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Clinicopathological changes in PL HIV on ART 2 after failure of ART 1 and causes of ART 1 Failure.

Dr. Narendra Singh, M.B.B.S, M.D. (Medicine), Senior Resident, Department of Medicine, Rama Medical College, Hospital and Research Centre, Kanpur, Uttar Pradesh. India.
E-mail. *narendrasingh0011@gmail.com*
Dr. Lalit Kumar, M.B.B.S, M.D. (Medicine), Senior Resident,
Department of Medicine , KPS PG Institute of Medicine, GSVM Medical College, Kanpur, Uttar Pradesh, India E-mail: *lalit85gsvm@gmail.com*
Dr. Desh Nidhi Singh, Associate Professor, Department of Microbiology, Rama Medical College, Hospital and Research Centre, Kanpur, Uttar Pradesh India. E-mail: *deshnidhisingh@gmail.com*
Dr. Vipin Kumar M.B.B.S, M.D. (Anatomy), Senior Resident, KGMU, Lucknow, Uttar Pradesh, India E- mail: *vipin.prathamdas@gmail.com*
*Corresponding Author: **Dr. Narendra Singh, M.B.B.S, M.D.** (Medicine), Senior Resident, Department of Medicine, Rama Medical College, Hospital and Research Centre, Kanpur, Uttar Pradesh, India. E-mail: *narendrasingh0011@gmail.com*

Keywords

HIV,
ART,
Pneumocystis jirovecii,
Haemoglobin,
Serum Bilirubin and
Serum creatinin

Abstract

Background: HIV is virus, cause of AIDS, belong to the family retroviridae and subfamily Lentiviruses was first recognized in United States in summer of 1981 when U.S. Centres for disease control and prevention (CDC) reported the unexplained occurrence of *Pneumocystis jirovecii*. Person with positive HIV serology who have ever had a CD4 lymphocyte count below 200celles/micro L and CD4 lymphocyte percentage below 14% are considered to have AIDS

Materials and Methods: This study was conducted in ART plus centre K.P.S. Post Graduate Institute of Medicine (tertiary care teaching hospital) G.S.V.M. Medical College, Kanpur, Uttar Pradesh, India and is clinical (assessment with investigation) continuous longitudinal, prospective and retrospective , observational, single centre hospital based study was screened 1st line ART taking subjects for treatment failure decided by SACEP from 2016 t0 2018.

Result: this study subjects was female (71) and male(47) and rural(65) and urban (53) area . Increase of subjects of haemoglobin< 9 (4 to 5) to serum bilirubin>1 (5 to 10) and serum creatinine>1.5 (6 to 10).Oral Candidiasis (28) and pulmonary tuberculosis(27) and mode of transmission through heterosexual(97) was maximum subjects.

Conclusion: In this study the maximum opportunistic infection were oral candidiasis and tuberculosis. Female and rural population with heterosexual mode of transmission was predominance .Haemoglobin, Serum Bilirubin and Serum creatinin was increase and general symptoms was present that decrease during ART 2 treatment.

Introduction

HIV is virus, cause of AIDS, belong to the family of human retrovirus (Retroviridae) and subfamily Lentiviruses consist of two distinct groups the human T lymphotropic virus(HTLV-1) and human T lymphotropic virus-2 (HTLV-2) are transforming retroviruses , human immunodeficiency virus HIV -1 and HIV-2 .HIV-1 have different group as M,N,O and P . M group is having nine subtype A,B,C,D,F,G,H,I and k and about 60 recombinant form presents .CRFs range from highly prevalent form such as CRF01 that is common in southeast Asia and CRF02AG from west and central Africa. HIV-1group M subtype C dominating as the global pandemic, came from Chimpazees and Gorila .HIV-2 was first identified in 1986 in West Africa, came from Sooty Mangabeys and spread from West Africa to other part of world. In India 95% of infection of HIV -1 and group C but in United States more infected population is from HIV-1 and group B. A confirmed HIV Case can be classify one of five stage that are 0,1,2,3, and unknown.

Table-1 Tabular representation of stages of HIV infection

Stage	CD4 Cell count (6year to adult)[cell/micro liter]	% of CD4 Count
0	negative HIV in 6 month after HIV infection	
1	>500	>25
2	200-499	14-25
3	<200	<14
UNKOWN	If no criteria applied because of missing CD4	

This show that stage 3 is the CD4 less than 200 and less than 14% this stage is known as AIDS.

