A STUDY ON
TUBERCULOSIS (TB) CO-INFECTION IN NEW HIV CASES VISITING ART CLINIC OF SUKRA RAJ TROPICAL AND INFECTIOUS DISEASE HOSPITAL TEKU, KATHMANDU, NEPAL

A DISSERTATION
SUBMITTED FOR THE PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE MASTER'S DEGREE OF SCIENCE [ZOOLOGY] WITH PARASITOLOGY AS A SPECIAL PAPER

BY
JHUMANATH ACHARYA
ROLL NO 2063-64-16
T.U. REGD NO: 5-3-28-139-2006

TO
CENTRAL DEPARTMENT OF ZOOLOGY
INSTITUTE OF SCIENCE AND TECHNOLOGY
TRIBHUVAN UNIVERSUTY, KIRTIPUR
KATHMANDU, NEPAL

TRIBHUVAN UNIVERSITY
INSTITUTE OF SCIENCE AND TECHNOLOGY
CENTRAL DEPARTMENT OF ZOOLOGY
KIRTIPUR,KATHMANDU,NEPAL

RECOMMENDATION

This is to certify that **Mr. Jhuma Nath Acharya** has completed hid dissertation work entitled **" The study of Tuberculosis (TB) Co-infection in the new HIV cases visiting the ART Center of Sukraraj Tropical and Infectious Disease Hospital Teku , Kathmandu, Nepal"** for the partial fulfillment of the **M.Sc. Degree in Zoology (Parasitology)** under our supervision . To the best of our knowledge, this is an **original** research study and has not been submitted for any other degree.

……..	…….
Supervisor	**Co-supervisor**
Mr. Janak Raj Subedi	Dr. Devi Prasad Bhusal
Lecturer	Chief Medical Officer
Central Department of Zoology	HIV Counselor
Tribhuwan University Kirtipur	ART Clinic STIDH Teku
Kathmandu, Nepal	Kathmandu Nepal
Date……	Date……

TRIBHUVAN UNIVERSITY
INSTITUTE OF SCIENCE AND TECHNOLOGY
CENTRAL DEPARTMENT OF ZOOLOGY
KIRTIPUR,KATHMANDU,NEPAL

.

RECOMMENDATION

On the recommendation of the Supervisor **Mr. Janak Raj Subedi** and Co-Supervisor **Dr. Devi Prasad Bhusal**, this dissertation of Mr**. Jhuma Nath Acharya** is approved for the examination and submitted to the Tribhuwan University as the partial fulfillment of the requirements for the **M.Sc. Degree in Zoology with Parasitology** as a special paper.

…….

Professor Dr. Ananada Shova Tamrakar

Head of the Department,

Central Department of Zoology

Tribhuwan University, Kirtipur

Kathmandu, Nepal.

TRIBHUVAN UNIVERSITY

INSTITUTE OF SCIENCE AND TECHNOLOGY

CENTRAL DEPARTMENT OF ZOOLOGY

KIRTIPUR, KATHMANDU,NEPAL

APPROVAL

We the members of the expert committee , evaluated the dissertation work entitled **" The study of Tuberculosis (TB) Co-infection in the new HIV cases visiting the ART Center of Sukraraj Tropical and Infectious Disease Hospital Teku , Kathmandu, Nepal"** and approved that Mr. Jhuma Nath Acharya is qualified for awarding M.Sc in Zoology with Parasitology as a special paper**.**

Expert Committee

……...
Mr. Janak Raj Subedi
[Supervisor]
Lecturer
Central Department of Zoology
Tribhuwan University Kirtipur
Kathmandu Nepal

……
Dr. Devi Prasad Bhusal
[Co- Supervisor]
CMO
STIDH Teku
Kathmandu Nepal

……..
Prof. Dr. Ananada Shova Tamrakar
Head of Department
Central Department of Zoology
Tribhuwan University, Kirtipur
Kathmandu, Nepal

……
External Examiner

…….
Internal Examiner
Dated:……

DECLERATION BY THE CANDIDATE

I hereby declare that the work title **"The study of Tuberculosis (TB) Co-infection in the new HIV cases visiting the ART Center of Sukraraj Tropical and Infectious Disease Hospital Teku, Kathmandu, Nepal"** is done by myself, and has not been submitted elsewhere for the award of any degree as per my knowledge. All sources of the information have been specifically acknowledged by reference to the authors or institution

Dated…

Signature of the candidate:…….

Jhuma Nath Acharya

Batch 2063-64

Roll No 16

Acknowledgement

I would like to express my highest degree of thanks and gratitude to my Internal Supervisor **Sir Janak Raj Subedi** Lecturer of Central Department of Zoology (Parasitology) and my co-supervisor **Dr. Devi Prasad Bhusal** the C.M.O. and the Counselor of HIV/ AIDS, Sukraraj Tropical and Infectious Disease Hospital (STIDH) Teku, whose keen knowledge and ability bestowed upon me during my entire research time despite of their busy scheduled. Their suggestions and helps are the pillar of my success.

I also like to extend my sincere thanks to **Prof. Dr. Ananda Shova Tamrakar** the Head of the Department, Central Department of Zoology, for providing the necessities for writing thesis work. My good thanks are to **Prof**. **Dr. Ranjana Gupta, Prof. Dr. P.N. Mishra, Ashok Bam Sir and Pitamber Dhakal Sir** Lecturers from Department of Parasitology for their visible or invisible help rendered to me to make my work complete.

I am equally thankful to the Director **Dr. Saroj Prasad Rajendra** of Sukraraj Tropical Hospital for Infectious Hospital, Teku for providing me the permission to undergo my thesis work in the hospital. My thanks are to **Dr. Shanti Gurung, Nani Baba Shrestha** , **Gyani Laxmi Maharjan**, **Shanta Bhatt, Lucky Pradhan and Deepa Shakya** and for their co-operation and help during my field work. To all the volunteers of different NGOs like Prerna, Sathi Samuha, Blue Diamond Society, Sparsa, Sneha Samaj, Youth Vision for their help during the field study.

Last but not the lest I express my heart full of thanks to my dear **"Durga"** my partner, who helped me throughout in arranging and formatting all the text and reached me to this final end.

……

Jhuma Nath Acharya

Roll No. 2064-65/16

TU Regd. No: 5-3-28-136-2006.

Date:

Abstract

Tuberculosis (TB) and HIV/AIDS had aroused as a serious public health problems since their emergence. The social and ethical impact brought about by these diseases in the community among the patients had made them to be in disguise because of the stigmatization and other social discrimination. The occurrence of TB in the HIV positives and HIV in the TB patients is found to be further deteriorating the global status of TB and HIV. The HIV positive patients are 50% more likely to get TB as an Opportunistic Infection than the non-HIV people. In most of the HIV cases TB arises as the earliest manifestation. It is the most common Opportunistic Infection among the HIV positive people. The current study was conducted to study the prevalence of Tuberculosis (TB) among the new HIV positive cases visiting the ART clinic of Sukraraj Tropical and Infectious Diseases Hospital, Teku. TB as the opportunistic infection was studied in 106 cases out of 390 HIV positive newly diagnosed cases which are 27.17 %. Among them were 80 males (75.47%) and 26 females (24.53%). The highest prevalence rate was found to be in the age group of 25-45 years with an average age of 35 years with 83.75%(67) males and 16.25% (22). More precisely the age group of 30-35 years has the highest prevalence rate with 38.67%. The prevalence rate was found to be highest in Seasonal Migrant Labor (44.28 %), primary and below level of educational status (51.88%), Smokers (79.24%) and with present TB status (57.54%). The new research on this area and implementation of such policies that can be useful to both the vulnerable population and the government will save as it says “A stitch in time saves nine”.

List of Tables and Figures

I. Tables

II. Figures

ABBREVIATIONS AND ACRONYMS

AIDS	Acquired Immune Deficiency Syndrome.
TB	Tuberculosis
HIV	Human Immune Deficiency Virus
USA	United States of America
ELISA	Enzymes Linked Immunosorbent Assay
STIDH	Sukra Raj Tropical and Infectious Disease Hospital
OI	Opportunistic Infection
FHI	Family Health International.
FSWs	Female Sex Workers.
MSWs	Male Sex Workers
BPKIHS	B.P.Koirala Institute of Health Sciences
ARV	Anti-Retro Viral
ART	Antiretroviral Treatment
CMI	Cell Mediated Immunity
HAART	Highly Active Anti-retroviral Therapy
LAV	Lymphandenopathy Associated Virus
IFA	Immuno Fluorescence Assay
ICRW	International Center for Research on Women
FPAN	Family planning Association of Nepal
NCASC	National Center for AIDS and STD Control
IDUs	Intravenous Drug Users
CSWs	Commercial Sex Workers
PTB	Pulmonary Tuberculosis
EPTB	extra Pulmonary Tuberculosis
SAARC	South Asian Association for regional Co-operation
MDRTB	Multi Drug Resistant Tuberculosis
DOTS	Direct Observation Treatment System
VCTCs	Volunteer Counseling and Testing Centers
PCP	*Pneumocystis carinii*

MSM	Man having Sex with Man
SEA	South East Asia
STDs	Sexually Transmitted Diseases.
NTC	Nepal Tuberculosis Center
STAC	SAARC Tuberculosis and HIV/AIDS Center
PMCT	Prevention for Mother-to-Child Transmission
MCT	Mother –To-Child Transmission

Chapter 1

INTRODUCTION

1.1 General Background

Human civilization has reached the canopy in this 21st century. The new invention and discoveries in the field of science and technology has made the globe smaller to reach as a whole. The invention and discoveries which are emerging today are all making human life more and more convenient as a result life has become more and more easy. But this application of whole of these technologies has not reached the nook and corner of the globe. Still there are plenty of nations where a large percentage of the population dies every year due to the out break of epidemic. There are no medication sufficient to prevent and control of these epidemic. Among these epidemics is H1N1 influenza, the brand new bursting globally; already existing are the HIV/AIDS and Tuberculosis which takes away large population every year. Due to poor economic growth and the poverty of the individual there has not been so good mechanism for the control and prevention of these fatal diseases.

The global HIV epidemic has emerged as a formidable challenge to the public health development and Human Rights. It has eroded the improvements in life expectancy and mortality in most of the HIV infected countries. Within a just a time of 25 years of its occurrence HIV has relentlessly spread virtually to all the countries of the world. Every day over 68000 persons are infected by HIV and an over 5700 dies from HIV /AIDS mostly due to inadequate access to HIV prevention and treatment service. Today it has remained as a challenging disease to the Public Health sector. This disease attacks people of all age and sex. The number of Children living with HIV is increasing incredibly year after year. This epidemic has mushroomed globally into an unforeseen and unpredicted night mare and the morbidity and mortality cost to societies and staggering and when crippled with the economic cost may will have exact an irrecoverable toll in many global nations. Its infections reveals varying patterns to transmission and have evidence suggests that the impact globally has disproportionately affected the more vulnerable and marginalized persons within the societies including children, women, person living with improved condition, commercial sex workers [CSW], Injecting Drug User [IDUs], Men who have sex with men [MSM] .The facts

are clear and staggering with 95% of the HIV infected persons living in less in industrialized nations. The prevalence of HIV increased markedly in Sub Saharan African nations, but the recent occurrence is seen in the several global nations including the countries of South Asia due to rapid explosion of the population. Although HIV/AIDS is of relatively recent occurrence and its prevalence is low, but has dramatically increased among high risk group. The moment of the people from one country to another, poverty, illiteracy, Commercial Sex Workers and Injecting Drugs Users and relatively high rate of sexually transmitted diseases in the developing nations make the population vulnerable to HIV/AIDS. The traditional values and the norms, discrimination of women, especially in the south Asian countries is making group of people more vulnerable to this fatal disease.

1.2 General background on Tuberculosis

Among the serious public health problem Tuberculosis as emerged as a serious challenge epidemic. It has become a global burden today. About 22% of the global population is affected by this disease. It has remained as a prevention and control challenge. It is the most common cost of the death from infectious disease among the adults. According to the WHO record of 22% global TB case only the South-Asian countries especially SAARC countries house 29% with three high burden countries including India, Bangladesh and Pakistan. Tuberculosis is the debilitating disease and major health problem which incur a heavy economic and social loss, which is borne by sick individual, their families and the countries. The social cost of Tuberculosis is immense, the family and the individual TB patient face a social stigma, and this is seen particularly in the South Asian Nations. As a result they are discriminated. Tuberculosis in the family has a serious implication in the children as well. Children face the stigma problem of them being from the family of the parental tuberculosis. Nearly one third global population is the victim of the attack of the *Mycobacterium tuberculosis bacillus* [MTB] and is at the risk of developing active clinical tuberculosis disease. Globally approximately 16 million people are suffering from active tuberculosis with the estimated 8-5 million persons developing active tuberculosis each year, resulting approximately 2 million death tolls every year. Tuberculosis has remained as one of the most difficult and serious public health challenges with severe impacts on the health and

the development of the many nations and in particular the third world nations. It is leading infectious cause of death among the adults aged 15-59 years in the developing nations. More women die due to tuberculosis then due to all combined cause of maternal mortality. It was estimated that with out urgent action about 70 million persons will be dying due to this disease within the next two decades.

1.2.a. Definition and History of Tuberculosis

As per the definition by the Health Encyclopedia Tuberculosis or TB is the chronic infection caused by the bacteria called *Mycobacterium tuberculosis* occasionally the other variants of the *Mycobacterium* genus. The disease usually involves the lung but other organs are also of the body are also involved. It is caused by the germ that is transmitted from one person to another by air droplets. Usually this infection is passed on as a result of very close contact, so family members of the infected person are endangered if the person continues to live in the same household and has not undergone proper treatment. The vast majority of the people who have TB germs in their body do not have active TB disease. Even if the disease is active the disease is quite advanced. TB in the children often occurs as childhood disease. The classical symptoms of TB are chronic cough with blood-tinged sputum, fever, night sweat, and weight loss. About one third of the global population today is suffering from this infectious disease and every new case occurs at the rate of one case per second. The proportion of people who become infected with TB each year is stable or falling worldwide but, because of the rapid population explosion the absolute number of the new cases is still found to be growing. The disease tuberculosis caused by the tiny *Mycobacterium tuberculosis* has been reported since human antiquity. The earliest unambiguous detection of is in the remains of the bison that dates back 18000 years ago. Weather TB originated in the cattle and then transferred to human or is diverged from common ancestor infecting different species is currently unclear but is evolved relatively recently. Skeletal remains of the Neolithic settlements in the Eastern Mediterranean shows prehistoric human 7000B.C. had TB and tubercular decay has been found in the spines of the Egyptian Mummies from 3000-2400 B.C. Phthisis is a Greek term for TB ; around 460 the times involving coughing up

blood and fever which was almost fatal. In South America the earliest evidence of TB is associated with the Paracas-Caverna culture. TB a White Plague called by Johan Banyan as the "Captain of all these men of death". In ancient Hindu text TB was referred to a Rogray and Rajayakshma meaning "The King of Diseases" (Grange et.al 1996). Certainly TB was well recognized by the time of Hippocrates (377-400 BC) who gave an excellent clinical description of disease called "**Pthisis"** a Greek word which means "to consume to spit and to waste away" (Grange, 1996; Miller 1982). Dutch Physician Franciscus Sylvis (1614-1672) deduced from autopsies that TB characterized by formation of nodules which he named tubercles (Lowell et.al, 1969). The word 'Tuberculosis' means small clump (Dobos. et. al, 1952). Several names have been used to refer TB in the years an acute progressive TB has been referred to as "Galloping Consumption". In the modern medicinal science Tuberculosis disease in human was first of all coined by Robert Couch.

1.2. b. Epidemiology of Tuberculosis in global scenario

Roughly a third of the world's population has been infected with *Mycobacterium tuberculosis* and a new infection occurs one in every seconds. However not all infection with *M.tuberculosis* causes TB disease and many infections are asymptomic.In 2007 an estimated 13.7 million people had active TB disease with 9.3 million new cases and 1.8 million died of active TB. The annual incidence rate varied from 363 per 100,000 in Africa to 32 per 100,000 in the America. TB is the world largest infectious killer disease of women of reproductive and leading cause of death among people living with HIV/AIDS.

The raise in HIV infection and neglect of TB control program has enabled a resurgence of TB. The emergence of drug resistance strains has also contributed to this new epidemic with from 2002-2004, 20% of the TB cases being resistance to standard treatment and 2% resistance to single line drugs. There is a varied occurrence rate of TB in the neighboring apparently due to differences in health care system.

In 2007, country with the highest estimated incidence rate of TB was Swaziland with 1200 case per 100,000 people. India has the largest total incidence with the estimated 2 million new cases. The Philippines ranking 4th in the world for the number of cases of TB and has highest number of cases per head in South East Asia. Almost two third of the

Filipinos have TB and up to an additional 5 Million people are affected yearly. In the developed countries TB is less common and is considered as the mainly the urban disease. In the United Kingdom the average of 15 per 100,000 in 2007 and the highest incidence rate in Western Europe were 30 per 100,000 in Portugal and Spain. The rates compared with 98 per 100,000 in China and 48 per 100,000 in Brazil. In the United States the overall TB rates was 4 per 100,000 in 2007. In Canada TB is still endemic in some rural areas.

