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Research Article

Retrospective study on cost distribution of antiretroviral therapy in a tertiary care hospital

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ABSTRACT

Background: Acquired immunodeficiency syndrome (AIDS) is caused by human immunodeficiency virus (HIV), which is an RNA virus. The first case of AIDS in human beings was reported in 1981, and now spread of HIV infection is alarmingly high with around 20 million deaths. The objective of the study was to determine the cost distribution of antiretroviral therapy among autoimmune deficiency syndrome (AIDS) patient attending the anti-retroviral therapy (ART) center of the tertiary care center.

Methods: The objective of the study was to determine the cost distribution of antiretroviral therapy among AIDS patient attending the ART center of the tertiary care center. The study was retrospective, 20 patients included in different age groups and categories the cost incurred toward patients were divided under different heads: medication, laboratory diagnosis, transport, and miscellaneous costs.

Results: It was found that major part of the cost is spent on drugs. The cost of transport and lab diagnosis varied based on age and stage of the disease. Miscellaneous costs were also high and were proportional to other costs.

Conclusion: HIV infected population is more likely to have a lower socioeconomic status which has varied effect on the effectiveness of highly active ART. Some of the problems faced by them are access to health care, transport, economic instability, etc. all these factors have an impact on outcome of treatment. Overall it can be found that preventive measure than treating has better impact on quality of life.

Keywords: Acquired immunodeficiency syndrome, Human immunodeficiency virus, Highly active antiretroviral therapy, Cost, Retrospective

INTRODUCTION

Acquired immunodeficiency syndrome (AIDS) is caused by human immunodeficiency virus (HIV), which is the RNA virus. The first case of AIDS in human beings was reported in 1981, and now spread of HIV infection is alarmingly high with around 20 million deaths.[1] HIV is mainly of two types AIDS is mainly caused by HIV1 but in some parts of West Africa HIV2 is responsible.[2] Over the past 35 years, HIV infection has emerged as a major global health problem, WHO in 2009 showed 33.3 million people worldwide living with HIV, India even though has low HIV prevalence but has 3rd largest population with HIV1 and HIV2.

In 1992, national AIDS control program was launched; and in IJ2004, National AIDS control organization (NACO) was established. NACO was mainly responsible for better control of AIDS. As per the WHO statistics of 2012 there are 35.2 million people living with HIV with 2.3 million fresh cases.[3] The number of people receiving antiretroviral therapy (ART) is 9,700,000. The national adult (15-49 years) HIV prevalence is estimated at 0.27% for year 2011; 0.32 among males and 0.22 in females. There is steady decline from 0.49% in 2001. About 1.48 lakh people died of AIDS related causes in 2011. It is free ART since 2004, has saved over 1.5 lakh lives in the country until 2011.[2,3]

The various routes of HIV transmission as per latest are heterosexual (88.2) parent to child 15%, homosexual 1.5%, injection drug use (1.7%). Blood and blood products (1%) and unknown (2.7%).[3,4] It is mostly concentrated among female sex workers, injection drug abusers, transgender, etc. The virus is found in greatest concentration in blood, semen, and cerebrospinal fluid. Lower concentration has been detected in tears, Saliva, breast milk, urine, cervical, and vaginal secretion. Have also been isolated in brain tissue, lymph node, bone marrow, and skin.[4,5]

Table 1: Drugs used in the treatment of HIV.[6,7]

Class	Drugs/dosage
NRTI	Zidovudine (AZT) - 300 mg - BD Didanosin (dd1) 400 mg - OD Stavudine (d4T) 300 mg - BD Lamivudine (3TC) 300 mg - OD Abacavir (ABC) 600 mg - OD Tenofovir 300 mg OD
NNRTI	Nevirapine (NVP) 200 mg OD then 200 mg BD Efavirenz (EFV) 600 mg OD
PI	Atazanavir (ATV) - 300 mg-OD Indinavir (IDV) 800 mg TDS/BD Nelfinavir (NFV) 750 mg TDS Ritonavir (RTV) 600 mg BD Saquinavir (SQV) 1200 mg TDS/1000 mg BD Lopinavir 400 mg BD
Others	Entry fusion inhibitors - Enfuvirtide; CCR5 receptor inhibitor-Maraviroc; Integrase inhibitor-Raltegravir