Table 2- Tabular representation of clinical staging of HIV infected patients

Sl no.	Clinical stage	Disease
1	Stage 1	1. Asymptomatic 2. Persistent Generalized Lumphadenopathy.
2	Stage 2	1. Unexplained moderate weight loss (< 10%) of presumed or measured body weight) 2. Recurrent respiratory tract infections (sinusitis, tonsillitis ,oitits media , pharyngitis) 3. Herpes zoster 4. Angular cheilitis. 5. Papular pruritic eruptions . 6. Seborrheoic dermatitis . 7. Fungal nail infections

3	Stage 3	1. Unexplained 2 severe weight loss (<10 % of presumed body weight) 2. Unexplained chronic diarrhoea for longer than one month. 3. Unexplained persistent fever (above 37.5OC intermittent or constant for longer than one month 4. Persistent oral candidiais 5. Oral hairy leukoplakia 6. Severe bacterial infectons (e.g. pneumonia ,emphysema ,bone or joint infections. 7. Acute necrotizing ulcerative stomatitis , gingivitis ,periodontitis . 8. Unexplained anaemia (<8/dl) , neutropenia (< 0.5 *109/litre) and or chronic thrombocytopenia.(<50*109/litre)
4	Stage 4	1. HIV wasting syndrome 2. Pneumocystic pneumonia 3. Recurrent severe bacterial pneumonia 4. Chronic herpes simplex infection (oralabial , genital or anorectal of more than one months duration or visceral at any site 5. Oesophageal candidiasis (or candidiasis of trachea , bronchi or lungs.) 6. Extrapulmonary Tuberculosis 7. Kaposi sarcoma 8. Cytomegalovirus infection (retinitis or infection of other organs 9. Central nervous system Toxoplasmosis . 10. -HIV encephalopathy. 11. Extrapulmonary Cryptococcosis. 12. Lymphoma 13. Atypical disseminated Leismaniasis.

This table show the different clinical symptoms present and diseases in HIV infected patients. The clinical feature of HIV infected patients appear when viral load of patient is increase and CD 4 count decrease 'WHO categorise the clinical staging in which stages 4 and stage 3 are recognized as AIDS

HIV was first recognized in United States in summer of 1981 when the U.S. Centres for disease control and prevention (CDC) reported the unexplained occurrence of *Pneumocystis jirovecii* in previously healthy homosexual men in Los Angeles And Kaposi sarcoma (KS) with and without *P. jiroveci* and other opportunistic infections in 26 previously healthy homosexual men in New York, San Francisco and Loss Angles. First time in 1983 Human Immunodificiency Syndrome (HIV) was isolated from a patient of lymphadenopathy and by 1984 it was demonstrated clearly the causative agent of AIDS .In 1985 A sensitive enzyme- linked immune sorbent assay (ELISA) was developed then Scope and Evolution of HIV among developing nations throughout world happened.

HIV attack on white blood cell, CD4+T cell and CD4 cell damage so CD4 count decrease .and immunity of body decrease as the result there are so many infection occurred in the body that are called opportunistic infections.

Table -3 Tabular representation of opportunistic infection and its causes

SL. N.	Opportunistic infection	Cause	Location
1	Candidiasis	Fungus	Mouth, Throat, Foot Vagina
2	Cytomegalovirus	Virus	Eyes, Lungs, Brains and Guts
3	Cryptococcosis	Fungus	Brain And spinal cord
4	Cryptospordiasis	Parasite	Gut
5	Mycobacterium avium complex	Bacterium	Gut lung, Skin
6	Mycobacteria. tuberculosis	Bacteria	Lung, Heart, Liver and Brain
7	PML	Virus	Brain
8	Toxoplasmosis	Parasite	Brain
9	Pneumocystis pneumonia	Fungus	Lung

There are different type of organism that can infect organs of human when body immunity become very low and CD4 count very low so patients on different CD4 count have different infection.

Table 4 Tabular representation of opportunistic infection on the basis of CD4count

SL.N.	CD4 Count	Opportunistic infection
1	<500	Tuberculosis, Bacterial Pneumonia, Heroes zoster, Oropharyngeal.candidiasis, Non Typhoid Salmonelosis, Kaposy sarcoma, Non Hodgkin lymphoma
2	<200	Pneumocystic Jirovecy Pneumonia,Cronic Herpes Simplex Ulcer,Oesophageal Candidiasis, Isospora Belli Diarrhea, HIVwasting syndrome, HIV Associated dementia
3	<100	Cerebral Toxoplamosis, *Cryptococal meningitis*, Cryptospordiasis, Microspordiasis, Cytomegalovirus infection and disseminated *Mycobacterium avium* complex Progressive multifocal leucoencephalopathy
4	<50	Cytomegalovirus infecton cryptococal meningitis lymphoma

This table show that as well as the CD4 count decrease the more serious infection occurred and more dangerous and life threatening symptoms happened.

HIV virus is transmitted through HIV infected patients to uninfected patients by number of way as

1. Sexual transmission
2. Transmission through injection drugs use
3. Transmission by transfused blood and blood products.
4. Occupational transmission of HIV
5. Mother to child transmission f HIV
6. By different body fluids

Table 5 - tabular representation of estimated per act probability of acquiring HIV from an infected source by exposure act

SL .No.	Type Of Exposure	Rout Of Exposure	Risk Per 10000 Exposure
1	Parental	Blood transfusion Injection drugs use Percutaneous	9250 63 23
2	Sexual	Receptive anal intercourse Insertive anal intercourse Receptive vaginal intercourse Insertive vaginal intercourse Recetive oral intercourse Insertive oral inter course	138 11 8 4 LOW LOW
3	Mother To Child	Vaginal delivery Breast feeding	1500 54
4	Other	Bititng Spitting Throughing body fluid sharing sex toys	Negligible Negligible Negligible Negligible

This table show that the blood transfusion is most common mode of HIV transfusion and oral intercourse is the lowest amount of transmission method and also bitting spitting have negligible mode of method transmission.