In the South East Asia region with an estimated 4.88 million prevalent case and an annual incidence of 3.17 million TB cases, carries one third of the global burden of TB. Five of the eleven members countries in the region are among the 22 high burden countries, with India accounting for over 20% of the global cases. Most cases occur in the age group of 15-54 years, with males being disproportionately affected. The male-female ratio among newly detected cases is 2:1. Though death due to TB have declined after the introduction of DOTS.

1.2. c. Epidemiology of Tuberculosis in context to Nepal

According to the status of WHO with the population of over 28 million, Nepal estimates an incidence of 173 cases of all forms of tuberculosis per 100,000 populations while the incidence of new smear positive is estimated as 77 per 100,000. TB is identified as a priority program within the Ministry of Health and Population. Since 2001 there has been a slow decline in the number of cases notified. Similarly there is a slight shift to the older aged group. This data suggest there is a decline of TB burden in Nepal in recent years. The case detection rate for new smear positive cases was 66% in 2007 with treatment success rate of 89% for the cohort of the patients registered in 2006.

1.2.d. Social and Economic status of Tuberculosis

A disease poses various threats to the individual and lots much socio-economic impact to the general population. Especially the communicable disease takes away a lot of lives and leads to greater loss to the nation. Since TB is debilitating disease and major health problem among the nations of the world. It incurs heavy socio- economic costs due to TB. These social and economic costs are borne by the sick individuals, their family and the country. As most (80%

in India) of TB cases are among the economically most productive age groups (15-54 years).The economic cost to the family and the countries are quite significant

It is estimated that an adult TB loses an average 3-4 months of work time during the course of illness. This would imply and estimate 20-30% loss of annual house-hold income. Similarly if a person dies an average of 15 years income is lost by the family and nation as well

The social costs of TB are also immense. The immediate social costs are death associated with TB when it is nearly a 100 % curable disease. Another significant social implication is the stigma that the TB patient and their family face. Women in South Asia are particularly the victims of such social stigma, as women in SAARC region are less empowered and face all kinds of discrimination. Because of social stigma many women with TB lose their status as wives and mother in the family. In India alone more then 100,000 women are dejected by their families on account of TB. TB in the family also has serious implication on children. Many children especially from the poor families are forced to leave the school to work as a result of the parental TB. It is estimated that in India more then 300,000 children leave school to work as a result of the parental TB.

The estimate of over all economic burdens in SAARC countries is not readily available. However estimate for India are indicative for the enormity of economic costs to the SAARC countries. Almost 95% of TB cases and 98 of death occurred within developing countries were 75% of cases are within economic productive age group

1.3.a Definition , background, discoveries and history of HIV/AIDS

Acquired Immuno Deficiency Syndrome or Acquired Immunodeficiency Syndrome (AIDS) is the disease of the human immune system caused by a retro virus called Human Immuno-deficiency Virus. The entry of this virus in the immune system, by which it begins to fall, leading to life-threatening opportunistic infection. Infection with HIV occurs by the transfer of blood, semen, vaginal fluid, pre-ejaculate, or the breast milk. Within these bodily fluids, HIV is present as both free virus particles and the virus within infected immune cell. HIV infection in human is considered to be pandemic by the World Health Organization. From this discovery in 1981 to 2006 AIDS has killed more than 25 million people. HIV infects

about 0.6% of the world's population. In 2005 alone AIDS claimed as estimated 2.4 to 3.3 million lives of which more then 570000 were children. A third of these deaths occur in Sub –Saharan Africa, retarding economic growth and increasing poverty. According to the recent estimates HIV is set to infect 90 million people in Africa, resulting minimum estimates of 18 million Orphans. HIV infects primarily vital cells in the human immune system such as T-helper cells more specifically the CD_4^+ T-cells. , Macrophages, and the dendrite cells. HIV infection leads to low level of the CD_4^+ T-cells through three main mechanisms. First direct vital killing of the infected CD_4^+ T-cells by CD8 cytotoxic lymphocytes that recognize infected cells when CD_4^+ cells declines below a critical level, Cell mediated immunity is lost, and the body becomes progressively more susceptible to opportunistic infection.

Most people infected with HIV eventually develop AIDS. These individuals die mostly from the opportunistic infection or maligencies associated with the progressive failure of the immune system. HIV progresses to AIDS at a variable rate affected by the viral, host and the environmental factors; HIV-specific treatment delays this process. Most will progress to AIDS within ten years of the HIV infection some will have progressed much sooner and some will take much longer time. Treatment with the anti-retroviral increases the life expectancy of the infected with HIV. Even after HIV has progressed to diagnosable AIDS, the average survival time with anti-retroviral therapy, some who has AIDS typically ides within a year.

It is likely that we never know who was the first person being infected with the AIDS and how it spread from the initial person. Scientists investigating the possibilities often become very attached to their individual infected with HIV. Clinically AIDS was first observed between 1980 and early 1981. A group of five men showed symptoms of *Pneumocystis carinii* (PCP).a rare opportunistic infection that was known to present itself in people infected with much compromised immune system. Sooner there after a set of men developed a rare-skin cancer called Kaposi's sarcoma (KP). Many more case of the PCP and KP quickly emerged. After recognizing a pattern of anomalous symptoms presenting themselves in patients, the task force of U.S. Center of Disease Control Prevention named this condition as Acquired Immune Deficiency Syndrome. (AIDS).

In the year 1983, two separate research group lead by Robert Gallo and Luc Montiagnier independently declared that a novel retrovirus may have been infecting AIDS

patients and published their findings in the same issue of the journal" Science" Gallo claimed that a virus his group had isolated from an AIDS patient was strikingly similar in shape to other human T-lymphotropic virus his group was the first to isolate. This virus was then called as HLTV-III. At the same time Montiagnier group isolated a virus from a patient presenting lymphandenopathy of neck and physical weakness. Two classic symptoms of AIDS. Contradicting the report from Gallo, Montiagnier and his colleagues showed that the core patient of this virus were immunologically different from those of the HTLV-III, Montiagnier group named their isolated virus as Lymphandenopathy-Associated Virus (LAV).

Whether Gallo or Montiagnier deserve more credit for the discovery of the virus that cause AIDS has been a matter of considerable controversy. Together with this Colleague Francoise Barre-Sinoussi, Montiagnier was awarded one half of 2008 Nobel Prize in Physiology or Medicine for the discovery of the Human Immuno-deficiency Virus.

1.3.b. Signs and symptoms of HIV/AIDS

Infection with HIV-1 is associated with a progressive fall in the CD_4^+ T-cells count an increase in the viral load. The stage of the infection can be determined by measuring the patient's CD_4^+ T-cells count and the level of HIV in the blood. HIV infection has basically four stages. They are the incubation period, acute infection, latency age and AIDS. The initial incubation period upon infection is asymptomatic and usually last between two-four weeks. The second stage, acute infection which last an average of 28 days and can include symptoms like fever, lymphandenopathy, phryngities, skin rash, myaligia, malaise and mouth and esophageal sores. The latency stage, which occurs third, shows few or no symptoms and can last anywhere from two weeks to 20 years and beyond. AIDS, the fourth stage of all and final stage of the HIV infection shows as symptoms of various opportunistic infection.

Pathophysiology of AIDS: The pathophysiology of AIDS is complex, as is the case with all syndromes. Ultimately, HIV/AIDS by depleting CD_4^+ T helper lymphocytes. This weakens the immune system and allows opportunistic infections. T- Lymphocytes are essential to the immune system response and without them, the body cannot fight infections or kill cancerous cell. The mechanism of CD_4^+ T cells depletion differs in acute and chronic

phases. During the acute phase, HIV-induced cell lyses and killing of the infected cells by cytotoxic T cells accounts for CD_4^+ T cells depletion, although apoptosis may also be the factor. During the chronic phase the consequences of generalized immune activation coupled with the gradual loss of the ability of the immune system to generate the new T cells appear to account for the slow decline in CD_4^+ T cells. Although the symptoms of immune deficiency characteristics of AIDS do not appear for years after a person is infected, the bulk of CD_4^+ T cells loss occurs during the first weeks of the infection, especially in the intestinal mucosa, which harbors the majority of the lymphocytes found in the body. The reason for the preferential loss of mucosal CD_4^+T cells is that the majority of the mucosal CD_4^+ T cells express the CCR5 co receptor, where as the small fraction of CD_4^+ T cells in the blood stream do so. HIV seeks out to destroy CCR5 expressing CD_4^+ cells during the acute infection. Vigorous immune response eventually controls the infection and initiates the latent phase. However, CD_4^+ T cells in the mucosal tissues remain depleted throughout the infection, although enough remain to initial ward off life-threatening infections. Continuous HIV replication results in the state of generalized immune activation persisting throughout the chronic phase Immune activation, which is reflected by the increased activation of the immune cells and release of the pro-inflammatory cytokines, result from the activity of the several HIV replication .Another cause of the breakdown of the immune surveillance system of the mucosal barrier caused by the depletion of mucosal CD_4^+ T- cells during the acute phase of the disease.

This results in the systemic exposure of the immune system to microbial components of the gut's normal flora, which in a healthy person is kept in check by the mucosal immune system. The activation and proliferation of the T cells that results from the immune activation provides fresh targets for HIV infection. However direct killing by HIV alone cannot account for the observed depletion of CD_4^+ T cells since only 0.01% to 0.10 % of the CD_4^+ T cells in the blood are infected. A major cause pf the CD_4^+ .

A major cause of the CD_4^+ T cells loss appears to result from their heightened susceptibility to apoptosis when the immune system remains activated .Although new T cells are continuously produced by the thymus to replace the lost ones, the generative capacity of the thymus is slowly destroyed by the direct infection of the lymphocytes by HIV. Eventually the

minimal number of CD_4^+ T cells necessary to maintain a sufficient immune response is lost leading to AIDS.

1.3. c. Diagnosis of HIV/AIDS

The diagnosis of AIDS in a person infected with HIV is based on the presence of certain signs or symptoms. Since June 5, 1981 many definitions have been developed for epidemiological surveillance. Many HIV positive people are unaware that they are infected with the virus. Like less then 1% of the sexually active urban population in Africa has been tested and this proportion is even lower in rural population. Furthermore, only 0.5% of the pregnant women attending urban health facilities are counseled tested or receives test result. Again, this proportion is even lower in rural health felicities. Since donors may therefore be unaware of their infection, donor blood and blood products used in medicine and medical research are routinely screened for HIV. HIV testing of initial screening with an Enzyme Linked Immunosorbent Assay (ELISA) to detect the antibodies to HIV-1. Specimens with the non-reactive result from the initial ELISA are considered HIV negative unless new exposure to an infected partner of unknown HIV status has occurred. Specimen with the reactive ELISA is tested in duplicate. If the results of either duplicate test are reactive, the specimen is reported as repetitively reactive and undergoes confirmatory testing with a more specific supplement test like Western Blot or less commonly Immuno Fluorescence Assay (IFA). Only specimen that is repetitively reactive by ELISA and positive by IFA or reactive by Western Blot are considered HIV positive and indicated of HIV infection. Specimen that is repetitively ELISA reactive occasionally provides an intermediate Western Blot result which may be either an incomplete antibody response to HIV infected persons of non-specific reaction in an uninfected person. Although IFA can be used to confirm infection in this ambiguous cases these assay is not widely used. Generally a second specimen should be collected more then a month later a retested for persons with intermediate Western blot result. Although much less commonly available, nucleic acid testing can also help diagnosis in certain situation. In addition a few tested specimens might provide an inclusive result because of low quality specimen. In this situation a second specimen is collected and tested for HIV. Modern HIV testing is extremely accurate. The chance of a false positive result in

the two step testing protocol is estimated to be 0.0004 % to 0.0007% in the general United States population.

1.3.d. WHO Staging System of HIV/AIDS

In 1990 the WHO grouped this infections and conditions together by introducing the staging system for patients infected with HIV-1. An update took place in September 2005 most of this conditions are opportunistic infection that are easily treatable in a healthy people. As per the staging system the disease can be grouped in four stages.

Stage I: HIV infection is asymptomatic and is not-categorized as AIDS

Stage II: Includes minor muco-cuteneous manifestation and recurrent, upper respiratory tract infection.

Stage III: Includes unexplained chronic diarrhea for longer then a month, severe bacterial infection and pulmonary TB.

Stage IV: Includes Toxoplasmosis of the brain, Candidacies of the esophagus, trachea, bronchi or lungs and Kaposi's sarcoma. These diseases are the indicators of AIDS.

1.3. e. Socio-Economic Impacts of HIV/AIDS

HIV/AIDS is one of the must burning issues which is creating havoc in the social life of the infected individual and also creating a terror among the non-infected for its speedy transmission. It has created a type of a social stigma and discrimination of the infected individual in the family and society. As a result of such discrimination about a million of people especially in the Indian sub-continent and other south Asian region, the children and women are in the greater risk of this socio-economic impact. The fear surrounding the emerging epidemic since 1980 is still fresh in many peoples' mind. At the time of the first history of the occurrence of this grave disease, very little was known about the risk of transmission, which made people scared of those infected due to fear of contagion. From early in AIDS epidemic a series of powerful images were used that reinforced and legitimized stigmatization.

HIV/AIDS related stigma is not a straight forward phenomenon as attitudes towards the epidemic and those affected vary massively. Even within one country reaction AIDS will vary between individual and groups of people. Religion, gender, sexuality, age and levels of AIDS education can all affect how somebody feels about the disease. AIDS related stigma is not static. It changes over time as infection levels, knowledge of the disease and treatment availability varies. In 2003 when launching a major campaign to scale-up treatment in the developing world WHO claimed that "As HIV/AIDS becomes a disease that can be both preventive and treated, attitudes will change and denial stigma and discrimination will rapidly be reduced". It is difficult to access the accuracy of this statement as level of stigma is hard to measure. A number of small –scale studies have however been conducted with fairly positive results. The fact the stigma remains in developed countries such as America where the treatment has been widely available or over a decade, also indicates that the relationship between the HIV treatment and stigma is not straightforward. An estimated 27% of AIDS related stigma and discrimination refers to prejudice, negative attitudes abuse and treatment directed people living with HIV/AIDS. They result in being shunned down families, peers, and wider the community: poor treatment, health care and education settings and erosion of the right, psychological damage and can negatively affect the success of testing and treatment. AIDS stigma and discrimination exist worldwide, although they manifest themselves differently across the countries, communities, religious groups and the individuals. They occur alongside other forms of stigma and discrimination such as racism, homophobia or misogyny and can be directed those involved in what are considered socially unacceptable activities such as prostitution and drug abuse. Stigma not only makes it more difficult for people trying to come to term with HIV and manage their illness on a personal level, but it also infers with attempts to fight the AIDS epidemics as a whole. On a national level the stigma associated with HIV can deter governments from taking fast and effective actions against the epidemic, whilst on a personal level it can make the individual reluctant to access HIV testing, treatment and care. Self-stigma and fear of negative community reaction can hinder efforts to address the AIDS epidemic by perpetuating the wall of the silence and shame surrounding the epidemic. Stigma also exacerbates problems faced by children orphaned by HIV/AIDS. AIDS orphans may encounter hostility from their extended families

and communities and may be rejected, denied access to schooling and health care and left to fend for themselves. There are certain factors that contribute to HIV/AIDS related stigma:

- HIV/AIDS is a life threatening disease and can therefore people react to it in strong ways.
- HIV infection is associated with behaviors like homosexuality, prostitution, promiscuity and drug addiction that are already stigmatized in many societies
- Most people get infected with HIV through sex which often carries moral baggage
- There is a lot of incorrect information about HIV that is transmitted creating irrational behaviors and misperception of personal risk.
- HIV infection is often thought to be the result of person irresponsibility
- Religion or the moral beliefs lead some people to believe that being infected with HIV is the result of moral fault that deserves to be punished.

1.3.e. Effects of Stigmatization

AIDS-related stigma has had a profound effect on the epidemics course. The WHO cites fear of stigma and discrimination as the main reason why people are reluctant to be tested, to disclose HIV-status or to take anti-retroviral drugs. The wide-spread fear of stigma is held accountable for the relatively low uptake of the prevention of Mother-to-child transmission programmes in countries where the treatment is free. In case of Botswana for example, despite the fact that the service is available at every center in the country only 26% of the pregnant women availed themselves of the opportunity to protect their unborn children. Over half refused to take a test, a nearly half of those who tested positive did not go to accept treatment. People with HIV may be turned away from health care services and employment or refused to entry to a foreign country.

In some cases they may be forced from home by their families and rejected by friends and colleagues. The stigma attached to HIV/AIDS can extend to the next generation, placing an emotional burden on those left behind.