NRTI: Nucleoside reverse transcriptase inhibitors,
NNRTI: Nonnucleoside reverse transcriptase inhibitors,
PI: Protease inhibitors

Table 2: WHO classification of stages of AIDS.[4,8]

Stages	Clinical manifestations
Stage 1	Asymptomatic, persistent generalized lymphadenopathy
Stage 2	<10% Loss of body weight, recurrent respiratory tract infections, herpes zoster, angular chelitis, recurrent oral ulcerations, popular pruritus eruptions, seborrhoeic dermatitis, fungal nail infections
Stage 3	>10% Weight loss unexplained chronic diarhoea, persistent fever, oral candidiasis, oral hairy leukoplakia, pulmonary TB, severe bacterial infections, ulcerative necrotizing stomatitis, gingivitis, periodontitis, unexplained anemia
Stage 4	HIV wasting syndrome, pneumocystis jiroveci/recurrent bacterial pneumonia, chronic herpes simplex infection, esophageal candidiasis, extrapulmonary TB, kaposi sarcoma, cytomegalovirus disease, CNS toxoplasmosis, HIV encephalopathy, extrapulmonary cryptococcosis, lymphoma, invasive cervical carcinoma, disseminated leishmaniasis

AIDS: Acquired immunodeficiency syndrome, TB: Tuberculosis,
CNS: Central nervous system, HIV: Human immunodeficiency
virus

Pharmacoeconomic is a branch of pharmacology as well as economics that is concerned with comparison of the cost of various therapeutic approach or modalities against the outcome. The objective is to allocate the funds according to the priorities, i.e., balanced distribution of the available finances.[8] The different methods for analysis in pharmacoeconomic are cost minimization, cost-effective cost benefit and cost utility. Economic burden of AIDS is of global importance, there is great need to carry out the pharmacoeconomic study of antiretroviral therapies, and hence the study was done.

METHODS

The basic aim of the study was to evaluate the cost estimation in AIDS. Patients who had underwent the treatment in controlled set up. Even though the drugs dispensed and investigations done to the patient were free of cost the government schemes. Cost incurred was calculated hypothetically based on standard charges. The above-mentioned parameters were evaluated for duration of 6 months from the time; they were diagnosed and started on standard therapy. The study is a randomized retrospective study conducted in the patients visiting the ART center attached to SIMS Shimoga. The patients (20) in number were randomly chosen 9 men 9 women and 2 children/adolescents. Only those who were regular in treatment and regular in scheduled visit to the hospital for general checkup and investigations were included in the study. While selecting the patients group, care was taken for equal distribution in terms of age and clinical stage of the disease.

Based on the WHO clinical stages patients from Stages 1, 2, and 3 were included. The distribution of patients included in the study was as shown in Table 3.

There are different models under pharmacoeconomic studies. The cost minimization analysis tries to provide the best treatment with minimum cost. The cost-effectiveness analysis is related with how to achieve an objective with minimal possible cost. The analysis includes cost of medicine, any investigations, or test adverse effects, etc., cost-benefit analysis is broader than cost-effective analysis. It is related with whether to pursue the objective or not and is concerned with the value of money for quality, as well as quantity of life. Cost utility analysis is basically comparison between the programs. The outcome of treatment is calculated based on computing the quality adjusted life years (QALY).

The cost incurred on the patient was divided into following heads
1. Cost for medications: this includes the costs (on all medications) antiretroviral drugs as well. Drugs prescribed for secondary infection
2. Cost for lab investigations: included the cost included in the laboratory, investigations done toward the diagnosis, Follow-up investigations done to access the effectiveness of antiretroviral therapy. Enzyme-linked immunosorbent assay, western blot, complete

Table 3: The groups and stage of AIDS patient chosen.

