29.5% (54) of patients had studied secondary education, 21.3% (39) had studied up to college and 25.1% (46) were illiterate and 24% (44) had only studied up to Primary.

Regarding routes of transmission, 97.3% (178) of transmission was due to heterosexual route, 1.6% (3) were from Mother to Child and 1.1% were Men having sex with Men (MSM).

Most (56.8%) of the patients who were registered were asymptomatic (WHO stage 1). Equal number of patients (18.6%, n=34) were in stage 3 and stage 4. Only 6% (11) were in stage 2.

BMI of the patients at the initiation of ART was as follows. 56.8% (104) had normal BMI, whereas 29.5% were underweight and 13.7% (25) were Obese. The mean basal CD4 count was 162.70.

Table 1: Clinical profile of the patients at presentation.

Parameters	Count n	Column %
Age category	<30	42 23.0%
	31-40	69 37.7%
	41-50	47 25.7%
	>50	25 13.7%
Education	College	39 21.3%
	Illiterate	46 25.1%
	Primary	44 24.0%
	Seconadary	54 29.5%
Route of transmission	Heterosexual	178 97.3%
	Mother to child	3 1.6%
	MSM	2 1.1%
WHO staging	1	104 56.8%
	2	11 6.0%
	3	34 18.6%
	4	34 18.6%
BMI Category	Underweight	54 29.5%
	Normal	104 56.8%
	Obese	25 13.7%

MSM: Men having sex with men

Out of 183 patients, 23.5% (43) had one or other side effects after initiation of ART. The details of the side effects are depicted in the (Table 2).

Side effects were more common among patients with less than 30 years (33.3%). It was common among females when compared to males, though not statistically significant. It was commonly seen among patients who were in WHO stage 2. Basal CD4 count, weight and BMI were correlated with side effects, but there was no statistically significant correlation with these factors. 25% of patients who had OI had side effects. But it was not statistically significant.

Table 2: Details of the side effects of anti retroviral treatment.

Side effects	Count n	Column %
Anemia	19	44.2
Hepatotoxicity	7	16.3
Vomiting	4	9.3
Rashes	3	7
Skin Rashes	2	4.7
Pancytopenia	2	4.7
TBM(IRIS)	1	2.3
SJS	1	2.3
Pancreatitis	1	2.3
Jaundice	1	2.3
Hepatotoxicity and rashes	1	2.3
Bicytopenia	1	2.3

TBM: Tubercular Meningitis, IRIS: Immune Reconstitution Inflammatory Syndrome

Anemia (44.2%) was the most common side effect seen, followed by hepatotoxicity (16.3%). This could be due to the zidovidine based regimen, which was the initial choice. 9.3% (4) developed vomiting. 1 patient developed

Tubercular meningitis (TBM) after starting ART. This could be part of Immune reconstitution Inflammatory syndrome (IRIS).

There were 18 deaths (12.2%). The relationship between death and certain clinical profile were correlated. Patients above 50 years of age were more prone to death compared to younger age group. There was not much difference between male and female patients. The death among males were marginally high. When education level were compared, death was more common among the extremes level of education i.e., illiterate and college educated. When WHO staging was compared, maximum death was seen among patients who were in stage 4 followed by stage 3 and stage 2 and 1. When BMI was compared with death, maximum death was seen among patients who come under malnutrition, and patients with a BMI of 19 ± 3.5 had a significant mortality ($p=0.03$). The patients whose basal weight was 49 ± 11.3 also died, which was statistically significant (0.026). When it was compared to the CD4 count, patients with low CD4 count died. Their mean CD4 count was 87.6 ± 78.5 and was statistically significant ($p=0.002$). The details are provided in the (Table 3 and 4).

Table 3: Correlation between various parameters and death.