Table- 6 Tabular representation of stages of HIV infection and their related symptoms.

S.l. no.	Stage of Infection	Symptom And Character
1	Primary infection	HIV virus inter to the body through the different way and inter to susceptible cell having CD4 via receptor CCR5 AND CXCR4 .In the cell it multiplied through replication process
2	Acute HIV infection	about 50 % to70% of individual with HIV infection experience an acute clinical syndrome about 3 to 6 week after primary infection. It has been reported that several symptoms of acute HIV syndrome .such as 1-Fever, 2-Pharangitis, 3-Lymphadenopathy, 4-Headache 5-Arthragia, 6-Lethargy/anorexia, 7- Weight loss, 8- Myopathy, 10-Encephalopathy

3	Asymptomatic stage (Latent stage)	This the stage in which the symptoms of infection is not present but HIV disease with active virus replication is ongoing and progressive. The HIV RNA level is very low level but in this stage when CD4 count decrease to the critical level and then the opportunistic infection occurred but symptoms of HIV infection is not present.
4	Symptomatic stage	Symptoms of HIV disease can appeared at any time during the course of HIV infection. The spectrums of illness that can be present as CD4 Count decline, More severe and life threatening complications of HIV infection occurred in patients with CD4 count is less than 200 /micro L. That are A -AIDS Defining illness-The diseases published by the centres of disease control and prevention that are associated with AIDS and used World wise as a guideline for AIDS diagnosis that are 1-Candidiasis of brochi, trachea or lungs 2-Candidiasis of oesophagus 3-Coccidiodomycosis 4-Cryptococcosis 5-Cryptospordiasis 6-Cytomegalovirus retinitis 7- Encephalopathy 8-Herpes simplex 9-Histoplasmosis 10-Isospordisis 11-kaposi,s sarcoma 12-Burkitts Lymphoma 13- Immunoblastic Lymphoma. 14-Mycobacterium Avium complex or Mycobacterium kanasi 15 –Mycobacterium Tuberculosis 16-*Pneumocystis jirovecii* Pneumonia 17- Progressive multifocal Leukoencephalopathy 18- Salmonella sepsis 19 –Toxoplasmosis of brains 20-Tuberculosis disseminated 21- Wasting syndrome 22-Cervical cancer 23-Pneumonia recurrent 24- Mycobacterium tuberculosis any site (pulmonary) B-Opportunistic infection stage-This is the infection occurred more often or more severe in people with weakened immune systems than in people with healthy immune systems. 1-Aspergillus sp 2- Candida albicans 3-Clostridium diffixile 4-Coccidioides immitis 5- Cryptococcus neoformans 6- Cryptosporidium 7-Cytomegalovirus

		8-Geomyces.destructans 9-Histoplasma.capsulatum 10-Isospora belli 11-Polyoma.virusJC.Polyomavirus 12-Kaposi Sarcoma 13-Legionaire disease 14-Microsporidium 15-Mycobacterium –avium complex 16 – Mycobacterium tuberculosis 17 –Pneumocystis jirovecuu 18 –Pseudomonas aeroginosa 19-Salmonella 20-Staphylococcus aureus 21- Streptococcus pneumonia 22-Streptococcus pyogenes 23- Toxoplasmosis gondii C-Non aids defining illness- 1- Non AIDS related cancer 2- Cardiovascular disease 3- Renal disease 4- Hepatic disease. 5-Hodgkins disease 5- Multiple myeloma 6- Leukemia 7- Melanoma
5	HIV Associated illness-	1- Cardiomyopathy 2- Enteropathy 3- Nephropathy 4- Lipodystrophy 5- Arthropathy 6- Fibromylgia 7- Neurocognitive disorder 8- Dementia 9- Encephalopathy 10- Myelopathy 11- Peripheral neuropathy
6	ART Associated symptoms-	The disease occurred during antiretroviral therapy as adverse effects. 1-Anemia 2- Thrombocytopenia 3 –Jaundice 4 –Abdominal pain 5-Pancreatitis 6- kidney injury 7- Hypersensitivity syndrome 8-Lipodystrophy 9-Nausea, Vometing, Diarrhea 10-Osteomalacia 11-Hyperglycemia 12Vertigo

This table show the presence of symptoms and the stage of HIV infection. This also show that After infection of patient by different mode the events in the body is happening that are

Biomarker that used for diagnosis and prognosis of HIV infected patients

1-HS CRP- is a potential biomarker for predicting long term disease progression, cardiovascular disease risk, predict mortality, disease progression and faster progression to AIDS .