Denial goes hand in hand with discrimination, with many people continuing to deny that HIV exists in their communities. Today HIV/AIDS threatens the welfare of wellbeing of people throughout the world. Combating stigma and discrimination people who are affected

with HIV/AIDS is vital ingredient for preventing and controlling the global epidemic. To overcome the stigma and discrimination, people attitudes towards AIDS must be changed. In some countries people altogether lack the knowledge of their right in their society. They got to be educated so they are able to challenge the discrimination stigma and denial that they encounter. Institutional and other monitoring mechanisms can enforce the right of the people with HIV and provide powerful means of mitigating the worse effect of the discrimination and stigma. However o policy or law alone combat HIV/AIDS related discrimination will continue to exist so long as societies as a whole have a poor understanding of HIV/AIDS and the pain and suffering caused by negative attitudes and discriminatory practices. The fear and the prejudice that lie at the core of HIV/AIDS discrimination needed to be tackled at the community and the national levels with AIDS education playing a crucial role. A more enabling environment needed to be created to increase the visibility of the people with HIV/AIDS as a 'normal' part of nay society. The presence of treatment makes this task easier where there is hope, people are less afraid of AIDS; they are more willing to be tested for HIV to disclose their status and to seek help if necessary. In future the task to comfort the fear-based messages and biased social attitudes in order to reduce the discrimination and stigma of people living with HIV/AIDS.

International Centre for Research on Women (ICRW) the possible consequences of HIV-related stigma to be:

- Loss of income / livelihood
- Loss of marriage and child bearing options
- Poor care within health sectors
- Withdrawal of care giving in the home
- Loss of hope and feelings of worthlessness
- Loss of reputation.

"We can fight stigma, enlightened laws and policies and key but it begins with openness, the courage to speak out. School should teach respect and understanding. Religious leaders should preach tolerance. The media should condemn prejudice and use its influence to advance social change from securing legal protection to ensuring access to health care" [Ban-Ki-Moon] General Secretary of United Nations Organization

"The epidemic of fear, stigmatization and discrimination has underlined the ability of the individuals, families and the societies to protect themselves and provide supports and reassurances to those affected. This hinders in no small way, efforts at stemming the epidemic. It complicates decisions about testing, disclosure of status and ability to negotiate prevention behaviors including the use of family planning services"

1.3.f. Epidemiology of HIV/AIDS

The HIV/AIDS widespread has engenders as much fear, revulsion and despaired and utter a helplessness since it first occurrence. It has spread in such a way that there are hardly any countries in the world which can remain aloof from infection of this disease. There are countries in the world that where one out of every three is infected with HIV. The epidemiology of this disease has left no countries left untouched There are countries where a large percentage of the HIV infected do not have the access to the medical assistance like testing counseling and treatment, thereby they are at the greater risk of dying as this infection decreases the immunity of the defense system and die due to various opportunistic infection. The individual do not have the knowledge of HIV and the opportunistic infection. The main reason of the wide and rapid spread lack of the knowledge and an access to the medical support or care.

According to the latest global estimates for UNAIDS and WHO , there were 33 million people living with AIDS in 2007,up from 29.5 million in 2001,the result of continuous new infection people living longer with HIV and general population. The global prevalence rate had leveled since 2000 and was 0.81 in 2007.Two million people died of AIDS in 2007 up from 1.7 in 2001but deaths are now declining due to the part to antiretroviral treatment (ART) scale-up. HIV is the leading cause of death worldwide and the number one cause of death in Africa. New HIV infection are believed to have peaked in the late 1990s and declined between 2001-2007, from three million to 2.7 million. The decline is attributable to natural trends in the epidemic and to prevention. Still there are more then 7,000 new HIV infection per day in 2007.Most of the new infection are transmitted heterosexually, although risk factors vary, in some countries, Men who have Sex with Men

(MSM), Injecting Drug Users (IDUs)and Female Sex Workers (FSWs), are at the significant risk. An estimated 8 in 10 people infected with HIV do not know it. HIV has lead to the resurgence of the Tuberculosis particularly in Africa and TB is the leading cause of the death for people with HIV worldwide. Women represent half of all people living with HIV worldwide more than half (50%) in Sub-Saharan Africa. Gender inequalities differential access to service and sexual violence increases women vulnerability to HIV, and women especially the younger women are biologically more susceptible to HIV. Young people age 15-24 accounts for new HIV infections. In sub-Saharan Africa the HIV prevalence rate among young women is nearly 3 times that of their male counterparts. Globally there were 2 million children living with HIV in 2007, 370,000 new infections among the children and 270,000 AIDS deaths. There are approximately 15 million AIDS orphans today most of whom (77%) live in the Su-Saharan region.

Sub Saharan Region: This is the hardest hit region is home to two-third (67%) of people living with HIV but only 11-12% of the world's population. Most children with HIV live in this region (90%).Almost all of the region's nations have generalized HIV epidemics that is their national HIV prevalence rate greater than 1%. In nine countries of this region more than 10% of the adults are estimated to be HIV positive. South Africa has the highest number of people living with HIV in the world that is 5.7 million and almost one in five South African adults is HIV positive. Swaziland has the highest prevalence rate in the world that is 26.1%. Recent data offer promising signs, with national HIV prevalence stabilizing or even declining in several countries in this region.

1.4 a. General background of HIV/TB Co-infection

The deadly and the synergenitic relationship between HIV and Tuberculosis which is better called HIV/TB Co-infection each potentiating the others. HIV promotes the development of active clinical TB disease in persons with both latent and recent acquired MTB infection. In fact tuberculosis is the earliest manifestation of AIDS in more than 50% of all the cases in developing countries and accounts for about third of AIDS death. HIV epidemic can facilitate the emergence of the multi-drug resistant strains of *Mycobacterium tuberculosis bacillus* which is very difficult to manage with the present armory of anti-TB drugs. Actually this co-infection has posed a bigger threat to present humanity with its gravest public health

challenge yet. These two TB and HIV/AIDS killer are positioned to deliver debilitating morbidity, mortality and associate economic costs. The co-infection of these two diseases is more devastating and can promote the emergence of the multi-drugs strains of MTB. Tuberculosis can stand as the most killer of the person with HIV. Tuberculosis is usually the initial manifestation of the AIDS in half of the all AIDS cases. The untreated infection leads to progressive infection being MTB infection. Tuberculosis in high HIV prevalence population is the leading contribution to morbidity and mortality with evidence that HIV infecting is accelerating the tuberculosis epidemic. Now the time has come to be very sensitive in formulating the national policies in the prevention of these two diseases and the co-infection too or else this co-infection will once again emerge as a powerful sword in killing the next tolls of the life in the world in the name of epidemic.

1.4.b. Definition of the illness

"Co-infection" refers to certain clinical manifestation of one disease to a patient who is already the victim of the disease. In the other word it is the occurrence of another severe infection of a disease which is so much closely associated with the previously existing disease. Therefore the prevalence of one new disease in a patient already suffering from another disease is clinically called co-infection. This secondary disease that is examined can be a type of opportunistic infection. This sort of condition as precisely used in the case of HIV/AIDS and other associated opportunistic infection. The existence of TB in the HIV/AIDS people is the most commonly appearing co-infection. Both of these diseases are equally fatal if they are not diagnosed and treated in time. Both of this disease is the major public health problem of the developing countries. The death due to this co-infection is increasing. The presence of TB in HIV/AIDS is now most prevalent infectious causes of the human suffering and death worldwide. HIV infected individuals co-infected with TB have an annual risk of 5-15 % of developing active TB. The South East Asian region of the World Health Organization accounts for nearly 40 % of all the TB cases globally and 18%of the world's HIV infected also live in this region. In India also TB is the most common opportunistic infection among HIV sero-positive patient. Moreover HIV and TB are so closely related with factors like malnutrition, poverty, and homelessness and overcrowding. As per the HIV/AIDS, ARV news letter of the estimated 44 million people living with

HIV/AIDS, 12 million are co-infected with TB. The prevalence of HIV in patients with TB is 12% in Thailand and Cambodia, 6.8% in Myanmar and 4% in Vietnam. TB kills about 350,000 HIV patients every year more than any other opportunistic infection. The HIV epidemic by increase the risk of reactivation of latent TB infection and by facilitating more rapid progression of TB disease. Unlike other Opportunistic infections TB can be readily transmitted to HIV negative households and other close contacts.

HIV/AIDS pandemic has caused a resurgence of TB, resulting in increased morbidity and mortality world wide. HIV and *Mycobacterium tuberculosis* have a synergetic interaction. : Each accentuates progression of the other clinical presentation of TB in early HIV resembles that observed in immunopotent person. In late HIV infection however TB is often typical presentation, causing extra pulmonary disease. Anti-tuberculosis treatment is however completed by frequent drug interaction with highly active anti-retroviral therapy (HAART) and drug resistant are more common among HIV infected patients. TB is leading cause of morbidity and mortality in patients with HIV/AIDS. The direct and indirect cost of this illness due to TB and HIV enormous, estimated to be more than 30 % of the annual household income in developing countries and have a catalytic impact on the economy in the developing world. Thus co-infection of HIV and TB is not only a medical malady but a social and economical disaster and hence is aptly described as “cursed duet”. The interface between TB and HIV in increasing in countries like India where both HIV and TB infection is maximally prevalent in people of 15-49 years age. With regard to Nepal, it is estimated that among 60,000 HIV in Nepal, more than 85 % are infected with TB. 2,665 cases of AIDS have been diagnosed in Nepal till 2003. The prevalence of HIV is increasing rapidly in Nepal and effective control measures for AIDS as well as for TB are important now than ever before. National Tuberculosis program is conducting regular surveys of how often HIV occurs in TB patients. In 2002, 2.4 % of the TB patients also were reported to have HIV infection. This could rise rapidly if the HIV increases. The next survey was planned for 2004-2005 biennium with the support from WHO which shows the HIV prevalence in TB increases to almost four folds in the last six years time.

1.4.c. Epidemiology of the Co-infection of HIV and TB

According to the recent estimates by the WHO and Joint Nations Program me on HIV/AIDS (UNAIDS), nearly 39.4 million people were living with HIV/AIDS worldwide, more than half them in the sub-Saharan Africa and nearly about a fifth in the South East Asia. About one third of the HIV positive population worldwide is co-infected with *Mycobacterium tuberculosis* this account to about 14 million people worldwide. Globally about 9 % of all the TB cases in adults are attributable to HIV. Studies from sub-Saharan Africa have recorded HIV sero prevalence rates of 50-70 % in patients with TB. In Asia where the HIV epidemic is still at early stage, the rate of HIV infection in TB patients has been lower. A HIV positive infected with *M. tuberculosis* has a 50-60 % life time risk of developing TB disease as compared to HIV negative that has only 10 % risk. This is especially important in Indian where the estimated that 40 % of the adults population harbor *M. tuberculosis*. Hospital based HIV seroprevelence studies amongst TB patients from different regions of India has shown greater variation-the prevalence rate varying 0.4 % -28.1 % have been reported. The prevalence of HIV infection among the patients of TB is raising at an alarming rate in the western parts of the country like Mumbai (2.56 %-10.15 %), Pune (10-25.75 %) and South India (0.59-8.89 %) but much more slower pace in North India. A rising trend of HV infection in patients of pulmonary TB has been seen in Lucknow (1.25-4.28 %). In India, there were an estimated 5.1 million people living with HIV at the end of 2002. Assuming that about 40 % 0f these persons are co-infected with TB, the estimated TB-HIV co-infected figure will be around two million.

The prevalence of HIV in patients with TB is 12 % in Thailand and Cambodia, 6.8 % in Myanmar and 4% in Vietnam. Public health implications are profound. TB kills about 350,000 HIV patients every year, more than any other opportunistic infection The HIV epidemic fuels the Tb epidemic by increasing the risk of reactivation of the latent Tb infection by felicitating more rapid progression TB disease. Unlike other opportunistic infection TB can readily transmitted to HIV negative households and other close contacts. The highest percentage of the co-infection rate of this double pandemic in seen in the developing nations.

1.4.d. Global Aspects of TB/HIV Co-infection

According to the recent estimates by WHO and joint UN program on HIV/AIDS, nearly 39.4 million people were living with HIV/AIDS globally. More than half of them are in Sub-Sahara Africa and nearly one fifth in Southeast Asia. By the end of 2000 about 11.5 million people were co-infected with HIV and *Mycobacterium tuberculosis* globally, 70% of the co-infected people were in Sub-Sahara Africa, 20 % in Southeast Asia and 4 % in Latin America and Caribbean. TB accounts for 13% of the related death globally. Globally 9% of all new TB (31% in Africa) were attributable to HIV/AIDS (Sharma et.al, 2005)

Over 4 million estimated HIV infections are existing in the SRRAC region (STC. 2003). As HIV prevalence rate in the SAARC region is still low, (<0.1% in Srilanka, Maldives, Bangladesh and Bhutan, where as >1.00 % in Nepal, India and Pakistan) the relatively low proportion of TB cases attributable to HIV-0.8% in India, 0.6% in Nepal and 0.1 % in Bangladesh (STC. 2003).According to the study made by Health Ministry of Government of Nepal TB/HIV co-infection is in rising trend. It was observed that the total TB/HIV co-infection co-infected cases were 14 in (1988-1991) followed by 99 (1992-1997), 312 in (1998-2003).A study of the "Surveillance of HIV infection with TB in Nepal" conducted out in 2002 in five different testing sites in various parts of Nepal such as Kathmandu, INF Nepalgunj, Tansen Palpa, NATA Biratnagar and RTC Pokhara showed that HIV prevalence among TB patients continuous to raise and had increased four folds in the past eight years

1.4. e Impact of HIV on TB

HIV is one of the strongest risk factors for developing active TB, while TB incidence is declining in the Western Pacific Regions rates of the HIV/TB co-infection is alarmingly increasing in sub-Saharan Africa. The HIV epidemic has the greater potential to worsen the TB epidemic. This is mainly because of the HIV increases the risk of reactivation of people with latent TB and become HIV infected persons are more susceptible to the new TB infection. These patients would add to the incidence of TB thereby leading to increase the new infection and re-infection. HIV is the most powerful risk factor for progressing of TB

infection to TB disease. Also HIV infected persons who become infected with *M. tuberculosis* rapidly progress to active TB disease.

Tuberculosis is the most common opportunistic infection and is the major cause of the morbidity among the HIV positive patients. It is the first manifestation of AIDS in more than 50% of cases in the developing countries. HIV by itself does not cause multidrug resistant tuberculosis (MDR-TB), but fuels the spread of this dangerous condition by increasing susceptibility to TB infection and also accelerating the progress from infection to disease.

In person with HIV/AIDS, factors such as, increased vulnerability to TB, increased opportunity to acquire TB due to overcrowding, exposure to patients with multi-drug resistant TB, increased hospital visit and malabsorption of anti-tuberculosis drugs resulting to sub-optimal therapeutic blood levels in spite of strict adherence to treatment regimen have all been postulated as possible cause for increased risk of acquired MDR-TB

Th-1 type immune system responses characterized by adequate cell-mediated immune system is the crucial host defense against *M.tuberculosis* HIV infection primarily affects those components of the host immune response responsible for cell-mediated immunity. Thus individual infected with latent TB infection the fine balance between the *M. tuberculosis* and the host immunity get tilted in favor of the former resulting in reactivation. Moreover the infection is poorly contained following reactivation resulting in widespread dissemination causing extra pulmonary disease. This is corroborated by experimental findings that when peripheral blood lymphocytes of patients with HIV-TB are exposed to *M.tuberculosis* in vitro, they produce decreased amounts of Th-1 type cytokines, as compared with HIV-negative patients with TB. The interaction between HIV in persons co-infected with them is bidirectional and synergetic. The course of HIV infection accelerated subsequent to the development of TB and the adverse between HIV viraemia and CD_4^+ counts gets right compared with the CD_4^+ counts matched HIV-infected control without TB, the relative risk of death and development of other opportunistic infection is higher in HIV/TB co-infected patients. Accelerated HIV progression is partly with HIV/TB. Further increased HIV and replication has been demonstrated locally, at the sites of disease affected by TB such as affected lung and the fluid in the patients with HIV/TB. Moreover genetic diversity of the locally replicating HIV-viral population is higher than that of circulating population and the

local immune system also favors the development of the latent HIV infection of macrophages dendrite cells thereby potentially enhancing dissemination of HIV.

1.4.f. Clinical Presentation

The clinical presentation of TB in infected patients varies depending on the severity of immunosuppressant. Clinical presentation of TB in person with early HIV infection has been found to be similar to the observed in immunocompetent and HIV negative patients. In Immunocompetent patient pulmonary tuberculosis encountered and accounts 80% of the cases. While extra pulmonary site is the lymph node. However, neurological, pleural, pericardial, abdominal and virtually everybody sites can be involved in HIV positive patients. Even in HIV infected patients PTB is the most common form of TB

1.4. g. Diagnosis

Diagnosis of TB in presence of HIV infection is very complicated by increase number of patient with PTB who are Acid Fast Bacillus (ABF) smear negative. Therefore the diagnosis required of TB is in HIV positive a patient requires a high index of suspicion and a combination of clinical radiography and bacteriologic investigation. The presence of the following symptoms should alert the clinicians to the possibilities of HIV infection in the patients with TB, weight loss more than 10 kg or more than 20 % of the original body weight, Pain and swallowing and burning sensation on the feet. Diagnosis of TB in HIV patients is difficult because of absence of fever and constitutional symptoms, negative sputum smears, atypical chest radiography high prevalence of PTB especially in the inaccessible sites, resemblance to other opportunistic pulmonary infections among others. However the conventional methods of smear and culture must be applied to sputum, body fluids and secretions. Attempts must also be made to procure materials for histopathological, cytopathological and micro pathological testing employing radiological guided procedure or minimally invasive diagnosis methods, like video assisted thoracoscopy, laparoscopy and colonoscopy, where relevant. A negative tuberculin skin test may reflect the immune deficiency status and does not rule out the presence of active TB. In HIV infected individuals the radiographic manifestation of PTB can be a typical or different. A study compared the

radiographic findings at base line and at the end of anti-tuberculosis therapy in HIV positive and negative patients with TB. The common radiographic presentation among HIV positive were diffused soft parenchyma opacities followed by cavities pleural effusion military TB and hilar lymphandenopathy cavities were more frequent among TB patients without HIV infection. On the completion of anti-tuberculosis treatment with HIV have less radiographic sequel in the form of fibrosis.