Parameters		Death				p
		No		Yes		
		Count n	Row %	Count n	Row %	
Age	<30	39	92.9%	3	7.1%	0.06
	31-40	65	94.2%	4	5.8%	
	41-50	42	89.4%	5	10.6%	
	>50	19	76.0%	6	24.0%	
Sex	Female	63	91.3%	6	8.7%	0.7
	Male	102	89.5%	12	10.5%	
Education	College	34	87.2%	5	12.8%	0.8
	Illiterate	41	89.1%	5	10.9%	
	Primary	41	93.2%	3	6.8%	
	Seconadary	49	90.7%	5	9.3%	
Route of transmission	Heterosexual	160	89.9%	18	10.1%	0.8
	Mother to Child	3	100.0%	0	.0%	
	MSM	2	100.0%	0	.0%	
WHO staging	1	96	92.3%	8	7.7%	0.7
	2	10	90.9%	1	9.1%	
	3	30	88.2%	4	11.8%	
	4	29	85.3%	5	14.7%	
BMI Category	Malnutrition	46	85.2%	8	14.8%	0.3
	Normal	95	91.3%	9	8.7%	
	Obese	24	96.0%	1	4.0%	

WHO: World Health Organization BMI: Basal Metabolic Rate SE: Side Effects

When death was compared to opportunistic infections, 18.1% (13) of patients who had some form of opportunistic infections died during the study period, which was very significant (p -value= 0.003) (Table 5).

Totally 39.34 % (72) patients had opportunistic infections during the study period, with 2 patients developing 2 OIs at the same time. Some of them had OI at the time of diagnosis and some developed during the course of the

disease. The commonest OI was tuberculosis 45(60.8%). Among the tuberculosis, 33 (73.33%) had extrapulmonary and 12 (26.6%) had pulmonary tuberculosis. One of the patient had tubercular meningitis (TBM) and cryptococcal meningitis (CM) at the same time. Next commonest was candidiasis (9.5%), followed by Herpes Zoster (8.1%) and CM (6.8%). The details of the opportunistic infections are provided in the (Table 6).

Table 4: Correlation between basal parameters and death.

	Death	n	Mean	Std. Deviation	P
Basal CD4 count	No	165	178.2	118.4	0.002
	Yes	18	87.6	78.5	
Basal Weight	No	165	55.7	12.1	0.026
	Yes	18	49.0	11.3	
BMI	No	165	20.9	3.8	0.03
	Yes	18	19.0	3.5	

P<0.05 significant, CD: Cluster of differentiation, BMI: Basal Metabolic rate

Table 5: Relationship between OIs and death, p=0.003.

Parameter	Death				
	No		Yes		
	Count n	Row %	Count n	Row %	
OI	No	106	95.5%	5	4.5%
	Yes	59	81.9%	13	18.1%

p<0.05 significant, OI: Opportunistic infections

Table 6: Details of the opportunistic infections.

Parameters	Count n	Column %
OIs Tuberculosis (pulmonary 12, extra pulmonary 33)	45	60.8
Candidiasis	7	9.5
Herpes Zoster	6	8.1
Cryptococcal Meningitis	5	6.8
Genital Herpes	1	1.3
Pneumonia	2	2.7
PCP	4	5.4
Diarrhoea	4	5.4

PCP: Pneumocystis Pneumonia

DISCUSSION

In this study, most of the patients registered were males (62.29%) compared to females. There were no transgenders. This is similar to most of the studies in India and other countries.⁶⁻⁸ When age was considered, most of the cases were seen in the age group between 31

to 40 years (37.7%) with least being above the age of 50 (13.7%). This is similar to the study done by Chakravarti J et al, from Banaras Hindu University where more cases were seen between 20 to 40 years of age.^{6,8}

In the present study, interestingly, most of the patients were educated, with only 25.1% being illiterate. Maximum number of patients had studied up to secondary education followed by patients who had studied up to the college or Primary School. This is in contrast to most of the studies, where maximum cases were seen among the illiterates.^{6,9} The major route of transmission among our group of patients was Heterosexual route (97.3%), followed by vertical transmission and homosexual route. This is similar to most of the studies where heterosexual transmission plays a major role in the transmission of this disease.^{6,10}

We adopted WHO staging at the time of initiating the ART. Interestingly most of the patients were asymptomatic (56.8%), followed by patients who were in WHO stage 3 and 4 (18.6%), meaning most of them had some major opportunistic infections. The least number of patients were in stage 2 (6%), meaning they had only minor opportunistic infections. But in a study done by Sun J et al, from Shanghai public health clinical center, maximum number of patients were in stage 3(75.3%) and 4 (23.1%) at the time of registration.¹¹