2-D-DIMER- is the marker of inflammation and endothelium activation and hyper coagulation and linked increase risk of non AIDS events in HIV +VE patient

3-CD4 COUNT- decrease when HIV is enter to infected cell and innocent bystander cells and use for monitoring of HIV progression.

4-CD8 COUNT-.CD8+Tcell developed a phenotype of HLA-DR+/CD38+ had aggressive course and poorer prognosis and whose CD8+T cell developed a phenotype of HLA-DR+/CD38- had stabilization of the CD4 counts .

5 –IL6 (INTERLEUKINE- IL6 can be used as a marker for inflammation in HIV infected patients and presence of diseases as cardiovascular, hepatitis and kidney injury. And monitoring of adherence and efficacy of PL based regimen.

6-IL-1 (INTERLEUKINE-1) - is mortality indicator have more chance of myocardial; infarction.

7-IP-1INTERFERON–(IFNY)- INDUCED PROTIEN10 – is a chemokine involved in trafficking immune cell to inflammatory site and related to degree of progression of PL HIV .

8-sCD14-is the inflammatory marker indicates the mortality of PL HIV.

9-HLA ALLELES— ALLELES as HLA-B57 and HLA-B27 is associated with slower disease progression and lower virologic setpoint .HLAB 35 is associated with faster progression to AIDS and higher viral load .HLA B 51 is having protective phenotype.

11-APOE GENE - a gene that have associated with several cognitive outcome.

13-CC-chemokine-It is the soluble factor and nonspecific are the potent suppresser of HIV replicatipon .

13-T-regulatory cells or T-regs- involve in dampening aberrant immune activation that propagates HIV replication.

The pathological test that are used for diagnosis of HIV infected patient is

1. **ELISA TEST-** IT test the presence of antibody of HIV and p24 Antigens .It have the 99.5% sensitivity. It used for screening test.
2. **WESTERN BLOT TEST-**It is the specific assay that is used for confirming test for HIV infection .it is 99% specific test for HIV infection.
3. **IMMUNE COMPLEX –DISSOCIATED P24 ANTIGEN CAPTURE ASSAY**- It is used for measurement of level of HIV -1 CORE protein in an EIA –based format following dissociation of antigen –antibody complexes by weak acid treatment .It can detected the p24 level up to 15pg/ml
4. **HIV RNA BY BDN-** Measurement of level of particle –associated HIV –RNA IN a nucleic acid capture assay employing signal amplification .It is reliable to 50 copies /ml of HIV RNA.
5. **HIV RNA BY TMA-** It is done by target amplification of HIV-1 RNA via reverse transcription followed by T 7 RNA polymerase. It is reliable to 100 copies/ml of HIV RNA .
6. **HIV RNA BY NASBA-**It is done by isothermal nucleic acid amplification with internal controls. It is reliable to 80 copies /ml of HIV RNA.
7. **HIV RNA by PCR-** It is done by target amplification of HIV 1 RNA via reverse transcription followed by PCR. It is reliable to 40 copies/ml of HIV RNA.

Standard combination of antiretroviral regimens are two NRTI together with an NNRTI, PROTEASE INHIBITOR (PI) or INTEGRASE INHIBITOR . Starting regime of dual NRTIs combined with an NNRTI or a PI or an INTEGRASE INHIBITOR .These regimen should be monitored for resistant testing. If resistant testing is not available then PI in second line regimens are preferable.

Monitoring of efficacy during art treatment.

A base line viral load should be measured prior to initiating treatment .Viral load should be repeated 4 to8 weeks after starting a new regimen when the count should show at least a tenfold decrease. After six month of ART The viral load should be suppressed defined as below the detection of the assay (usually less than 50 copies /ml).

WHO defined immunological failure as fall in CD 4 Count to base line or a 50% fall from peak on ART or persistent count below 100cell/mm.

Failure of art is defined as Viral load become detectable after Suppression typically more than 400 or more than 1000 Copies/ml).

First time ART should consists of two nucleoside reverse transcriptase inhibitor (NRTI) +One Non nucleoside reverse transcriptase.7

The second line ART regimens comprised of zidovudine (ZDV), lamivudine (3TC), tenofovir (TDF), and boosted Lopinavir/ritonavir (LPV/r) have been introduced recently in a phase wise manner at limited centres. The criteria to switch on second line ART includes clinical and/or immunological and/or virologic failure in a patient who had received 6 months or more of standard first-line ART. The patient qualify for second line ART if they demonstrate CD4 decline to pre-ART values, CD4 drop to less than 50% of peak on-treatment value, failure to achieve CD4 greater than 100 c/mm^3 (immunologic failure), or develop a new WHO stage III/IV AIDS-defining illness (clinical failure) or those with HIV RNA 10,000 c/ml or greater (virological failure).

The Second line treatment programme is still relatively new with little experience in India population. Without resistance testing and 6 monthly virological monitoring the consequences of second line therapy outcomes are unclear. It is therefore, critical to assess the clinical, virological and immunological effectiveness and treatment outcome over the first year of follow-up in the patients switched to second line therapy at public sector tertiary care center.