Sputum microscopy is the corner stone of the diagnosis of TB even in high HIV prevalence area's patients suspected of having TB should have three sputum specimen examined for AFB . HIV infected smear positive patients tend to excrete significantly fewer organisms per ml of sputum than HIV negative patients which can led to AFB being missed if the appropriate number of samples as well as high power field is not examined my microscopy. In early HIV, smear positive PTB is as common as the non-HIV positive. The sputum negativity leads to increase as the HIV disease and the immune suppression progress. In Indian studies AFB smears negativity has been reported as high as 82 %.

TB can occur at any time during the course of HIV infection. Even in HIV infected patients PTB is the common one. The clinical presentation of TB depends upon the degree of immunosuppressant in the patients. The presentation of TB in the early stage of HIV infection is similar to that in HIV negative patients, often resembling the post primary PTB with upper lobe of HIV infection the presentation of TB often resembles primary disease with infiltrative lesions, lower lobe disease intra-thoracic lympathodenopathy and the sputum smear results are often negative. It is often difficult to distinguish other HIV related pulmonary complication from PTB. Hence the extent the over diagnosis of smear negative PTB is uncertain. It is important to follow the diagnostic algorithm outlined for the diagnosis of PTB even in HIV positive individuals in order to diagnosis smear negative TB. The following conditions in TB patients should arouse the suspicion of the HIV infection.

- Oral/esophageal Candidiasis
- Chronic diarrhea for more than a month
- Weight loss more than 10 % of Total Body weight in 6 months time.
- Fever for more than a month
- Herpes Zoster
- Recurrent pneumonia

- Typhoid
- Oral hairy leukiopikia
- Kaposi's Sarcoma
- Present or post genital ulceration
- Generalized dermatitis

The detection of HIV infection in TB patients can be achieved by referring the patients to the VCTCs. The rapid HIV test kits consisting of three different antigens are used for the diagnosis of HIV infection. The first test is performed by comb aids kit and if it is positive a second test is performed by capillus kit and if the second test is positive the third is performed by using the Tridot kit. If all three tests are positive then the person is declared a positive for HIV infection.

Similar to the TB patients HIV positive persons who show the following symptoms should be suspected of having TB and must be further investigated for diagnosis and treatment.

- Cough for prolong time about three weeks or more
- Fewer for more than two weeks
- Weight loss
- Fatigue listlessness
- Unexplained dysponea/ chest pain
- Haemoptysis
- Lymph node enlargement
- Head ache , vomiting alteration of sensorium or convulsion

Patients who are HIV positive should be referred to the nearby hospital for further medical examination.

1.4. g. Prevention, Control and Treatment of the double endemic

The synergetic relationship between the two diseases Tuberculosis and HIV /AIDS has made the condition of the patients who are co-infected more vulnerable. Those patients living with AIDS have a greater risk of acquiring TB due to the low immune system which is rendered weak by the HIV virus. Therefore the treatment of the patient who is being co-infected with HIV/AIDS and TB are more complicated due to the drug interaction between the HIV retro-

viral treatment and TB medication. If people living with HIV have not yet started with treatment, the recommendation may be to treat first before introducing HIV anti-viral treatment. This decision could be made by the doctors after examination or the CD_4^+ counts. In case people already receiving the ARV treatment for HIV, it may be necessary to make changes to the treatment. Due to the impossible complication it is essential that the practioners who have knowledge in both TB and HIV manage the treatment.

It is essential to start standard anti tuberculosis treatment promptly following DOTS strategy in HIV patient's diagnosis to have TB as majority of these patients respond well to the standard anti tuberculosis treatment. It is known HIV positive individuals with active TB category I is to be used. Treatment regimens recommendation under RNTCP is the same irrespective of patients HIV status. The duration of the therapy will be as per treatment regimen and category. The availability of highly active anti-retroviral therapy has significantly improved the outcome of HIV/AIDS in terms of prevention of TB has been demonstrate in South Africa, and outcome of the patients with HIV-TB co-infection has improved over years attributable to improvements in anti-retroviral and anti-tuberculosis treatment. Thus understandably both anti-tuberculosis treatment and HAART are indispensably in the management of the patients with HIV-TB.

Till date no cure is available for HIV/AIDS. It is only the opportunistic infection emanating from the disease that can be treated antiretroviral drugs used to treat HIV/AIDS are effective in slowing down the action of the virus and prolong the life of the patients. The treatment for TB is same for HIV infected and HIV non-infected. The TB-HIV infected individuals receives Category I treatment if they are new smear positive cases. WHO recommends that people with TB/HIV complete their TB therapy prior beginning the ARV treatment, unless there is a high risk of HIV disease progression and death during the period of TB treatment.

Table No I. Anti-retroviral therapy for individuals with TB Co-infection WHO recommendation 2002

	Situation	Recommendation
1 2	Pulmonary TB and CD_4^+ count <50 per mm^3 or Extra pulmonary TB	Start Tb therapy. Start one of the following regimens as soon as the TB therapy is tolerated - ZDV/3TC/ABC - ZDV/3TC/EFV - ZDV/3TC/NVP - ZDV/3TC/SQV/r
	Pulmonary TB and CD_4^+ 50-200 per mm^3 or total lymphocyte count < then 100-1200 per mm^3	Start Tb therapy. Start one of these regimens after two months of TB therapy - ZDV/3TC/ABC - ZDV/3TC/EFV - ZDV/3TC/NVP - ZDV/3TC/SQV/r
3	Pulmonary TB and CD_4^+ >200 per mm3 or total lymphocyte count more than 1000-1200 per mm^3	Treat TB , monitor CD4+ counts if available start ART

ZDV: Zidovudine, 3TC: lamivudine, ABC: Abicabir, NVP: Neverapine, EFV: Efavirenz, SQV/r: Squanivir/low dose titonvir

1.5 STUDY AREA

The study area selected was the ART Clinic of the Sukraraj Tropical Hospital for Infectious Disease Teku. It is a separate department of the Hospital which is funded by NCASC and Global Fund under the Health Ministry. It is under the supervision of Dr Devi Prasad Bhusal who is the counselor and the co-coordinator of the Clinic. Along with it is DOTS clinic for T.B. This hospital is located in the heart of the city just to the side of Department of Information, Ministry of health and Population Govt. of Nepal. The advantage of its location

is that there is the National Public Health Laboratory almost attached with it but is a separate organ.

1.6 . JUSTIFICATION

This study area is selected as my research area/field due to many advantages. It is one of the most populous ART clinics where about 1700 patients from different places in and around valley visit for their consultation, counseling and ART treatment. . Different agencies involved in the prevention and treatment of this fatal disease come to this center for the consultation and medication. The clinic supplies the ARV treatment free of cost to all the PLWHA where CD_4 count is below 200. Most of the new cases of the suspected PLWHA visit this center for VCT counseling and treatment. The another factor is due to the location of NPHL where all most all the cases are referred for the CD_4 count and other medical test related with HIV, like LFT test, TB test ,Hepatitis test which makes the patients convenient to go to this centre and hence I can collect necessary information from them.

Chapter 2

OBJECTIVES OF THE STUDY

2.1 General Objective

To study the rate of prevalence of the HIV/TB co-infection among the new HIV positive patients visiting the clinic

2.2 Specific Objectives

- To study the age and gender -wise prevalence rate of HIV/TB co-infection
- To analyze the profession wise prevalence rate of the TB/HIV co-infection
- To study the prevalence rate of the TB/HIV co-infection in different educational level.
- To analyze the prevalence of TB/HIV in the smokers and non smokers.
- To study the prevalence rate of co-infection after and before diagnosis of HIV

CHAPTER 3

LITERATURE REVIEW

3.1 Background on HIV/AIDS

The origin of AIDS and HIV has puzzled scientists ever since the illness first came to light in the early 1980s. For over twenty years it has been the subject of fierce debate and the cause of countless arguments, with everything from a promiscuous flight attendant to a suspect vaccine programme being blamed. So what is the truth? Just where did AIDS come from? The discovery of HIV, the Human Immunodeficiency Virus, was made soon after. While some were initially resistant to acknowledge the connection (and indeed some remain so today), there is now clear evidence to prove that HIV causes AIDS.

It is now generally accepted that HIV is a descendant of a Simian Immunodeficiency Virus because certain strains of SIVs bear a very close resemblance to HIV-1 and HIV-2, the two types of HIV.

1998 analysis of the plasma sample from 1959 suggested that HIV-1 was introduced into humans around the 1940s or the early 1950s.In January 2000, the results of a new study suggested that the first case of HIV-1 infection occurred around 1931 in West Africa. This estimate (which had a 15 year margin of error) was based on a complex computer model of HIV's evolution. However, a study in 2008 dated the origin of HIV to between 1884 and 1924, much earlier than previous estimates. The researchers compared the viral sequence from 1959 (the oldest known HIV-1 specimen) to the newly discovered sequence from 1960. They found a significant genetic difference between them, demonstrating diversification of HIV-1 occurred long before the AIDS pandemic was recognized.

The question of exactly where the transfer of HIV to humans took place, and where the 'epidemic' officially first developed has always been controversial. Some have suggested that it is dangerous to even try to find out, as AIDS has frequently been blamed on an innocent person or group of individuals in the past. However, scientists remain keen to find the true

origin of HIV, as most agree it is important to understand the virus and its epidemiology in order to fight it.

It is likely that we will never know who the first person was to be infected with HIV, or exactly how it spread from that initial person. Scientists investigating the possibilities often become very attached to their individual 'pet' theories and insist that theirs is the only true answer, but the spread of AIDS could quite conceivably have been induced by a combination of many different events. Whether through injections, travel, wars, colonial practices or genetic engineering, the realities of the 20th Century have undoubtedly had a major role to play. Nevertheless, perhaps a more pressing concern for scientists today should not be how the AIDS epidemic originated, but how those it affects can be treated, how the further spread of HIV can be prevented and how the world can change to ensure a similar pandemic never occurs again

3.2 Background on Tuberculosis

The historic origin of tuberculosis in the human population is unknown. For some time it was assumed that human tuberculosis was derived from bovine tuberculosis in domestic cattle. It may be, however, a disease endemic in some animals rather that a 'crowd' disease sustained only in human hosts. It is now known that tuberculosis is maintained in a variety of wild animal reservoirs. These include buffalo and wild bird populations.

Robert Koch isolated the tubercle bacillus in 1882. The infection is usually airborne. Large numbers of people carry the bacillus. For most people, the infection is a silent, benign event. Read that sentence again. On average, infected people have only a 3 percent chance of developing active disease during their lives and a 1 percent of coming down with lethal disease. With the onset of the AIDS epidemic, the incidence of TB has increased alarmingly amongst persons infected with HIV.

Tuberculosis probably first appeared in the Iron Age. TB is reported to have appeared as isolated cases in Germany and Denmark during the Neolithic. It was not common in Britain until Roman times and became a significant disease burden only in the Middle Ages. How do we know this? TB leaves characteristic traces on the ribs and tends to destroy the bodies of

lower (lumbar) vertebrae, producing a characteristic angle in the lower spine. Years ago, TB was one of the greatest killers of mankind. It has often been called 'the white plague.' In recent times, the TB epidemic really began in Europe about 400 years ago. The last large area to be reached by TB was New Guinea in the 1940s, ironically when effective chemotherapy was developed half way around the world--a triumph of biomedicine. For a time, the disease was seen in a religious or moralistic manner. People so afflicted 'deserved it as punishment by the Lord.' It was even 'fashionable' amongst writers and the upper classes to have consumption (the term then used for TB). The sallow, thin appearance was even considered beautiful.

3.3 Background of HIV/TB Co-infection

Tuberculosis is the leading cause of death among people living with HIV in Africa and accounts for nearly 25 percent of deaths among persons with HIV worldwide.TheWHO's Global TB Control 2009 report estimated that at least one-third of the 33 million people living with HIV worldwide are infected with TB, and they are 20–30 times more likely to develop active TB than those without HIV. The global burden of TB disease among people with HIV is concentrated, like the HIV pandemic itself, in sub-Saharan Africa. According to the WHO's Global TB Control2009 report, 456,000 people globally died of HIV-associated TB in 2007. When infection is diagnosed and drugs are available, TB is curable. Because people living with HIV are more likely than non-HIV-infected persons to have extra pulmonary or smear-negative pulmonary TB, the disease is often inaccurately diagnosed, and this—along with diagnostic delays caused by poverty, the expense of transport to a facility to diagnose TB, alongside HIV related comorbidty—is a significant cause of the higher TB-related mortality among people with HIV.

TB/HIV is a leading reason why TB control is failing worldwide. In response to the impact of TB/HIV and learning from the contribution that HIV activists have made in mobilizing political will behind HIV care programs, the WHO's Stop TB Department revised its TB control strategy in 2006 to include policies that recommend national TB programs and their partners to address TB/HIV co infection as well as empower TB patients and their communities to improve TB/HIV collaborative policies and mobilize resources and political will for TB.

3.4. Literature review in Global Context

Muller *et a*., (1989-1993) conducted a study in 458 co-incident cases of HIV and TB identified in Chicago in United States. In the result the co-infected cases increased from 8.00% in 1989 to 15.00% in 1993. During the same year he obtained non-Hispanic black accounted for 50 % of the AIDS, 62 % of the TB and 71 % of the TB/HIV co-infection where as Hispanic black accounted 14-17 % of the TB/HIV co-infection.

Elloite *et al.*, (1990) conducted a cross-sectional study in Zambia University Teaching Hospital, Lusaka, Zambia, Central Africa in 1990 and showed that out of 346 adults patients with TB, 206 were positive for HIV. The peaks for both TB and HIV infection were aged 25-34 years and women of 14-24 years. Of patients with conformed PTB, 73/149 was positive for HIV. HIV positive patients with sputum positive smear and their chest X-ray films less often showed classic upper zone disease. Of 72 patients who fulfill clinical criteria for AIDS 17 were negative for HIV.

Helbert et *al.*, (2007) reported that out of 207 homosexual bisexual patients with AIDS 24 were the AIDS related complex, 39 were asymptotic HIV infection 32 patients were found to have *Mycobacterium* infection. *M.tuberculosis* was found in 13 patients with AIDS and 2 with AIDS related complex

De Cook *et al*., (1991). showed that in his study the prevalence of the rate of HIV/TB co-infection in Abidjan of Ivory Coast that 35 % of the total co-infected cases studied were attributed to HIV-1 and 4% to HIV-2.

De Cook *et al*., (1992). conducted a study in different parts of South Africa; the prevalence rate of the TB/ HIV co-infection cases was found to be 20-67%.

Steen and Mosinki (1993). conducted a study among 214 Tuberculosis patients in Botswana in South Africa to determine the prevalence of HIV co-infection by ELISA method and

found 45 out of 214 were HIV positive. The HIV seropositivity reached 29 % in the age group of 15-49 years, 25.00% of females with average age of 34 years and 18 of the males with an average age 39 years were HIV positive. 18 (40.00%) of the HIV positive had AIDS, no significant difference was found between HIV positive and HIV negative with regards to clinical type of tuberculosis.

Doli *et al.,* (1994) reported that in Indonesia the person infected by only *Tubercule bacilli* HIV negative cases had about 10% chances of developing to active TB during the remainder of their lives, thus they had less than 0.5 % chances developing to overt disease annually, but in contrast to HIV positive people already infected with TB has about 8% chances of developing to overt disease annually or up to 50% chances of developing TB during the rest of their relatively short life span.

Hsieh *et al.,* (1996) studied that in his study 24.6 % of the patients of HIV had TB with an average age of 37 years in National Taiwan University Hospital which was alarmingly high.

Alverez *et al*., (1996) conducted a study to determine the prevalence of TB in HIV infection between April to June in 1996. Among the population of the participants in the risk control programme in the town of Heidi servei Obret deLleida. Out of 150 patients 45 of whom were newly enrolled participants 80% were male averaging 31.1 years of age. The prevalence TB infection was 27.3% being higher among former prison inmates. The prevalence of HIV infection was 36.1 being greatest among those who had been using heroin longer than 11 years.

Berhance *et al.,* (1999) conducted a study to analyze the TB/HIV co-infection prevalence rate in Ethiopia.The study concluded that 54.8% of the HIV positive had TB co-infection.

Carvalho *et al.,* (1999) assessed the prevalence rate of the dual infection of the TB with the HIV positive people in Malawi. The studied resulted that the prevalence rate of the HIV/TB co-infection was 26.7 %.