Age group	Group 1 <20 years	Group 2 21-35 years		Group 3 36-50 years		Group 4 above 50 years		Total
		Male	Female	Male	Female	Male	Female	
Stage 1	1	1	1	1	1	1	1	07
Stage 2	1	1	1	1	1	1	1	07
Stage 3		1	1	1	1	1	1	06
	02	03	03	03	03	03	03	20

AIDS: Acquired immunodeficiency syndrome

Table 4a: Cost of individual drugs (INR).[9]

Drug dose (mg)	Minimum	Maximum
Zidovudine 100	100	536
Zidovudine 300	153	215
Lamivudine 100	76	280
Lamivudine 150	85	230
Tenofovir 300	400	997
Didanosine 250	240	417
Didanosine 400	390	650
Efavirenz 200	270	275
Efavirenz 600	690	774
Indinavir 400	190	257
Abacavir 300	470	784
Nelfinavir 250	234	400
Nevirapine 200	136	195
Ritonavir 100	275	300

Table 4b: Cost of drug combinations (INR).[9]

Combination	Dose (mg)	Min	Max
Lamivudine+zidovudine	150+300	198	820
Lopinavir+ritinavir	133.3+33.3	400	500
Lamivudine+zidovudine+nevirapine	150+300+200	225	240
Efavirenz+zidovudine+lamivudine	600+300+300	1080	1100
Stavudine+efavirenz+lamivudine	30+600+150	940	950
Lamivudine+stavudine	150+30	109	115
Lamivudine+stavudine	150+40	114	240
Nevirapine+lamivudine+stavudine	200+150+30	215	230
Nevirapine+lamivudine+stavudine	200+150+40	222	240
Didanosine+efavirenz+lamivudine	250+60+300	1110	1260

blood count, absolute CD4 lymphocyte count, CD4 lymphocyte percentage, HIV viral load tests, B$_2$-microglobulin, and p24 antigen

3. Cost for transport: Transport cost included the cost by the patient for traveling from his home to the hospital for treatment

4. Miscellaneous costs included the subsidiary costs, costs on medications and lab investigations other than AIDS such as treatment for diabetes mellitus, hypertension and cancer. It also includes the cost increased by the patient towards his attendants. The costs on the medications were calculated based on WHO guidelines, standard drug therapy. It should be noted that we have not included the cost on hospitalization due to aggravation of disease.

National pharmaceutical pricing authority revised prices of 418 drugs in 2014, of which zidovudine, lamivudine, stavudine, nevirapine, and indinavir are the antiretroviral drugs included in list of essential drugs, but other newer and more effective drugs are not included. It was found that cost of first line drugs in therapy was cheaper compared to the second line antiretroviral drugs.

RESULTS

Cost of treatment on younger age group was relatively less compared to elderly. The cost of medications increased proportionally with the age group and stage of the disease. In some cases, the secondary infections and associated complications were responsible for increased cost. The cost incurred on lab investigations also increased proportional to age group, as well as stage of the disease. Higher investigations were needed and frequency of lab investigations done increased with stage of the disease; this increase was also seen with age. The transport related costs did not vary much but still it was higher in an elderly and late stage of disease as they needed ambulatory services, which increased the cost. The miscellaneous costs increased proportionately in relation to other costs, with age and stage of the disease.

DISCUSSIONS

Prevention and treatment are the modes for control of AIDS, but still it is found that prevention is better than cure. Prevention can be done by proper education and creating awareness on the spread of HIV among the public. Safe sex be encouraged sharing of razors, needles in IV abusers should

Table 5: Different regimens specified by NACO for ART.

First-line antiretroviral regimens			Second-line antiretroviral regimens		
Regimen	App* cost/day (INR)		Regimen	App* cost/day (INR)	
	Max	Min		Maximum	Minimum
Preffered 3TC+AZT+NVP	45	48	PI component LPV, ATV, SQV, IDV, NFV	LPV (240), IDV (114), NFV (210)	LPV (300), IDV (154), NFV (360)
Alternative 3TC+AZT+EFV 3TC+d4T+EFV 3TC+d4T+NVP	 108 91 43	 241 100 46	NRTI components Tenofovir+ABC dd1+ABC Tenofovir+AZT Tenofovir+3TC	 134 118-133 60 57	 256 198-222 207 146
Other 3TC+Tenofovir+NVP 3TC+Tenofovir+EFV 3TC+AZT+tenofovir	 84 126 80	 184 220 266	 dd1+AZT dd1+3TC	 44-149 41-88	 59-172 56-111

NACO: National AIDS control organization, ART: Anti-retroviral therapy

Table 6: The various expenses (average) incurred in different groups.