Aims & Objectives

Clinicopathological changes in PLHIV on ART2 after failure of ART1 and causes of ART1 failure**.**

Materials and Methods

This study will be conducted in ART plus centre K.P.S. Post Graduate Institute of Medicine (G.S.V.M. Medical College, Kanpur) tertiary care teaching hospital from Dec 2016 to Dec 2018

Type of Study: Single centre hospital based study

Study Design:

This will be clinical (assessment with investigation) continuous longitudinal, prospective and retrospective, observational, single centre hospital based study at ART plus Centre, G.S.V.M. medical college Kanpur Uttar Pradesh, India.

Study Subject:

All the patient on 1st line ART treating in the centre will be screened for treatment failure based on clinical, immunological and virological criterias as decided by SACEP.

Inclusion Criteria:

1. Patient over the age of 18 years at pre-inclusion and monitored under outpatient condition.
2. Documented HIV-1 (group m) infection regardless of clinical stage and CD4 lymphocyte count (taken in 6 months)
3. Patient with treatment failure after first-line antiretroviral treatment with a combination including a non-nucleoside reverse transcriptase inhibitor and two nucleoside reverse transcriptase inhibitors, failure.
4. Adherence (>80%) to first-line antiretroviral treatment (questionnaire) at pre inclusion.
5. Patient agrees not to take any concomitant medication during the trial without informing the investigator.
6. Informed consent
7. For women in childbearing age: negative pregnancy test at inclusion, with no plan of pregnancy in the coming 12 months and agreeing to use mechanical contraception (with or without hormonal contraception) during the study.

Exclusion Criteria :

1. Infection with HIV-2 or HIV-1 groups O or N or HIV 1+2.
2. Adherence (<80%) to first-line antiretroviral treatment at pre inclusion.
3. Participation in any other clinical trial.
4. Presence of an uncontrolled, ongoing opportunistic infection or of any severe of progressive disease.
5. First-time treatment with a protease inhibitor, Abacavir.
6. Not interested to participate in study.
7. Severe hepatic insufficiency.
8. Creatinine clearance calculated by Cockcroft-Gault formula <50 ml/min.
9. Hb≤ 8 g/dl
10. Platelets < 50,000 cells / mm^3

11. Neutrophiles<500 cells / mm^3
12. Pregnancy or lactation.

Blood sample collection

On admission, 10 ml of peripheral venous blood was collected from the ante cubital vein by an autoclaved syringe using 20 gauze needles. The blood was allowed to clot at room temperature for at least half an hour. The glass tube with clotted blood was centrifuged at 2000 rpm for 20 minutes and the centrifugation was repeated once more to remove the red cells completely. The supernatant serum, devoid of cellular elements, was separated from the clot and placed in two acid cleaned small test tubes.

Viral load testing

Patient of HIV suspecting first line ART failure send to BHU Vanaras Department of Microbiology, IMS BHU Banaras.

For estimation of viral load
In BHU viral load is tested quantitatively real time PCR from HIV RNA by PCR machine.

Measuring

Viral load is typically reported as copies of HIV in a milliliter (mL) of blood. Changes in viral load are usually reported as a log change (in powers of 10). For example, a three log increase in viral load (3 Log10) is an increase of 10^3 or 1000 times the previously reported level, while a drop from 500,000 to 500 copies would be a three-log-drop (also 3 Log10).

CD4 count is done by BD facts flow machine by kit and report is analysed and given same day.

Results

Table 5 tabular representation of mode of transmission in study subject

Mode of transmission	No. of patients	%age
Heterosexual	97	82%
Unknown	6	.05%
Blood transfusion	11	.09%
Ten tracker	2	.01%

In this study the most common mode of transmission of HIV infection was heterosexual and least common is tracker. blood transmission mode of transmission is also present in .09%

Table 6: Tabular representation of Hb in study subject before one year and one year after

Criteria	1 year before of ART 2	1 year after of ART 2
<9	4	5
9-10	4	5
>10	101	108

In this study the hemoglobin level in the study subject is increase in the subjects, more than 10 the hemoglobin was increase in 101 subject to 108 subjects

Table 7: Tabular representation of serum bilirubin in study subject before one year and one year after

Criteria	1 year before of ART 2	1 year after of ART 2
<1	113	105
>1	5	13

In this study the serum bilirubin level is increase in the subject more than 1 in subject 5 to 13 subjects

Table 8: Tabular representation of serum creatinine in study subject one year before and one year after

Criteria	1 year before of ART 2	1 year after OF ART 2
<1	86	84
1-1.5	16	24
>1.5	6	10

In this study the serum creatinie level is increase from 6 to 10 and in more than 1.5 and less than 1 decrease in the subject of 86 to 84 and also increase the subject 16 to 24 of serum creatinine level 1 to 1.5.