Kwesigabo *et al*., (1999) conducted a study in Government Regional Hospital of Kagera Tanzania to estimate the hospital prevalence rate of HIB/TB co-infection found that the over all age adjusted HIV-1 prevalence was 32.8% (n=1422) and there was no significant difference in the age adjusted sex specific prevalence. The highest prevalence (53.3%) was found in the age group 25-34 years as well in the Gynecological and Medical ward (41.2% and 40.4% respectively) The patients who were HIV-1 infected were more likely to have a history of previous hospital admission and were at the increased risk of developing TB . The diagnostic categories with the HIV-1 infection prevalence were clinical AIDS (88.5%) Herpes Zoster and other HIV-1 skin manifestation combined (87.7%) and PTB (58.3%).

Girard *et al*., (1999-2000) conducted a study to analyze the data taken from 271 patients diagnosed in Italy during 1999 to 2000. The results of the study showed that out of 271 patients diagnosed 20 patients (7.4%) had previous TB where the treatment was not completed, 81 (29.9%) were diagnosed with HIV at TB diagnosis and 108 (39.8%) were aware of their HIV status but were not on ART and 82 (30.3%) were on ART.

Espinal *et al*., (2000) made a several studies and showed that HIV and TB co-infected cases were less in infection in transmission of *Mycobacterium tuberculi bacilli* than non-co-infected patients, in the Dominican Republic 61% of the households contact of HIV positive TB patients were positive tuberculin as compared to 76% among the households contact of HIV negative cases.

Diez *et al.*, (2001) studied that the rate co-infection of HIV/TB among the population who attended the hospital for the test there were 17.7 % co-infected in Spain.

Chimzizi *et al.,* (2001) conducted a survey to determine the prevalence of the co-infection of TB among the HIV patients in Malawi. The study found that 61% of the HIV positive patients were also co-infected with TB.

Thomas *et al*., (2001) showed in his study that 47% of the HIV positive patients studied in Chennai in South India was co-infected by TB.

Nkoghe *et al.*, (2001) conducted a study in Gabon between June 25th till August 31st 2001 concluded that among 358 patients examined, there were 141 females and 217 males. The male/female sex ratio was 1.50 and average age of 32 years. Proportion of new patients reached 61%. 91% of the patients suffered from PTB, 58 % smear positive and 26% were HIV -1 Positive.

Gracia *et al*., (2001) carried out a study using the epidemiological registering of TB-HIV /AIDS cases from health Secretariat of Bogotá. Only TB cases with HIV positive test were included in the study. Of 950 TB cases reported in Bogotá 113 (11.9%) were indicated to have TB and HIV tests, epidemiological information was recorded from 103 of them. Most cases were males, 38.8 % were between ages 25-34 years, and 40.8 % of the cases belong to contributive regimen. 82% were new cases. Of the 105 cases 62% were classified with PTB, 30 % with node TB, diagnostic criteria were recorded from only 55 patients. However, 78% were confirmed with microscopic smears.

Duke *et al*., (2002) reported that in a cross-sectional study made in Santa Domingo to assess the prevalence rate of the HIV/TB co-infection. The result of the study showed that there 14.6 % of the total being co-infected with TB.

Sharma, Kumar and Patnaik (2002) conducted a study in India to see the clinical, bacteriological and radiological features of HIV/TB patients. Over a period of two years a total of 301 TB patients were suspected to have HIV/AIDS co-infection and upon testing 42 patients were found to have seropositive. Most of the patients were Manual Labor followed by truck drivers. Sexual (heterosexual) route was found to me the risk factor of HIV/AIDS. The most common symptoms of the disease was cough and expectoration followed by fever and weight loss. AFB smear positive were found to be 21.4%. On chest skiagram infiltrative lesure were commonly seen in 61.9 % patients EPTB manifestation was seen in 45.6% of the HIV/TB cases.

Thakker *et al.,* (2002) found that the prevalence rate of the co-infection of TB in the HIV positive patients in India was increasing alarmingly year after year that is from 5.9%,6.3%,7.2%,7.9% to,8.0% from 1997 to 2001.

Dash *et al.,* (2002) conducted a survey on the study of the prevalence of the co-infection of TB among the HIV positive patients attending various VCT centers in Pakistan. The study found that 15.9% of the HIV patients included in the study were co-infected with TB.

Leslie *et al*., (2003) reported that the incidence rate of *Mycobacterium tuberculosis* among the HIV patients was 36.00% in Zimbabwe.

Salami and Katiba (2000-2004) conducted a study in HIV infected patients in University of Ilrin Teaching Hospital Nigeria from January 2000 till December 2004. The study resulted that TB/HIV co-infection occurred in 40% (297) of 744 new cases of TB seen in the last 5 years. HIV/PTB occurred in 79 % and HIV/EPTB occurred in 21 %. Above 47 new cases of the HIV/PTB and 12 of HIV/EPTB were diagnoses of the previous year.

Mohammad *et al.,* (2004) conducted a descriptive study to access the prevalence of the HIV among the TB cases diagnosed from 1998-2001 at Kota Bharu Hospital in Malaysia and obtained the majority of the patients were male (94.6%) within the average age of 34 years.

Bhagyabati *et al.,* (2004) conducted a study in Calcutta in India and found that 50% of HIV positive patients had TB which was significant statically ($P<0.001$). This contrast with the findings in another study but higher than that of Calcutta with 27.7% only.

Geoghagen *et al.,* (2004) conducted a review work in the children of age 0-12 years attending the University Hospital of the West Indies during January 1999 to December 2002. There was a significant increase of active TB cases. With 24 children diagnosed over this period all of these children received the BCG vaccine. 11(46%) of these were HIV co-infected and via Mother-To-Child. HIV infected children were statically more likely to be older than non-infected children.

Carvalho *et al*., (2005) carried out a study to evaluate factors related to TB development in HIV infected patients who were being treated at the Infectious Disease Hospital in Fortaleza Ceara, Brazil from January 2004 to December 2005, out of 171 patients who were diagnosed to have both HIV and TB. Among these co-infected patients, most (81%) were males, co-infected more frequent (87.8%) among patients over 40 years of age and those with lower educational level (less than 8 years of schooling) . 41% of the patients in the study had no smear positive culture test for AFB

Yayoi *et al.,* (2006) conducted a survey of HIV seropositive patients with *Mycobacterium* infection in Japan and found that out of 86 total, 48 (55.8%) were reported to have co-infected with *Mycobacterium tuberculosis.*

Lawn *et al.,* (2006) concluded in his study in Gugulethu Community health Center in South Africa that in a sample size of 1002, 67.00% of the patients were with prevalent TB at the start of the ART.

Kung *et al.,* (2006) conducted a surveillance study of HIV testing among patients with TB at University Hospital in Taiwan. The study reported was assessed among the patients diagnosed with TB. Out of 3643 patients diagnosed with TB and 49 with HIV infection prior to TB diagnosis were excluded in the study. Of the 3594 patients with unknown HIV status before TB diagnosis, 1035 (28.8%) were offered HIV testing. There was an increasing trend of providing HIV testing to TB patients that ranged from 16.1 % to 43.7 % ($P<0.001$) and the over all prevalence rate of HIV infection among TB patients was 5.6% of those tested compared with TB patients without HIV infection Those with HIV infection were more likely to be of age less than 50 years.

Gabunia *et al., (*2006) conducted a prospective observational study and has conducted in Georgia since January 1st 2006. All newly diagnosed HIV positive persons were screened for active and latent TB and the prevalence rate was identified up to 22% of HIV positive individuals were found to have active TB and 22.4-32.6% had latent TB. The prevalence of

HIV among thee TB patients ranged from 1.7% to 2.2%. The study showed significance prevalence of TB among HIV patients.

Moore *et al.,* (2007) made a report in his study in Toro in Uganda that there was an existence of 3.9 % of Co-infection of the TB in the new HIV positive cases at the start of the ART out of a total of 1044 population included in the study.

Cain *et al.,* (2007) conducted a cross-sectional study and a cohort retrospective study of patients newly diagnosed with HIV or TB from October 2003 till February 2005 found that out of 574 TB patients in Cambodia , 216 (38.00%) were diagnosed as HIV positive and TB was found in 124 (24.00%) HIV infected persons. . Of 108 TB patients with HIV infection and a recorded treatment outcome, 49 (27.00%) died compared to 17 (5.00%) with out HIV infection. HIV infected TB patients with smear-positive pulmonary disease died less frequently than those with smear-negative pulmonary disease.

Bendayan *et al.,* (2007) conducted a study in 1059 TB cases hospitalized in Shmule Harofe Hospital Thailand during January 2000 till December 2006 and found that there were 93 cases who were co-infected with TB and among them maximum were from the epidemic areas of the country.

Lee e*t al.,* (2007) studied the low adherence of guidelines for preventing TB among persons with newly diagnosed HIV infection in USA found, that out of the population size of 1093 persons diagnosed with HIV within January1995-1997 in Seattle , the person receiving the tuberculin test (TST), following HIV diagnoses resulted that 53.7% had TST following the HIV diagnosis 6.6 % were reactive to HIV

Sriprapa (2007) reported that in Thailand there were 17.00% of the HIV patients with TB and 15470 by end of 2007 were estimated to have HIV and 27.00% of them would be co-infected by TB.

Memon *et al*., (2007) conducted a study to determine the frequency of dual TB/HIV infection in patients presenting at tertiary cares Centers at Karachi in Pakistan whose result showed that out of the total of 196 patients of TB and HIV who were screened for the co-infection , 38(19.39%) were co-infected with co-infection. During the same duration 70 patients of TB were screened for HIV and was tested positive for HIV. History of elicit sexual relationship was found in 121cases and 25 of them were homosexuals.

Ngowi *et al.,* (2008) conducted in Haydo Lutheran Hospital Manaya region Tanzania between September 2006 to March 2007 to study TB among people living with HIV/AIDS attending the care and treatment in rural region of Tanzania showed that the prevalence rate of the HI was 8.5% among the 233 cases of Tuberculosis included in the study.

Sume *et al*., (2008) Conducted a retrospective study in Nylon Hospital , Douala, Cameroon showed the prevalence rate of HIV infection in TB was 51.6%. Smear positive pulmonary was the most frequent (65.00%) form of TB diagnosed but extra pulmonary tuberculosis and smear negative pulmonary TB were more frequently associated with HIV co-infection (80.00%, 68.5% respectively). While men and women presented equally with TB, women (61.4%) were significantly ($P< 0.0001$) more Tb/HIV co-infected than man (42.00%). The co-infected rate was highest among individuals aged between25-44 years (61.4%) and least among the age-group 0-24 years (22.5%). The increase in TB/HIV co-infection rate monotonic over time with stronger trend among females aged 25-44 years ($P<0.037$) and above 45 years ($P<0.001$).Over all prevalence rate of the co-infection of the country was 32.00% among the adult TB patients.

Walter *et al.,* (2008) studied that 6.4 % prevalence rate in his survey of 290 HIV patients who were under the ARV treatment and 53.3% were in those who are without ARV treatment in Cape Town in South Africa.

Datiko *et al.,* (2004-2005) reported in their study made in Jamaica to study the rate of TB-HIV co-infection depends upon the prevalence of HIV infection in the community . In all TB patients and pregnant women attending the health institution for the TB diagnosis and treatment and ANC care were consecutively enrolled in 2004-2005. Of the 1308 TB patients

enrolled (18%) were HIV positive. The rate of HIV infection was higher in TB for urban 25.00% than rural areas 16.00%. Of the 4199 pregnant women attending the ANC 155 (3.8%) were HIV positive. The rate of HIV infection was higher in pregnant women from urban (7.5%) than rural areas (2.5%)

Jiang *et al*., (2008) conducted a cross-sectional study of HIV and TB co-infection cases in the mainland of China in 241 cases. Among the 241 there were 183 males and 58 females with pulmonary and extra pulmonary Tuberculosis or both were accounted. Among 241 cases HIV/TB co-infection, 76.8% had CD_4^+ count 200 per mm^3 and 58.5% were of 100 $mm^{3.}$ Treatment for TB and HIV were provided to the patients and the mortality attributable to co-infection was reported for 15.8% of the cases.

Thiruvalluvan *et al.,* (2009) conducted a study to access the prevalence of HIV among TB out patient attendees in Rajaji Hospital Madhurai, India. Among 165 cases included in the study it was found that 54.66% chest symptomic attending TB out patient ward was HIV positive. An analysis of high risk profile versus positive result showed that 47(n=75) and 48(n=90) who admitted and denied high risk behavior respectively, found to be positive to HIV screening test.

Shah *et al.,* (2009) Conducted an Intensified TB case finding among HIV infected persons from VCTCs in Addis Ababa Ethiopia found , to evaluate commonly available screening test for Pulmonary Tuberculosis in HIV infected persons attending the Volunteer Counseling and Testing Centers showed that out of 438 HIV positive persons 265 (61.00%) females with an median age of 34 years (range 18-65 years) , overall 32 (7.00%) were diagnosed with TB of whom 5 (16%) were asymptotic but culture confirmed TB cases.

Crespo *et al*., (2009) conducted a study to find out the *Mycobacterium* infection among the HIV infected patients in Cali in Colombia. The study showed that out of 155 individual included in the study who are infected with HIV, the prevalence of TB was 6.5% in comparison with 0.04% among the group of HIV negative. Non-tubercles tuberculosis

present in 43 patients were significantly more frequent than *M.tuberculosis* (27.7% versus 6.5%, X^2=24.78, P=0.000001).

Reutar (2009) stated in his interview that about 83% of the TB patients in Swaziland are co-infected with HIV. One out of four sexually active adults has HIV/AIDS and the life expectancy has fallen to 32 years. Currently 18 % people are infected with TB die in this country annually. Most of the patients die at the first two months because they are also infected with HIV and were not put on ARV treatment fast enough or because they are infected with drug-resistant TB and were not diagnosed early enough.

3.5 Literature review in context to Nepal

Sherchand *et al*., (2001) conducted a study in Kathmandu valley to access the prevalence rate of TB/HIV co-infection. They found that the TB prevalence among the HIV patients in Kathmandu valley was 6.1%.

Dhungana *et al.*, (2002) conducted a study to determine the prevalence rate of the HIV/TB co-infection in Tansen Mission Hospital in Palpa , Nepal. They found that the prevalence of the HIV/TB co-infection was 10.26%.

Gautam (2003) reported in his study that the prevalence of the co-infection of HIV/TB in Kathmandu valley was 22.22%.

Dhungana *et al.*,(2004-2005) conducted a cross-sectional study during January 2004 to August 2005 in 100 HIV infected patients visiting the Tribhuwan University Teaching Hospital Kathmandu, Nepal and about dozens of HIV care centers of Kathmandu with the objective to characterize the different microbial species in HIV/AIDS patients. Among the 100 HIV infected patients 66 (66%) were males and 34 (34%) were females. 60 % of the cases were of age-group 21-30 years. Microbial were detected in 23 cases (23%) HIV cases of which 15 (65.2%) were in age group 21-30 years. 17 (74%) were males and 6(26%) were females. Among 23 co-infected cases 22 were culture positive for *Mycobacterium.* Among

these the predominated one was *Mycobacterium avium* complex (MAC) 9 (41%), followed by *Mycobacterium tuberculosis* 6 (27%), *Mycobacterium kansasi* 4 (18%), *Mycobacterium fortritum* 2 (10%) and *Mycobacterium chelonae* 1 (4%). Significant relationship was established between smoking /alcoholism and the subsequent development of TB (X^2=7.24, P<0.05) for smoking habit and (X^2= 4.39, P<0.05) for alcoholism. 14 (16%) co-infected cases presented with weight loss and cough whereas diarrhea was presented only with these patients with typical mycobacterial co-infection which was as high as 5 (56%) in patients with MAC co-infection

Luitel *et al*., (2004) in their study reported that among the HIV positive people in United Mission Hospital Tansen the prevalence of the TB increased from 10.8% in 2002 to 39.5% in 2004

Dharmadhikari *et al.,* (1997-2005) carried out a cases record study for TB among the 287 sex trafficked girls and women repatriated to a single, rehabilitation non-governmental organization in Kathmandu Nepal between 1997-2005. There were 17 cases of TB that developed after rescue within the sample of the girls and women who were aged 7-32 years when they were trafficked. The majority of the cases (70%) were likely PTB. Nearly 9 in every 10 individual who developed TB were HIV co-infected.

Dhungana (2005) studied in a cross-sectional study conducted among the 100 HIV cases 66(66.00%) were males and 34 (34.00% were females. 60.00% of the cases were of age group 21-30 years. Majority of them were smokers (41.00%), alcoholics (34.00%), illiterates were 54.00% and unemployed were 59.00%. Heterosexual activity (51.00%) was found to be the most risk factor of HIV infection. Of the total there were 23(23.00%) co-infected with tuberculosis.

Sherchand *et al*., (2006-2007) a study was conducted in the DOTS center , Maharajgunj and Infectious and Tropical Disease Research and Prevention Center, Tripureshowr . A total of 300 patients with respiratory tract symptoms and cough for more than three weeks suggesting symptoms pulmonary tuberculosis and having risk behavior towards HIV infection were

screened for TB by sputum microscopy, AFB culture, and radiology and HIV infection by standard ELISA method. The result concluded were that out of 300 patients 79 were diagnosed as PTB and 34 as HIV seropositive. Co–prevalence of TB/HIV was 4.33 % (13/300). Among these 13 there were 12 males and 1 female. HIV co-infection in Pulmonary TB cases were 16.46% (13/79). More cases were found in young adults age ranged from 21-40 years. Males dominate the females in occurrence.