Most of the patients in this study had a normal BMI (56.8%), with 29.5% underweight and 13.7% obese. According to the study done by Bacchetti P from the university of California BMI among men varied from 17.2-43.2 with a mean of 24.9±3.9.¹² Similarly in a study done by Nancy Crum-Cianflone et al, from Naval Medical Centre, San Diago, 2% were underweight, 52% were normal weight, 37% were overweight and 9% were obese. The mean BMI at diagnosis was 25.¹²

The mean CD4 count at the time of initiation of ART was 162.70. Rohit Goel from India reported much less CD4 count (81.69).⁷ Whereas Vajpayee et al reported a median CD4 count of 203.¹³

Of the patients who were initiated on ART, 23.5% of patients had one or the other side effects. Anemia (44.2%) was the most common side effects seen, followed by hepatotoxicity (16.3%). Anemia could be due to the zidovidine based regimen, which was the initial choice. 9.3% developed vomiting.⁴ One patient developed TBM after starting ART. This could be part of Immune reconstitution Inflammatory syndrome (IRIS). A study done in Ethiopia by Tamir Z et al, showed that 32.7% of patients on zidovidine developed anemia.¹⁴ Hepatotoxicity could be due to efavirenz, nevirapine or rarely zidovidine itself.^{15,16}

There were 18 deaths (12.2%). The relationship between death and certain clinical profile were correlated. Patients above 50 years of age were more prone to death

compared to younger age group. There was not much difference between male and female patients. The death among males were marginally high. When WHO staging was compared, maximum death was seen among patients who were in stage 4 followed by stage 3 and stage 2 and 1. This is similar to the study done by Zachariah R et al, from Medecins sans Frontieres, Operational Research, Brussels, where patients in WHO stage 4 had about twice the risk of dying than those in WHO stage III.¹⁷ 18.1% of patients had some form of opportunistic infections, which is very significant.¹³ Patients with low CD4 count died. Their mean CD4 count was 87.6 and was statistically significant. This is similar to the study done by Palella FJ et al, as part of the multicentric. The HIV Outpatient Study (HOPS) study from US, where mortality was more among patients who had a low CD4 count at the initiation of ART.¹⁸ A similar trend was observed in a study done by French AL et al, from Chicago, where low CD4 was associated with mortality.¹⁹

When BMI was compared to death, it was observed that patients with low BMI died compared to normal or obese patients. Similar findings were found by French et al.¹⁹ When death was compared to the presence of opportunistic infections, there was a significant association between the two. A 18.1% of patients who had OIs during the study period died. According to a study done by Bonnet F et al, from France, 27% died of at least one OI.²⁰

A 39.34 % (72) patients had opportunistic infections during the study period, with 2 patients developing 2 OIs at the same time. Some of them had OI at the time of diagnosis and some developed during the course of the disease. The commonest OI was tuberculosis 45 (60.81%). Among the tuberculosis, 33 (73.33%) had extrapulmonary and 12 (26.6%) had pulmonary tuberculosis. One of the patient had Tubercular meningitis (TBM) and Cryptococcal meningitis (CM). Next commonest was candidiasis, followed by Herpes Zoster and CM, which were 6 and 5 respectively.⁷ According to Rohit goel from India, tuberculosis (58.96%) was the commonest opportunistic infections, followed by chronic diarrhea (26.56%). This was followed by skin infections and oral candidiasis (11.99%).⁷

Limitation: HIV viral monitoring, which is a better and early indicator to know whether the patient is responding to the medications or not could not be done at the time of initiating ART or as part of monitoring due to the cost involved.

CONCLUSION

It can be concluded that the detection and management of HIV has come a long way from just treating the opportunistic infections to initiating Antiretroviral agent to control the further progress of the disease. The guidelines for initiating ART have evolved over a period

of time. Patients with low CD4 count, low BMI are more prone for Opportunistic infections and death. Early initiation of ART can prevent such incidences and improve the quality of life of HIV positive patients. Better drugs are now available which have got least side effects.

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