Table 10 Tabular representation of opportunistic infections in study subjects

Opportunistic infection	No. of subjects	%age
Oral candidiasis	28	23%
LRTI	10	8%
Pulmonary tuberculosis	27	23%
Chronic Diarrhea	5	4%
TBL	3	2%
Tuberculosis of pericardium	1	0.8%
TBM	3	1%
Extra pulmonary tuberculosis	14	11%
Abdominal Kocks	2	1%
NO infection	25	21%

Magnitude of opportunistic infection in study subject Our study show that oral candidiasis is maximum in no of subject(28) 23% and then second maximum is pulmonary tuberculosis(27) 23% (but overall total no of subject of pulmonary tuberculosis 23%, tuberculosis of pericardium 0.8% ,extra pulmonary tuberculosis 11% and pulmonary kocks 1% ,tubercular meningitis 1% and tubercular lymphadenitis 2%) is 36% that is maximum. LRTI was 8% and chronic diarrhea is 4%

Table –11 Tabular representation of base line characteristics of the patients in study.

Sl.no.	Characteristic	No. Of patient	Percentage
1	Gender		
	Male	47	39%
	female	71	61%
2	Age		
	20 -30years	23	19%
	30 -40 years	54	45%
	40 -50 years	29	25%
	50 -60 years	11	9%
	60-70 years	1	.001%
3	Geographical area		
	Urban	65	55%
	Rural	53	45%
4	Habit		
	Smoking	13	11%
	alcohol	53	45%
	tobacco	8	7%

5	Regime I TLE ZLN	 90 28	 76% 24%
6	Regime 2 TLATV/R ZLATV/R TLLP/R ZLLP/R	 35 74 5 4	 30% 59% 4% 3%
7	Clinical symptoms Weight loss Fever Diarrheal COUGH	One year before 105 34 56 24	One year after 20 5 5 12
Adverse Effect	Nausea Vomiting Diarrhoea Anaemia Abdominal pain Jaundice Kidney abnormality Headache Muscle pain Skin rash	30 46 25 37 20 28 5 24 46 18	25% 38% 21% 31% 16% 23% .04% 20% 38% 15%

This study consider the basic characteristics and also the data are taken as age, sex geographical area habit regime and clinical symptoms in base line study.

This study was conducted in ART plus centre KPS PG Institute of Medicine (G.S.V/M/ medical college Kanpur) considering total no of 118 subjects and All went Laboratory investigation .In 118 subject all the subject analysed and in all there was 94 subject have opportunistic infection and 25 was not having infection . In which Oral Candidiasis was found about 28 subject and Pulmonary Tuberculosis was found in 27 subjects Overall in subjects there was 50 subjects have Tuberculosis in which Pulmonary Tuberculosis was 27 Tubercular Lymphadenitis in 3 subjects ,TBM IN 3 subjects, Abdominal Kocks in 2 subjects and Extrapulmonary Tuberculosis in 14 subjects, so Individually Oral Candidiasis (28) is most common and Pulmonary Tuberculosis(27) is second most common but all kind of tuberculosis is most common about 50 subjects.

This study was considered as TLE AND ZLN regime in first line regime and TLATV/R, ZLATV/R, TLLP/R/ and ZLLP/R in second line of ART.

Discussion

Virendra Chandrashekhar Patil and Harsha V, Patil:[1] Clinical manifestation and outcome of patient with Human Immunodifficiency virus infection at tertiary care Teaching hospital .This considered 111 patients as observational retrospective study and in which about 75 were male and 36 were female and there was pulmonary tuberculosis and community acquired pneumonia is present. In this study the oral candidasis and lymphadenitis was present in 6 patients. In our study there was pulmonary tuberculosis anaemia LRTI, chronic diarrhoea is seen. In our study the male was less and female was more.

Neha Wal, Vimla Venkatesh ,G.G Agarwal ,A.K. Tripathi,[2]**:** Clinical feature of HIV Positive patients attending a tertiary care hospital of North India ;There was enrolled 317 patients in this study in which 193 was male and 124 was female patients ,Mean age of patient was 34.2 years and most was in the age group of20 to 40 year of age. In this study mostly was from rural background 83.9%.In this study the common symptoms was weakness body ache, joint pain lethargy, fever weight loss, cough and loss of appetite. Tuberculosis is also most common opportunistic infections. In our study the age group mostly infected was 30 to 40 year of age ,rural and female were mostly infected .pulmonary tuberculosis is more common of opportunistic infection. The symptoms more common are weight loss, fever, muscle pain ,chronic diarrhea and cough was present.