Ghimere *et al., (*2008) conducted a research to determine the recent prevalence of the TB co-infection among the new HIV cases being reported to Palpa Mission Hospital and concluded that the prevalence rate was 10.76%.

Jha (2008) studied that the prevalence rate of the HIV infection on the TB patients attending the DOTS clinic of BPKIHS was 4.7%. Among the 300 newly TB patients, 14(4.7%) patients were HIV positive. All 14 TB/HIV co-infected patients were males. Among these 8 (57.2%) were in 31-40 years and the rest 6 (42.8%) in age group 21-29 years.

Chapter 4

METHODOLOGY

4.1 Materials and Methodology:

The Sukra Raj Tropical Hospital for Infectious Diseases is located in Teku which is just attached with the Information Department of Health and Population Ministry, Government of Nepal. It is one of the hospitals where maximum cases of the PLWHA come for the ARV treatment.

A cross-sectional study was conducted in the ART clinic of the Hospital from January 1st 2009 till 31st December 2009. In total 390 new cases visited the ART clinic for the diagnosis and the treatment of the HIV with various symptoms like fever skin infection , loss of body weight continuous diarrhea , from different parts of the valley and the nearby towns to the ART clinic for the diagnosis and other medical examination. These new cases were interviewed to collect the information required for the research after they report to the clinic with the results of CD_4 count and other related medical examinations. They were categorized into two groups in terms of the already existing TB cases that are they had a past history of TB [relapse, failure, and return after default] and new TB cases after diagnosis of the HIV. Those who could not be interviewed in the first visit were then interviewed in the first follow up date that is after 14 days and in still missing ones their information were collected from their medical record file with the prior permission of the medical in-charge of the ART section and the Counselor. A structured questionnaire was prepared in English prior to the interview date and was dully consulted with the medical-supervisor. The information regarding the Knowledge Attitudes and the Practices about HIV/TB co-infection were asked to the patients. Prior to the interview they were counseled regarding the purpose of the interview. They were asked the questions in Nepali and were filled in the questionnaire by the interviewer. The collected data were kept confident and were coded using their ART number and were used only for the study. These collected data were analyzed and the findings were presented in the tables and graphs.

4.2 Data Collection, Processing and Analysis

4.2a. Data Collection:

Data were collected directly by the questionnaire filling in the direct interview with the respondents.Some of the data were collected by the reference of the medical record files of the patients

4.2.b.Edition of Data

Data were collected by the various means that is by the direct filling of the questionnaire, referring the record files of the patients and other universal data were collected from the journals and the facts sheet provided by the Information Department of Ministry of Health and many were collected from the different websites. Once the data were collected they were edited as soon as possible to find out the errors, in order to make sure the collected and edited data were accurate authentic and reliable uniform and are well arranged

4.2.c.Coding of the data

The information was coded so as to make their classification and tabulation will be made easy and convenient.

4.2.d.Tabulation and Classification of Data

To match to the objective and requirement of the research the coded data were classified scientifically and all thus classified data were than tabulated to summarize the entire data and were displayed statistically.

4.2.Analysis of Data

The data tabulated and classified was then analyzed by means of various demographic means like by means of table, bar diagram, pie chart, column graph line graphs.

Teku Hospital

ART/DOTS Clinic

ART Regimen

ART Regimen


A patient appearing in the interview during their hospital visit


Nurse counseling and dispatching the medicine to the Patient


Chapter 5

RESULTS

5.1 Introduction:

The HIV epidemic is associated with lots of socio-economic and psychological consequences are relatively new phenomenon and have so far, not been serious consideration given in the development planning by most of the affected countries The rapid and the hidden spread of this epidemic is effecting the suffering societies psychologically, socially and economically. More over the synergetic relationship with HIV and other Opportunistic Infections (OIs) are further making the problem more and more serious as a result the death of the HIV /AIDS is increasing.

5.2 Demographic Characteristics of the Respondents

5.1. a. Age and Gender wise distribution of TB/HIV co-infection data

From the study it was found that out of this 106 there were 80 males which were 75.5% and 26 females making 24.5 % of the total. The lowest frequency of the co-infection was found in 5-10 years age group where a single female was found to be co-infected, which was 0.94% of the occurrence rate. Likewise the highest frequency of the occurrence rate was studied in age group 35-40 years, which comprised 41 co-infected cases making 38.67% of the total occurrence rate. Among these 41 cases there were 32 males (78.04%) and 9 females (21.96%).The average age of the co-infected patients . The below table shows the age and sex wise prevalence of the HIV/TB co-infection.

Table No: I. Age and gender wise distribution of the HIV/TB co-infection

Age Group	Males		Females		Total	
	Number	Percent	Number	Percent	Number	Percent
0------15 Yrs	1	1.25	0	0.00	1	0.94
16----30 Yrs	8	10.00	9	34.61	17	16.03
31----45 Yrs	61	76.25	15	57.69	76	71.69
46----60 Yrs	10	12.50	2	7.69	12	11.32
> 61 Years	0	0.00	0	0.00	00	0.00
Total	80	100	26	100	106	100

5.2.b. Profession wise distribution of TB/HIV Co-infection data

In the present study, made to analyze the co-infection of TB/HIV prevalence , out of the total 390 cases of HIV , there were 106 TB/HIV co-infected cases which was 27.17 %.It has been alarmingly increasing then the previous study made . It was studied that out of 106 total 48 of the co-infected cases were from Seasonal Migrant Workers which was (45.28%). Among the 48 cases there were 41 males (51.25 %), and 7 females (26.92 %).Similarly among the 73 house wives of the seasonal migrant labor having HIV/AIDS 11 of them were found to be co-infected by the TB which was 15.06 % and is 42.30 % of the total females included in the study. Among the 32 farmers who were diagnosed as HIV positive 16 of them were also co-

infected with TB that was 50.00 % and was 15.09 % of the total. Among these 16 were 15 (18.75%) males and 1(3.84%) female. Out of 34 students having infected with HIV there were 8 who were also co-infected with TB which was 23.52 %.Of these 8 co-infected cases there were 6 males (7.50%) and 2 females (7.69%).Of the sex workers studied to have HIV infection there were 4 being co-infected with TB which was (30.76%) and among them there were 2 males (2.50%) and 2 (7.69%) females. Similarly 10 drivers who were found to have HIV positive and among them 5 (50.00%) were found to have being co-infected with TB and were all males (6.25%). Of the 14 HIV positive cases who denied expressing their profession 7 were found to be co-infected with TB (50.00%) and among them were all males (8.75%). The rest of the others were 7 (6.60%) cases were involved in other different professions and 4 were males (5.00%) and 3 females (11.53%). The profession wise distribution of the co-infected cases is represented in the given pie diagram.

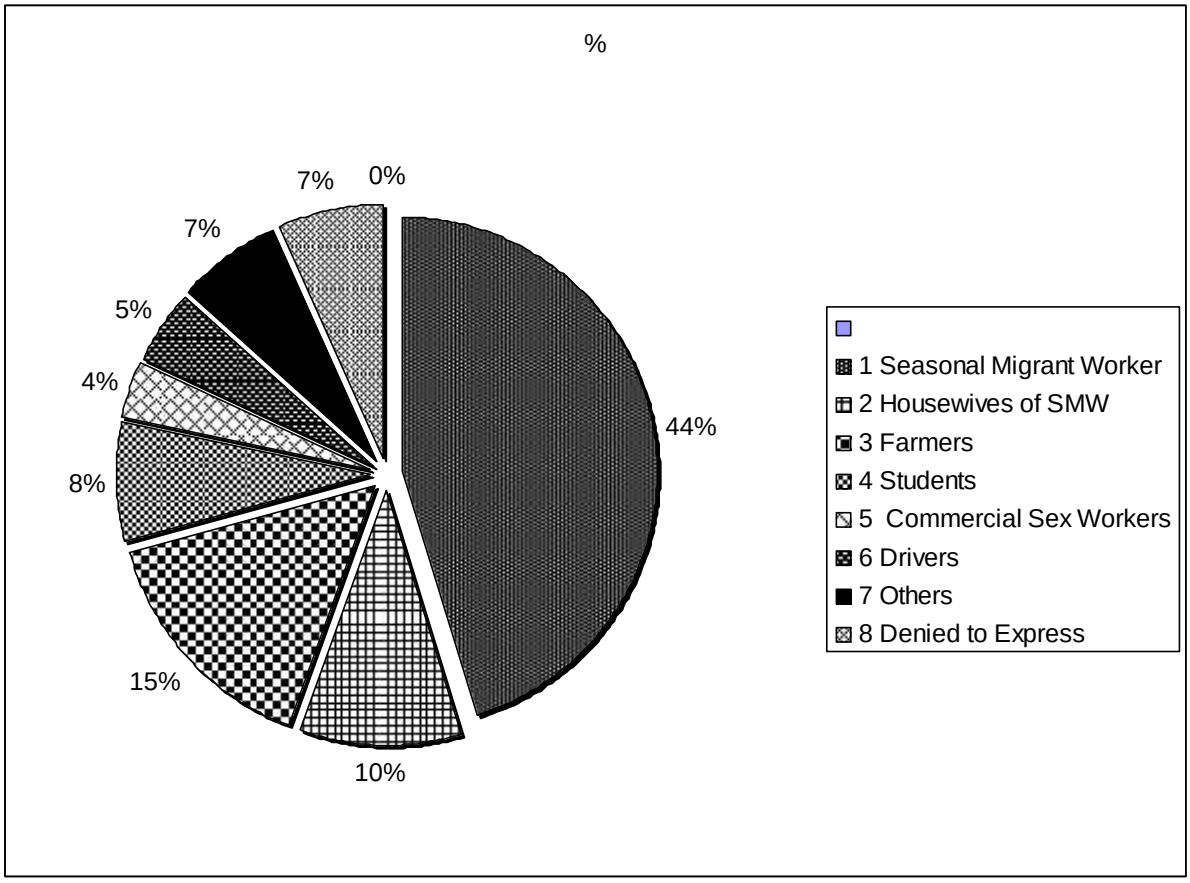


Fig No: 1 Numbers of HIV/TB Co-infected cases in different professions

5.2.c.Educational status wise distribution TB/HIV Co-infection.

This study determined to study the prevalence of TB/HIV co-infection among the patients with different educational status, visiting the hospital for ART treatment. The result was then tabulated. A total of 106 co-infected cases 61 (57.5%) can read and write in which 46 males (57.50%) and 15 females (57.69 %). The rest 45 (42.46%) of them were illiterate. Among the illiterate group 34 males (42.50%) and 11 females (42.30%). The highest frequency of the literate was in the level of primary and below which was 55 out of the total that was 51.88%. Among these cases there were 43 males (53.75%) and 12 females (46.15%). Likewise the numbers of the co-infected attaining lower secondary level of education were just 3 which were 2.83 %. Among them were 2 males (2.50 %) and 1 female (3.84%).Similarly attaining secondary level were just 2 which was (1.88%) and among them were 1 male (1.25%) and 1 (3.84%) female. There was just single female attaining Higher Secondary Level of education which was 3.84 % of the female co-infected and 0.94 % of the total population co-infected. There were no individual found to have higher level of education than this.

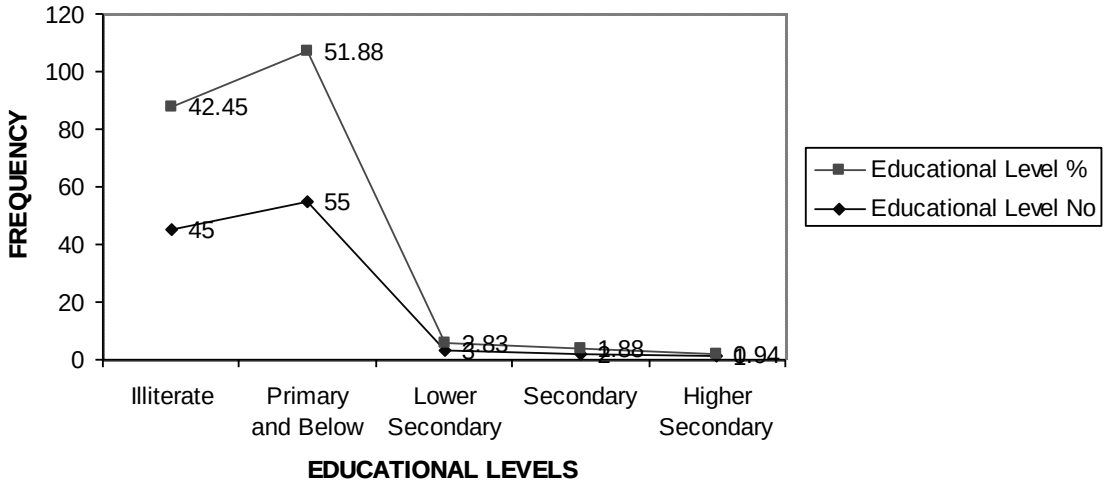


Fig.No.2 Percentage and number of the co-infected patients in different educational levels.

5.4. c. Distribution the TB/HIV Co-infected in terms of Smokers and Non-smokers

In the present study made to analyze the number of smokers and non-smokers among 106 co-infected cases with HIV/TB it was found that 84 of them were found to be the smokers which was 79.24%. Among these 84 smokers there were 66 males (82.50%) and the rest 18 were females (69.23 %). Of these 84 smokers 8 (9.53%) of them left smoking due to their bad health condition and 76 (90.47%) of them still continue to smoke. Among these who still smoke were 65 males and 11 females. This result shows that the smokers were more vulnerable for entering the dual epidemic. The graph below shows the number of smokers and non-smokers among the TB/HIV co-infected patients.

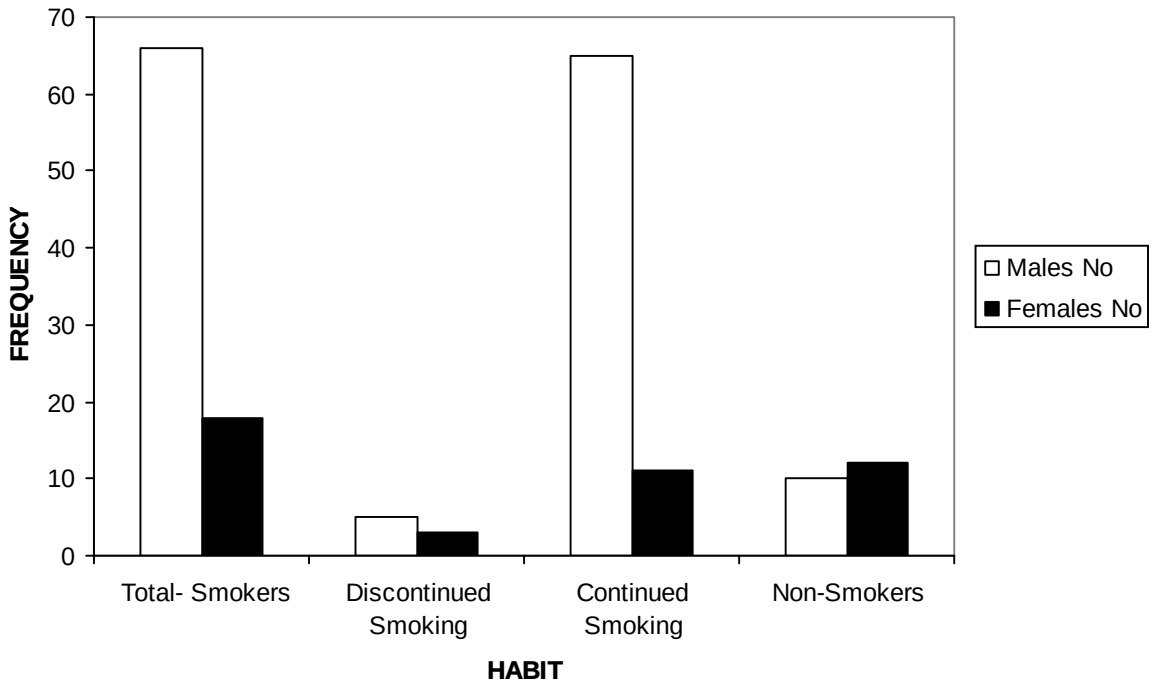


Fig No 3 Numbers of the HIV/TB Co-infected patients with respect to their smoking habits.

5.4. d. Distribution of the HIV/TB Co-infected patients with post and present Tb status

In the present study made to access the status of the TB cases in the HIV patients it was found that those who had TB treatment started before ARV treatment and those who do get the treatment for both treatment simultaneously. Among the 106 total TB/HIV co-infected cases there were 45 cases which was 42.45 % of the total had TB before diagnosis of HIV and 61 (57.55%) cases were those TB is diagnosed after the diagnosis of being HIV positive. Of the 45 patients with post TB cases there were 30 males (37.50%) and 15 females (57.69%). Likewise among the 61 cases of present TB cases there were 50 males (62.50%) and 11 females (42.30 %). This result shows that the prevalence of TB is more common after the diagnosis of HIV infection then early manifestation. The line graph below shows the data of the post and the present TB cases in the co-infected patients attending the ARV treatment.