Costs incurred	Various groups						
	Group 1	Group 2 (M)	Group 2 (F)	Group 3 (M)	Group 3 (F)	Group 4 (M)	Group 4 (F)
Medication	11646	15936	16064	18780	20943	21258	21130
Lab diagnosis	2000	3500	4000	3667	4100	4133	4533
Transport	1600	2233	2000	2600	2267	3133	2800
Miscellaneous	6405	8764	9638	10329	12565	12754	12678
Total	21751	30433	31702	35376	39875	41278	41141

Table 7: The average cost incurred in various stage.

Cost incurred	Stage 1	Stage 2	Stage 3	Total	Average
Medication	11723	18807	21710	52240	17413
Lab diagnosis	2614	3400	5616	11630	3876
Transport	1785	2000	3683	7468	2489
Miscellaneous	6448	12103	20155	38706	12902
Total	22570	36310	51164	110044	36681

be discouraged women suffering from AIDS or who are at high risk of infection should be advised to avoid pregnancy. Educational guidelines are made widely available, mass media channels should also actively participate in educating people on AIDS. High-risk groups should be urged to refrain from donating blood, body organs, sperms, and tissues. All blood samples are screened for HIV1 and HIV2 before transfusion. Strict sterilization practices should be ensured in hospitals and clinics, presterlize disposable syringes, and needles should be used as far as possible. The treatment of HIV infection is prolonged, needs expertise, strong motivation and commitment of the patient, overall it is complex and complicated. In 25 years of history of antiretroviral therapy the failure in treatment is mainly due to emergence of resistance. Monotherapy with drugs is contraindicated it has been mandated highly active

antiretroviral therapy (HAART),[10] where combination of three or more drugs are used. HAART rapidly kills >99% virions, a small number survive within the resting CD4 lymphocytes and invariably gives rise to relapse in the treatment. HIV reverse transcriptase is a highly copying error prone and rate of mutation is high with progress of disease in population HIV becomes genetically complex and diverse with susceptibility to drugs.[10,11]

It is characterized by marked inflammatory reaction against organisms to reestablish immune functions. NACO recommends two types of regimens for postexposure prophylaxis depending on the magnitude and risk of HIV transmission. In case of low risk two drug regimen zidovudine 300 mg + lamivudine 150 mg BD daily for 4 weeks.[12] In high risk cases expanded three drug regimen zidovudine 300 mg

BD + lamivudine 150 mg BD + Indinavir 800 mg TID for 3 weeks. There is no data to evaluate the value of prophylaxis after sexual exposure; the same regimens for needle stick may be used. HIV may be transmitted from mother to child either through placenta or during the delivery. There is the highest risk (70%) of transmission during birth process. The first line NACO regimen for pregnant women is (zidovudine + lamivudine + nevirapine).[11,12]

QALY is the unit of health measurement that combines the quantity (duration) of life with its quality. The quality of life is comprised of physical mobility, freedom from pain and distress, capability for selfcare, engage in normal work and social interaction.[13] An appropriate treatment saves or extends the life expectancy; although life is extended quality of life is low and not worth to extend it at all. Global health sector strategy on HIV/AIDS for 2011-15[2] stresses on these four strategic directions. Optimize HIV prevention, diagnosis, treatment and care outcomes, (a) leverage broader health outcomes through HIV responses, (b) building and sustainable health systems, (c) address inequalities and advance human rights. As the study was retrospective we had to rely mainly on the available data and past records and we could not follow the patient. Errors due to confounding and bias are more common as in any other retrospective studies. The advantage here was it could be conducted in a smaller scale and required less time to complete and analysis was better with multiple outcomes. Even though the study was restricted to only 20 subjects the results are effective enough to extrapolate for larger group. If still larger population was considered for analysis, we could have come out with better and accurate outcomes.

CONCLUSION

None of the currently available regimens can eradicate HIV from body the goal of therapy is to maximally and durably inhibit viral replication. So, treat the patient can attain and maintain effective immune response against secondary infections. Immune reconstitution syndrome usually occurs after institution of HAART in patients with latent or partially treated opportunistic infections. The pharmacoeconomic studies play a vital role in assessment of the cost-effectiveness of the treatment, so also in this case it's a vital tool to access the cost-effectiveness in HAART in HIV patients. The majority of the patients coming to the ART center are from the lower socioeconomic status they face many financial related problems. NACO provides free treatment, when we look at the quality of life of these patients it seems there is need to work more in his direction. Overall we find that preventive measures for disease, educating the public on AIDS and its grave effects will be more effective in control and eradication of disease.

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