Matin N, Shahrin L, Pervez MM ,Banu S,Ahmad D and Khatun M : Clinical profile of HIV/AIDS [3] – Infected patients admitted to a new specialist unite in DHAKA ,BANGLADESH -a low prevalence country for HIV-This study was considering about 109 patients and was a retrospective study .in this study mean age was 33.4 and 62% patients were male and 41% patients were female. This study showed that the heterosexual transmission was recorded in 87 (80%) patients .pulmonary tuberculosis oral candidiasis is found 25 and 11 patients. In our study there was maximum no .of HIV patient in age group of 30 to 40 years that was 54 (45%) and second most common age was 40 to 50 year of age group that was 35 (29%) and minimum no of subject is in age group of 60to 70 year of age group 1(.001%). It meant there was HIV infection maximally occurred in more sexually active person and also more economically productive group. There was life span of HIV patient is 50 to 60 year of age. In our study female was having more HIV disease that was 71(61% out of 118 subjects and male was having less HIV disease that is 47(39%) out o 118 and this study show that mode of transmission was most common was heterosexual mode that was 97(82%) Blood transfusion mode of transmission was second most common that is 11(9%) last was truck driver and injection drug user was last that is 2 (less than 1%)..Pulmonary tuberculosis and oral candiasis is opportunistic infection was present.

Mary Mahy, Christine S. Autenrieth, Karen Stanecki, and Shona Wynd;[4] Increasing trends in HIV prevalence among people aged 50 years and older: evidence from estimates and survey data of. AIDS. This study show the HIV-prevalence rates among people aged over 50 have increased steadily in the recent years. Care and treatment services need to address the specific needs of older people living Increasing trends in HIV prevalence among people aged 50 years and older: evidence from estimates and survey data.In our study the maximum number of patients was in age group of 30 to 40 year and life span of PL HIV subjects was 50 to 60 year of age

Anant A. Takalkar, G.S. Saiprasad, V .G. Prasad, Narendra S.and Madhekar Study of Opportunistic Infections In HIV Seropositive Patients Admitted to Community Care centre (CCC),[5] This study stated that out of 110 cases, 60.9% were males and 39.1% females. 77.2% respondents agreed that HIV could be transmitted through sexual means (96.2%), blood transfusion (96.7%) and sharing of sharp objects (92.5%). A few of the respondents believed that HIV can be transmitted through sharing of drinking cups (9.4%) and mosquito bites (13.6%)with HIV.Distribution of case as per presenting symptoms is shown in table1. In 79(71.8%) patients commonly observed symptoms were fever (82.2%), followed by weight loss (65.8%), cough and dyspnoea (45.5%), diarrhea (41.7%) and ulcers in orophyrangeals needed to incorporate Biomedical Research 2012; 23 (1): 139- and symptoms improve after the treatment of ART our study also have the symptoms as weight loss chronic dirrhea, fever cough and the symptoms were decrease one year after the .ART2. Opportunistic infections Number Percentage Pulmonary tuberculosis 33 52.3 Oral candidiasis 24 39.0 Cryptosporidial diarrhea 19 30.1 *Pneumocystis Carinii* Pneumonia (PCP) 09 14.2 Bacterial infection 08 12.6 Scabies 04 6.3 Dermatitis 04 6.3 Herpes zoster 03 4.7 Remaining 20% did not respond to the question on pattern risk behavior followed. Pattern of the opportunistic infections is given in table 3 and its comparison with various other studies in table 4. One or more opportunistic infections were observed in 63 patients (57%).Commonly observed opportunistic infections were pulmonary tuberculosis (52.3%), candidiasis (39%), cryptosporidial diarrhea (30.1%) and PCP (14.2%).

Dishank Patel, Mira Desai, A. N. Shah, and R. K. Dikshit [6] Early outcome of second line antiretroviral therapy in treatment-experienced human immunodeficiency virus positive patients This study was considering 126 patient in which 82 received regimen v (zidovudine +lamivudine +tenofovir bosted Lopinavir/r and 44 receive regimen Va (3TC

(Lamivudine) +TDF(Tenofovir) +LPV /r a significant body weight increase and marked reduction in number of patients categorized as WHO stage ¾ was observed .Our study also considered 118 patients and in which TLATV/R regime was taking that was by 35 subject and ZLATV/R was taking by 74 subjects rest TLLP/R REGIME BY 5 SUBJECT and ZLLP/R regime was taken by 4 subject.

Chauhan N S,Shah Sp. Desai MK, Shah A:[7] A safety analyses of different drugs regimens in immunodifficiency virus –positive patient; This study considering 2983 subjects and taken TLE and ZLN regime and at result there are Zaduvudine containing regime having anemia .In our study the anemia is the adverse effect is seen.

.**Dorina Onoya · Kamban Hirasen, Liudmyla van den Berg, Jacqui Miot · Lawrence C. Long· and Matthew P. Fox-**[8]: Adverse Drug Reactions Among Patients Initiating Second- Line Antiretroviral Therapy in South Africa: This study was considering about 7708 patients initiating second line ART .Anemia is was most common and experience in 2389 cases .second kidney problems was also found . Gastrointestinal problems was also found in this study.In or study Anemia , kidney problems and gastrointestinal problems was present. Anemia was present in Zaduvudine containing regimens and kidney probloms in Tenofovir containing regimen. In our study there was opportunistic infection present that maximum in oral candidiasis that is 28 subject(23%) but overall tuberculosis is maximum in 49(42%) that is maximum in which pulmonary tuberculosis is 27 subject (23%) ,extra pulmonary tuberculosis 14 subjects (11%) tubercular lymphadenitis 3(2%) subjects and tubercular pericarditis 1(0.008%) subjects ,Abdominal kocks 2 (1%) subjects ,TBM 2 (1%)subjects .One patient is also reported tubercular pericarditis in our study. LRTI is having 10 subject (12%) and chronic diarrhea 5(4%). But 25 subject is having no any opportunistic infections.