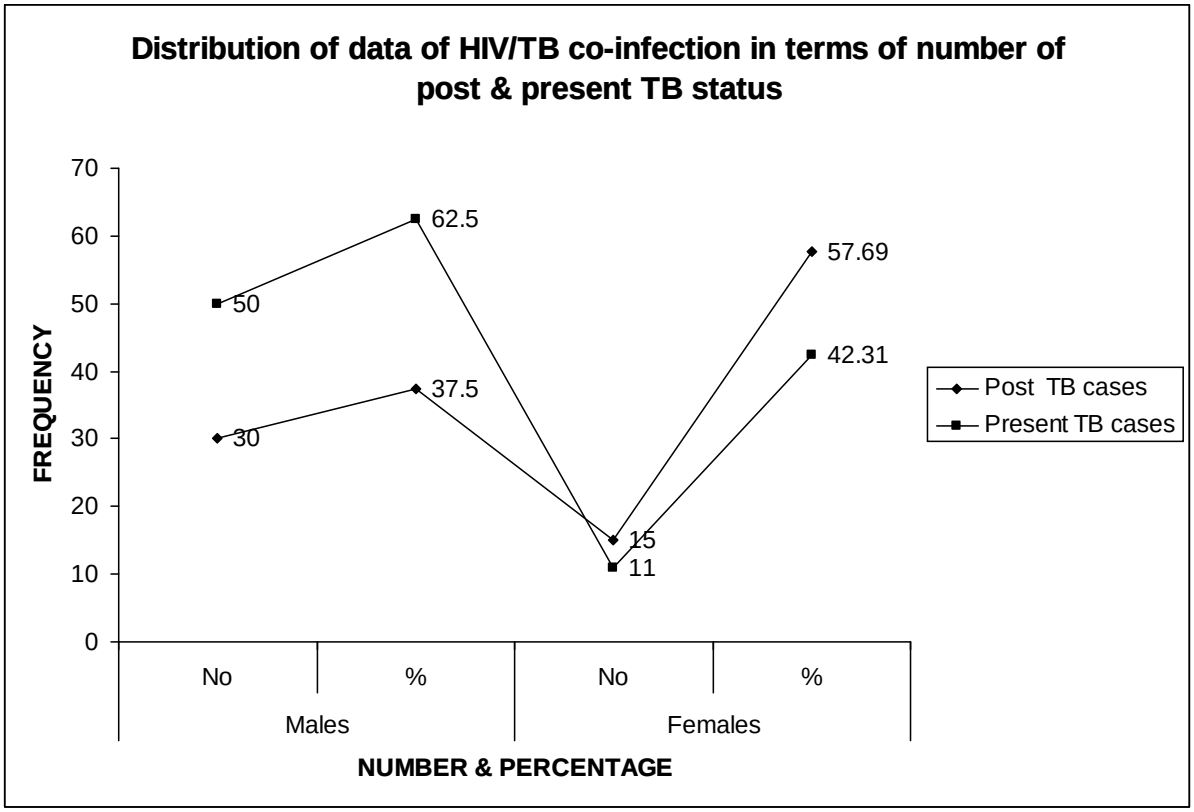


Fig No 4.Numbers and Percentages of the HIV/TB Co-infected cases in terms of Post and Present TB status

Chapter 6

DISCUSSIONS

When the entire world in is being becoming closer and closer due to the advent of various technology of science, there has been a rapid explosion of more and more life threatening epidemic are becoming pandemic. In the recent years TB and HIV/AIDS are creating the global havoc. They have aroused as a major public health problem and every year eroding a large toll of lives and national property for the prevention and control for it. The various steeps taken by national and global steeps are not found to be successful in finding out a durable and long lasting solution so much of these investments and trails seem to be thrown in the ashtrays. Globally there are more than 39.4 millions of people living with HIV/AIDS (UNAIDS), of which more than a half in the Sub Sahara Africa and one fifth in south east Asia. A country by the name Swaziland in Africa is the world most deadly affected country by HIV/AIDS and its attributable infections. It has about 85% of its population being infected by HIV/AIDS and among them 35% are co-infected by TB. The life risk has been reduced by this co-epidemic for the last few years. By the end of 2000 about 11.5 million people were co-infected by TB and HIV globally, 70 % of these co-infected live in Sub Sahara Africa, 20 % in South East Asia, 4 % in Latin America and Caribbean. TB accounts for 13 % of HIV related death world-wide. Globally 9% of the all new TB cases (31% in Africa), were attributable to HIV/AIDS (Sharma *et al.,* 2005). Over 4 million estimated HIV infections are found existing in the SAARC regions. (STC: 2005)As the HIV prevalence rate in the SAARC region is still low (>0.01% in Sri Lanka, Bangladesh, Maldives and Bhutan) where as <0.01>1.0 % in Nepal India and Pakistan. The available data show that relatively low proportion of TB cases attributable to HIV is in India 0.8, 0.6% in Nepal and 0.1% in Bangladesh. (STC: 2003).

There has been a tremendous work done in finding out the status of HIV and its co related infection in National regional and International level but sufficient work on finding out the rate of TB/HIV co-infection is comparatively low. Government of Nepal has set up many VCT centers in order to collect the available data of the cases and give the necessary help

and care to the HIV cases. These VCT has become the entry point for overall HIV and AIDS related services. It is provided free of cost to Most at High Risk Population (MARP) all over the country. Non-governmental organizations like FHI, FPAN are also involved to avail the necessary assistance to the infected people and bring them to the treatment centers. As per the fact sheet (NCASC November 2009) there are 14,787 HIV positive cases and 13,005 are enrolled under the HIV care, 3423 are under treatment. But the exact latest data on this co-infection is not available. As per the study made by Ministry of Health and Population made between 1988 till 2003 states that there were just 14 co-infected cases during 1988-1991, 99 cases in 1992-1997 and 332 in 1998-2003. This shows that there is an alarming trend of increment of co-infection in our country. A similar Surveillance of HIV infection in patients with TB in Nepal" a study conducted in 2002 in five different testing sites in various parts of Nepal such as NTC Kathmandu, INF Nepalgunj, PMH Tansen, NATA Biratnagar, and RTC Pokhara showed that HIV prevalence among TB patients continuous to raise and had increased four folds in the past eight years time.

In this present study made among the new 390 HIV cases reporting Sukraraj Tropical for Infectious Disease, Teku Kathmandu from January 1st 2009 till December 31st 2009, altogether there were 106 TB/HIV co-infected cases reported. The observed rate was 27.17 %. Among these 106 case there were 80 males (75.47%) and 26 (24.55%) females. Among these co-infected cases there were 45 cases that had TB before HIV confirmation and 61 of them had confirmed TB after HIV diagnosis.

This observed ratio was relatively higher than the similar study made in Kathmandu (22.22%) by Gautam D. (2003); almost a same finding was also made by Dhungana G.P. (Dissertation) Central department of Microbiology Tribhuwan University, Kirtipur (23%) in 2005. A study made by Ghimere P. *et al*., in Tansen Mission Hospital documented that the rate of co-infection of TB /HIV increased from 10.8 % to 39.5 % in 2004. The study made by the NCASC Teku official data states that the prevalence rate was found to be 66.0% among AIDS cases during 1993-2002 showed the prevalence was higher than the present finding. Lower percentage of findings was made by Sherchand *et al*., during 2002 in Kathmandu where the HIV prevalence among the HIV patients was found to be 6.1 %.In the global

scenario in 2003 (Leslie G. Louie *et al*.,) made a study stating the incidence of the co-infection was 35% among the HIV positive patients. Similar result was stated by De. Cook *et al*., in 1991that in Abidjan, Ivory Coast, 35 % of the co-infection cases were attributable to HIV-1 and 4%to HIV-2. Hsieh *et al*., in 1996 found 24.6% had TB where the mean age of the HIV patients was 37 years as observed in Taiwa University Hospital between January 1988 till September 1995.A study made by Thaker *et al.,* 2002 in India observed that the prevalence rate of HIV/TB co-infection was increasing each year by 5.9%, 6.3%, 7.2 %, 7.9% to 8% from 1997 till 2001 respectively. Berhanc *et.al*.1999 (Ethiopia), Carvalho, *et al.,* 1999, Chimziz, *et al.,* 2001 (Malawi), Diez, *et al.,* 2001 (Spain); Duke, *et al.,* 2002 (Santo Domingo),Dash, *et al*., 2002 found the rate of TB and HIV co-infection was 54.8 %, 26.7 %, 61%, 17.7%, 14.6 % and 15.9 % respectively. Muller, *et al.,* 1993 observed that during 1989-93 that proportion of co-infection of TB/HIV increased from 8 % (1983) to 15% in (1993). According to UNAIDS report 2009 one of the sexually active adults one of the sexually active adults in Swaziland (Africa) has HIV /AIDS and an enormous 80 % of the tens of thousands of people have TB, where the co-infection rate is 35 %. As per the international Journal of Respiratory Medicines “Thorax” February 2007, out of 30,670 TB cases reported in England and The Wales 5.7% were co-infected with HIV.

In the present study there was no such a big difference in the sex and age with the co-infection., although most of the co-infected cases were males and between the age of 25-45 with an average age of 35 years. The co-infection rate was maximum at this age group (83.96%) with (63.20%) males and (20.75%) females. The children below 15 years and adults above 60 years were observed to be comparatively less. This might be due to the fact that this is the economically productive age and they get involved in various activities for making the economy of the family and get into the epidemic while working in high risk areas. More over this age is the age of biological potentially or sexually active so there is higher chances of indulging into sexual activities while away from their partners and fall into the epidemic. Among them also most of the males are found to be the victim than the females of the same age. This might be due to women less involved in the outside environment and other income generation activities and remain at home looking after the children and the elderly members of the family. Similar results were also obtained by Dhungana *et al.,* in

2002 in Tansen. As majority of the of HIV infected people were higher in age0group of 21-31 years there might be higher chances of development of TB in this age-group of HIV people because it had already been verified that TB /HIV co-infection were statically significant. In addition people of this age group relatively high exposure to out side environment and hence there may be chances of development of TB. The same study also documented that TB/HIV co-infection was higher in males than females and is supported by this present study. A study made by Dhungana G P, among 100 HIV infected persons 23% were co-infected of which 65.2% and 26 % in 31-40 years were in the age group 21-30 years with higher prevalence rate in the males.. The sex wise distribution of the HIV infected in our society was studied to be higher in males (75.47%) than females (24.53%) which were similar to the data made available by NCASC which documented 72.7% males and 27.3 % females. A study made in Chennai (South India) by Thomas *et al.,* in HIV positive people showed 47 % of the HIV positive people were in age group 15-29 years, among them higher prevalence was seen in males than females. A similar study made in 149 HIV infected TB cases diagnosed from 1998-2001 at Kota Bharu Hospital Malaysia by Mohammad *et al.,* 2004 found that majority of the patients were males (94.6%) with an average age of 34 years. Hsieh *et al.*, (1996) documented 24.6 % of the TB/HIV co-infection were of mean age of 37 years in Taiwan University Hospital during the study period between January 1988-September 1995 which is similar to the present study.

In the present study of the total of 106 HIV/TB co-infected patients there was a significant difference between the profession of the patients and the rate of co-infection. The maximum (45.28%) cases were studied to be the Seasonal Migrant labor to different cities of Nepal, Indian and even overseas. Similarly farmers were found to be next follower with a co-infection rate of (15.09%). TB and HIV cause a great economic and social loss because 85.32 % of the infected patients are in the productive age group between (20-45) years. Unemployment and illiteracy governs most of these cases. This might be due to the involvement of this sexually active group in many illegal sex works due to lack of any job opportunity in the due course of searching a fertile economic pasture. So they might fall in the ditch of this epedimic.The housewives of the seasonal migrant labor might have acquired

from their infected counterpart and there is a high risk of transmission to their siblings as well.

In the present study there was also a relative difference with the rate of co-infection and educational status. Those who were completely uneducated and are just at or below level of primary education makes the greater part of the study population which was (51.8%). There were high number of males and the females under this category. This might be because of the reason that those who are uneducated and less educated do not have the idea of the diseases and their consequences and ignore them. Their knowledge attitudes and the behaviors regarding the disease were also found to be very low as a result these sections of the study population are found to be comparatively more infected. With regards to the studied sample population much of the respondents do not like to disclose the status due to the problem of social stigmatization. They would be discriminated and will be treated bad by the community by which their children will become the victim of the parental disease. This also might be due to the reason of lack of sufficient education and knowledge about these diseases. As the educational level increased the rate of co-infection was studied to be declining so might be more and more people are aware of the results and the consequences of the disease and keep them selves safe and in safety than the illiterate and less educated groups.

In this study there was a significant difference between the smokers and the non-smokers. Out of the total of the 106 co-infected cases there were 84 people who smoke which was 79.24 %. . Smokers might have acquired pulmonary TB due to smoking as smoking cause PTB sharply then those who do not smoke and particularly with those who have HIV positive test are very prone of getting TB as their immune system is made weaker by the virus so smoking aggravates the development of TB in HIV patients. Those who smoke further deteriorate their HIV status and increase the risk of reducing the life longevity.

In this study the percentage of those who had a post history of TB showed a little difference in the occurrence rate. Of the total cases there were 45 (42.45 %) patients who had TB before the HIV was disclosed to them and had undergone treatment before their ART treatment and the rest 61(57.53%) had their TB diagnosed after they were identified as HIV positive by

the medical examination. This study showed that there is high chances of development of TB after HIV infection might be due to the weakness of the immune system made my the depletion of the CD_4^+ T-lymphocytes. A study made by Stylbo 1990, and Daley *et al.,* 1992 showed that the HIV infected are also at the higher risk of rapid progression of active TB from the latent TB. The annual risk of development of active TB among HIV non- infected persons exceeds 10% of TB infected persons will develop active TB in absence of HIV and 40% in presence of HIV infection (Stylbo-1990, Godfrey Faussel, *et al.,* (2002). In a study made by Gautam D, among the 72 HIV/AIDS, 14 (19.44%) of them were found to have PTB and 2 (2.77%) were EPTB which was higher than findings made by Sherchand, *et al.,*2002 in Kathmandu which was 6.70 in the general population which suggest that the incidence rate of TB is increasing among the HIV/AIDS in Nepal indicating the threat of transmission to the greater population in the due course of time. Walter *et al.,* (2008) Cape Town in South Africa studied that 6.4 % prevalence of co-infection, 290 HIV patients who were under ART and 53.3 in those who are without ART. A study conducted in 129 HIV cases, TB co-infection was seen in 11.3 % with prior TB and 3 % with no prior TB (Seyler, *et al.,* 2005)in Abidjan Cote d' Ivory. Moore *et al.,* 2007 in 2007 in Toro, Uganda 3.9 % of all the patients with ART out of 1044 had been detected to be co-infected with TB. Lawn, *et al.,* 2006, in Gugulethu Community health Center South Africa, in a sample of 1002 cases 67 % of the patients were with prevalent TB at the start of ART a similar finding to this recent work.

Discussion on Awareness and KAP of the HIV/TB Co-infection

Most of the respondents were found to be less aware about HIV/AIDS and its consequences in detail. Most of them answered that HIV/AIDS is a dangerous life taking disease and never be cured. But they do not know about the relation of TB and HIV and nothing about other opportunistic infection Some of the educated respondents were found to be well aware of the HIV/AIDS and it transmission and the role to be played by the infected to prevent it further spread but had less knowledge about co-infection TB. Most of the respondents were of the view that avoiding unsafe sexual contact will prevent from the spread of this epidemic. Some were of the view that use of condom will prevent the transmission. The illiterate group of the respondents seems know very little about HIV and its attributable infections. These all

suggested that there is a lag of education and the information regarding HIV /AIDS and other Opportunistic Infections to minimize the rate of new occurrence of this epidemic.

Chapter 7

CONCLUSION

The study made in Sukra Raj Tropical Hospital for Infectious Diseases, Teku, Kathmandu from January 1st 2009 till 31st December 2009 to study the prevalence of TB/HIV co-infection among the new HIV positive cases the following conclusions were made:

The overall prevalence rate of HIV/TB co-infection in the new HIV positive patients attending the ART clinic of the hospital for ART was found to be 27.17%.The male prevalence rate was (75.47%) and the female prevalence rate was studied to be (24.52%) The highest prevalence rate was studied to be in the age group of 35-40 years (43.46%) with an average age of 35 years and the least prevalence was found to be in age group 0-10 years. (0.94%) The post TB prevalence rate was found to be (42.45%) and the current TB co-infection rate was found to be (57.54%) This co-infection has emerged as a serious public health challenge and is a serious problem in developing nations including Nepal. The lower literacy rate, looping unemployment, ignorance, inadequate health facilities, poverty are the main reason. The driving force of the Nepalese youth to the nearby cities of Indian sub-continent and over seas for better economic pastures is importing this disease.

The prevalence of the TB in the HIV patients is due to the weak immune system made by the declining of the CD_4^+ T-lymphocytes due to the entry of the HIV virus. There are many more cases which are yet to be declared and enrolled for the treatment due to the social stigmatization. They harbor other Opportunistic Infections too, these should be needed to be identified and need encouragement to get expose for medical treatment.

Chapter 8

RECOMMENDATIONS

After coming to the conclusion of the study made to determine the prevalence rate of HIV/TB co-infection among the newly diagnosed HIV positive patients visiting the ART Clinic of Sukra Raj Tropical Hospital for Infectious Diseases, the following recommendations are made.