Michael O Iroezindu, Eugenia O Ofondu,Harry Hausler and Brian Van Wyk: [9] Prevalence and Risk Factor s Opportunistic infections in HIV Patient Receiving Antiretroviral Therapy in a Resource – Limited setting in Nigeria; This study is concluded that the pulmonary tuberculosis and oral candidiasis is the most prevalence of opportunistic infection in PL HIV . Our study also concluded that over all tuberculosis is most prevalent but pulmonary tuberculosis is second most prevalence and oral candidiasis is most prevalence of opportunistic infection.

Dereje N, Moges K,Nigatu Y,and Holland R;[10] prevalence and predictor of Opportunistic infection among HIV Positive Adult On Antiretroviral Therapy (On-ART) Versus Pre ART in Addis Ababa Ethiopia: A Comparative Cross- Sectional study This study show that the prevalence of opportunistic infection in pre ART is more common than post ART time Pulmonary tuberculosis is most common in both time and also oral candidiasis is also present in our study the oral candidiasis and pulmonary tuberculosis is most common and present in during ART taking period.

Fithamlak Bistegen Solomon, Bachalem. Nega, Angore , Hailu Chare Koyra,Efrata gairma Tufa, tezera Moshago Berheto and Mahlet Admasu.[11] Spectrum of opportunistic infections and associated factors among people living with HIV/AIDS in the era of highly active anti-retroviral treatment in Dawro Zone hospital ;A retrospective study- This study concluded the overall prevalence of OIs inthe era of HAART is higher as compare with previous studies in the country . Significance level of AIDS defining illness was noticed and WHO staging2 and 3, CD4 level. our study is also have the opportunistic infection that are during ART treatment and have also indication of presence of decrease CD4 count and may be ART failure.

Kyser M, Buchacz K Bush TJ colney L J, Hammer J, Henry K et al:[12] This study considered 528 patients taking antiretroviral were enrolled from march 2004 to June 2006 and show that patients taking more indulge to alcohol have less adherence to antiretroviral therapy. Smoking and tobacco chewing produced cytokines that have decrease effectiveness of ART2. Our study also taking alcohol and smoking and have less adherence to ART 1 and have cause of ART 1 failure.

Alexander Biliouse Gertrude Nakigozi and Steven J Renold:[13] this study considered 1841 participant initiating Antiretroviral therapy in Rakai Health Science programme between JUNE 2005 AND JUNE 2011. There were followed with viral load monitoring after 24 weeks with good counseling for adherence .there was found that the adherence of ART regimen was increase and VIRAL LOAD suppression occurred .In our study patients considered and monitored the viral load after good adherence the viral load suppression occurred .

Conclusion

HIV has infection more in no in rural area and female are more affected and mode of transmission was heterosexual transmission.

HIV infection mostly occurred in 30 to 40 year of age group that most economical group of age group and most sexually active group.

Symptoms in PL HIV have weight loss, chronic diarrhea, and fever and cough more in paitents but after treatment number of patient decreased.

In our study haemoglobin decrease, serum bilirubin increase and serum creatinin was increase so, should be monitored during ART 2 treatment .

In this study there was opportunistic infection present that maximum in oral candidiasis but overall tuberculosis is maximum in which pulmonary tuberculosis ,extra pulmonary tuberculosis, tubercular lymphadenitis and tubercular pericarditis ,Abdominal Koch,s and TBM are included LRTI and Chronic Diarrhea is also present. The opportunistic infection mostly Oral Candidiasis that occur when subject come for visit and it can justified that the patient have decrease CD4 count and check for ART failure so it is good for monitoring of ART failure The cause of ART1 failure is due to not good adherence to ART regime and also having the subject smoking, alcoholism and tobacco chewing

In our study the symptoms were present as

A -Acute HIV Syndrome –

1- Weight loss
2- Fever
3- Muscle pain
4- Chronic diarrhea
5- Nausea

B- Opportunistic infections-

1- Pulmonary tuberculosis
2- LRTI(Lower Respiratory Tract Infectoin)
3- TBM(Tuberculous meningitis)
4- TBL(Tuberculous lymphadenitis)
5- Tuberculous pericarditis
6- Oral candidiasis
7- Abdominal kocks
8- Extrapulmonary tuberculosis

C -ART Associated symptoms-

1- Nausea
2- Vomiting
3- Aqbdominal pain
4- Skin rashes
5- Anemia
6- Kidney injury
7- Jaundice

D -AIDS Defining illness

1- Tuberculous pericaditis

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