- There is a need of further studies about TB and its role in HIV/AIDS prevention and control.

- High TB prevalence was found in HIV infected patients so TB and HIV prevention control program should work in close tandem.

- There is a need of serious steps by all level to bring the awareness to all level of people through different media may be through Radio, FM, News papers, Bulletins and magazines that reaches to the lower level of the people also.

- TB and HIV cause a huge Socio-economic loss because most of the infected patients are in the economic active population (20-45) years. Illiteracy, unemployment and ignorance are found to be the major risk factor for the infection so it is recommended that the Public health Sector socio-economic sectors are in the hour of the working in close collaboration.

- TB/HIV co-infection is the major risk for the HIV patients for death so there is a need of intervention to control TB in high HIV prevalence population.

- There is a need to identify the opportunistic parasites to determine the parasitic load among the HIV/TB co-infected patients

REFERENCES

Arora, D.R., Gautam, Sethi, S and Arora, B. (2004). Sixteen years study of HIV seroprevelence and HIV-related diseases in a teaching tertiary care hospital in India. *Int. Journal of STD AIDS*, 15(3): 178-182.

Alvarez, R. and Garcia, P. (1999). Prevelence of Tuberculosis and HIV infection among participants in IDUs risk control Programme. *Rev Esp salud Publica* , 73(3): 375-81.

Annual report: National Tuberculosis Control Programme, Nepal; 2006/2007.

AIDS News letter: Quarterly (2061; Asoj). Women Girls HIV and AIDS, 53:13-17.

Asrath, U., Sah S. and Jha, N. (2006). Awareness and high risk behaviors among migrant workers in relation to HIV/ AIDS a study from eastern Nepal**.** *SAARC Journal of Tuberculosis, lung diseases and HIV/AIDS,* 111(1): 5-12.

.

Acharya, R.P. and Bhattarai, M.D.(1999). HIV/AIDS prevention and control. *Journal of Nepal Medical Associatio*n, 38: 106-108.

Berhane, K., *et al.*, (1999). HIV testing among TB patients in Tigray region, Ethiopia, implications, TB treatment policy. *International journal of TB and Lung Diseases* .

Bhadwaj, A., Biswas R., and Shetty, K.J. (2001). HIV in Nepal: Is it rarer or the tip of an iceberg? *Trop Doct*, 31: 211-213.

Williams,B.G., Granich,R., Chauhan, L.S., Dhamshaktu, N.S. and Dye, C.(2005). The impact of HIV/AIDS on the control of Tuberculosis in India *Proc Natl Acad Sci* USA .

Barkare, N. and Miller, V. (2007). HIV/TB co-infection: Meeting the challenges, Report of Forum for Collaboration, HIV Research and TB and HIV working group to stop TB partnership. Sydney, Australia.

Cain,K.P., Kanara, N. and Laserson, K.F. (2007). The epidemiology of HIV associated TB in rural Cambodia, *Int. J Tuber Lung Dis* , 11(9):1008-13.

Crespo, M.P., Heli, R., Alzate, A., Carrasquilla, G. and Sanchez,N. (1999) . Mycobacterial infection in HIV infected patients in Cali, Columbia, USA, *Revista Panamericana de salud Publica,* 6(4): 249-55.

Chhetri, G.G. (2002). Prevalence of Tuberculosis among the suspected HIV patients visiting TUTH and their Antimicrobial Resistance Patterns (Dissertation) Central Department of Microbiology, Tribhuwan University

Chin, J. (2007). The AIDS Pandemic the collusion of the epidemiology with politically correctness. Oxford Redcliffe Publishing

Country report on HIV/AIDS provided by National HIV/AIDS Control Programme of Sri-Lanka to STAC in April 2008.

Country Cooperation Strategy 2006-2011, Nepal,

Cointinho, C., Brandes, E., Pardinas, M. and Rivas, C. (2004). Dissemination of mycobacteral infection in patients with HIV/AIDS. Evaluation of blood cultures, *Revista Argentina de microbiologia,* 2(3): 13-18.

Carvalho,B.M. (2008). Factors related to HIV/TB co-infection in a Brazalian Reference Hospital, *Braz. Jour Infect Dis,* 12(4):281-6.

Dhungana, J.R. (2002). Tuberculosis HIV Co-infection in UN Mission Hospital Tansen, Palpa, Nepal.

Dey, C., Scheele, S., Dolin, P., Pathania, V. and Raviglion, M.C. (1999). Global Burden of Tuberculosis. Estimated Incidence, Prevalence and Mortality by Country. *JAMA*, 282(7):677-686.

Dhungana, G.P., Ghimere, P., and Sharma, S. (2008). Characerization of Mycobacterial in HIV/AIDS patients in Nepal. *Jour. Nepal Med. Asso,* 47(169): 18-23.

Dhungana, G.P., Ghimere, P., Sharma,S. and Rijal. B.P. (2007). Tuberculosis and other clinical presentation of HIV/AIDS in patients with or without undergoing ART in Kathmandu, *Kathmandu University Med. Jour,* 5(1):22-6

Dharmananda, A.S., Gupta, J., Decker, M.R., Rai, A. and Silverman, J.G. (2005). Tuberculosis and HIV: global menace exacerbates via sex trafficking. *Jour of Med.Assoc of India,* 4(4); 153-56.

Datiko, D.G., Yassin, M.A., Kebeto, L.E., Lindtjorn, B. and Chekol, L.T. (2008). The rate of TB-HIV co-infection depends on the prevalence of the HIV infection in the community, *BMC Public Health* Jul 30; 8(1): 266.

Editorial Tuberculosis and Poverty, (2002). *International Journal of Tuberculosis and Lung Diseases;* 6(9): 745-746.

Elliot , R. and Simon, P. (1990). Impact of HIV on TB in Zambia, a cross-sectional study. *Biomedical Journal,* 301(6749): 412-5.

Gautam, D. (2005). Prevalence of Respiratory Tract Pathogens in HIV/AIDS Patients in Kathmandu A (Dissertation), Central Department of Microbiology, Tribhuwan University, Kirtipur Kathmandu Nepal.

Garcia, I., Merchan, A., Chaparro, P.E. and Lopez, L.E. (2004). Overview of the HIV/TB in Bogotá Colombia. *Biomedica* , 5(4): 132-7.

Girard, E., Antonucci, G. and Vanacore, P. (2004). Tuberculosis in HIV infected persons in context of wide availability of high active ART. *Eur. Respir Journal* , 24(1);11-7

Gurubacharya, V.L. and Gurubacharya, D.L. (2004). HIV Prevalence among Nepalese Migrant labor working in Nepal and Indian Cities. *Journal Nepal Medical Association* Vol.43, No-154.

Global Tuberculosis Control 2009-WHO.

Ghimere, P., Dhungana, J.R., Bam, D.S., and Rijal, B. (2004). TB and HIV Co-infection status in United Mission Hospital, Tansen-Western Nepal. *SAARC Journal of TB and Lung Diseases & HIV/AIDS*, 1(1): 32-38.

Gabunia, P., Salakaia, A., Kendelaki, G. and Kiria, N. (2006). TB-HIV co-infection in Georgia USA, *Georgian Med. News* , 1(65):7-10.

Gautam, D. (2004). The prevalence of the Respiratory Tract Pathogens (Bacterial) in HIV/AIDS patients of Kathmandu, abstract book. First SAARC conference on TB/HIV and Respiratory Dis, 14(17): 66.

Girard, E., Antonucci, G. and Vanacore, P. (199-2000). Tuberculosis in HIV infected persons in the context of wide availability of highly active ART. *Eur. Respir Jou*; 24(1): 11-7.

Geoghagen, M., Farr, J. and Hamblenton, I. (2004). Tuberculosis and HIV co-infection in Jamaican Children, *West Indian Med. Journal* , 53(5): 339-45.

Helbert, M., Robinson, D., Buchanan, D., Hellyer, T., Mc Crathy, M., Brown, I., Pincing, A.J., Mitchell, D.M. (1990). Mycobacterial infection in patients infected with HIV. *Thorax*, 45(1):45-48.

HIV/AIDS in Pakistan, World Bank, August 2008.

HIV/AIDS in Sri-Lanka, World Bank, August 2008.

HIV/AIDS in India, World Bank August 2007.

HIV/AIDS in Nepal, August 2008.

HIV/AIDS Health profile, USAID/Nepal

HIV Situation in India, NACO 2007 An Update.

HIV/AIDS in Bangladesh, World Bank, August 2008.

HIV/AIDS in Bhutan, World Bank August 2008.

HIV/AIDS in South East Asia Region, WHO-SEARO, March 2007.

Harris, A.D. and Maha, D. (1997). WHO Tuberculosis HIV Clinical manual

Haar, H.C. (2006).HIV prevalence among TB patients in Netherlands, 1993-2001: trends and Risk Factors. *The International Journal of Tuberculosis and Lung Diseases* , 10(7).

International Union against Tuberculosis and Lung Disease. Treatment regimens in HIV infected tuberculosis patients: an official statement of International Union against Tuberculosis and Lung Diseases, Paris, 16th September 1997. *Int. J Tuberc Lung Dis*. 1998; 2, 175.

Jiang, X., Lu, H. and Zhang, Y. (2008). a cross-sectional study of HIV and TB co-infection cases in Mainland of China, *South Med. Journal,* 101(9): 914-17.

Jha, K.K., Shrestha, L., Karki, K.B., Piryani, R.M. and Rhaman, M.M. (2005). HIV prevalence among diagnosed TB patients – A cross-sectional study in Nepal. *SAARC Journal of TB and Lung Diseases & HIV/AIDS, 3*(1): 60-64.

Kung, H.C., Sun, H.Y. and Chen, M.Y. (2009). HIV testing among patients with TB ay University Hospital Taiwan, *Jour. Formosa Assoc,* Apr; 108(4):320-7.

Kwesigabo (1999). Prevalence of HIV infection among hospital patients in North West Tanzania. *AIDS Care,* 11(1): 87-93.

Kumar, P., Sharma, N., Sharma, N.C., and Patnaik, S. (2002). Clinical Profile of TB in Patients with HIV /AIDS. *Indian Jour Chest Dis Allied Sci,* 44(3): 159-63.

Lee, L.M., Buskin, S.E., Morse, A., Cista, O.S. and Lobato, M.N. (1995-1997). Low adherence of the guidelines for preventing TB among the persons with newly diagnosed HIV-infection in USA, *Int. Jour. of Tuberc. And Lung Dis.*

Leibe, E., Li, L., Wu, Z., Rotheam-borus, M.J. and Guan, J. (2006). HIV/STD stigmatization fears as health seeking barriers in China. AIDS and behavior, 10 (5): p463-71.

Luitel, B.R., Lamgade, A., Bhusal, L. and Nepal, T. (2005). Trend of HIV co-infection in UN Mission Hospital A Retrospective glimpse, *Journal of Nepal Medical Association*, 44: 16(63).

Maher, D., Floyd, K. and Raviglion, M. (2002). TB/HIV Strategic Framework to Decrease the Burden of TB/HIV. Stop TB Department, WHO.

Mukadi, Y.D., Maher, D. and Harries, A.D. (2001). Tuberculosis cases fatality rates in high HIV prevalence population in sub Saharan Africa, 15:143-152.

Memon, A.R., Memon, M.A., Shah, S.A., Zuberi, B.F., Quden,R., Afsa, S. and Altaf, A. (2007). Frequency of Dual TB/HIV infection in patients presenting at the tertiary care centers in Karachi, *Jour. Coll. Physicians Sing Pak,* 7(10): 591-593.

Migliori, G.B. and Borghesi, A. (1992). Study of TB and HIV infection association in rural district of Northern Uganda, *Tuber Lung Dis,* 73(5):285-90.

Ngowi, B.J., Mfinenga, S.G., Bruun, J.N. and Morkve, O. (2008). Pulmonary TB among people living with HIV/AIDS attending care and treatment in rural Tanzania, *BMC Public Health ,* 30; 8:341.

Nkoghe, D. (2005). HIV surveillance among TB patients in Nkembo Hospital, Libreville, Gabon. *Bull Soc Pathol Exot,* 98(2):121-2

National Tuberculosis Center, Nepal Surveillance of HIV infection in Patients with TB in Nepal. Annual Report 2001/2002.

Newell, J.N., Baral, S.C., Pande, S.B., Bam, D.S. and Malla, P. (2006). Family-member DOTS and community DOTS for tuberculosis control in Nepal: cluster-randomised controlled trial. The lancet Vol.367, Issue 9514, pp 903-909.

National framework for joint TB/HIV Collaborative activities, India, February 2008.

Otsuka, Y. (2006). Survey of HIV seropositive patients with *Mycobacterium* infection in Japan, *Journal of Infection,* 51(5): 364-74.

Popilska, J., Marczyriska, M., Szczepariska, M. and Dobosy ,S. (2006). Tuberculosis in HIV infected Children, *Przeglad epidemiology,* 66(1):65-70.

Godfrey-Faussett, P., Maher , D., Diul, Y., Mukadi, M., Nunn, P., Perrie, J. and Mario Raviglion.(2002). How human immunodeficiency virus voluntary testing can contribute to tuberculosis control? *Bulletin of World Health Organization***,** 80(12).

Pakistan HIV/AIDS Situation and Response Analysis 2006.

Prakh, P., Gupta, G. and Rizal, S. (2006). HIV AIDS related knowledge, attitudes and risk perception amongst health professionals in BPKIHS. 13th annual celebrations scientific programme abstract book, Dharan, Nepal.

Sharma, S.K., Maha, A. and Khadiram, T. (2005). HIV/TB Co-infection Epidemiology, diagnosis and management, India. *Journal of Medical Research.*

Shah, S. and Demissie, M. (2009). Intensified case finding among HIV infected person from Volunteer Counseling and Testing centers in Addis Ababa, Ethiopia.

Sherchand, J.B., Bam, D.S. and Sherchand, S. (2001). HIV infection in Tuberculosis patients of Nepal. *Journal of Nepal Association of Laboratory Science* Vol-4, No: 4, Pp 1-5.

Sherchand, J. B., Maharjan, S., Bam, D.S., Singh, A. and Cuevas, L.E. (2008). Human Immuno Deficiency Virus co-infection in suspected TB patients. *Journal of Inst. Of Med*, 30(1): 6-10.

Salami, A.K. and Katiba, I.A . (2004). HIV associated TB patients and trends in the University of Ilorin Teaching Hospital. *Afr. Jour Med Science*, 35 (4); 57-60.

Sriyabbaya, N., Silurug, N. and Chunnchiviboonwat, D. (2002). Increasing Surveillance notification of TB cases extending to all region of Thailand in situation of the HIV/AIDS epidemic. *International Journal of TB and Lung Diseases* Vol. 2 No: 2, Pp11-2.

Sonia, J., Khatter, P., Singh, B., Arora, J., Rana, T., Seth, P. and Urvashi (2008). Mycobacterial infection in HIV virus seropositive patients; *Indian Jour. Tuber and Lung Dis*, 55: 28-33.

Subedi, B.K. (2003). HIV/TB Co-infection in Nepal. *Journal of Institution of Medical Association of Nepal* , 25: 19-21.

Steen, T.W. and Mosinki, K.T. (1993). Tuberculosis and HIV infection in Kweneng district, Botswana, *Jour. Tidsskr Nor Laegeforen*, 113(29): 3568-71.

Sume, G.E., Etogo, D., Metchinndie, J.N. and Kabore, S. (2008). Seroprevelence of HIV infection among TB Patients in Nylon District Hospital TB treatment Center.*East Afr.Medi. Journal* , 85(11): 529-36.

SAARC Tuberculosis Center /SAARC – Canada regional Tuberculosis and HIV/AIDS Project (STC), 2003a. *Articles on Tuberculosis and HIV/AIDS in the SAARC Region***,** Kathmandu, Nepal.

SAARC Tuberculosis Center /SAARC - Canada regional Tuberculosis and HIV/AIDS Project (STC). 2003b. *HIV/AIDS in SAARC Region***,** Kathmandu, Nepal

SAARC Tuberculosis Center/SAARC Canada regional Tuberculosis and HIV/AIDS Project (STC). 2003c**.** *Tuberculosis in the SAARC Region*, Kathmandu, Nepal.

SAARC *HIV/AIDS Update*, SATC 2008.

Sridhar, C.B., Kini, U. and Subhash, K . (2002). Comparative cytological study of lymph nodes Tuberculosis in HIV-infected individual and in patients with diabetes in the developing country. *Diagnosis Cytopathology*, 26(2), 75-80.

Senagupta, D., Lal, S. and Shrinivas,D. (1994). Opportunistic infection in AIDS. *Journal of Indian Medical Association,* 92 (1), 24-26.

Subedi, L.P., Khanal ,A., Sharma, B., Rana,P., Raut, R.K. and Subedi, I.P.(2004). Soci-economic impact of DOTS strategy in combating tuberculosis in Bhaktapur district of Nepal. *Journal of Nepal Health Research council,* Vol.2 No.1, p 43-50.

Sherchand, J.B., Bam, D.S. and Sherchand, S. (2001) . Human immunodeficiency Virus (HIV) information in Tuberculosis patients of Nepal. *Journal of Nepal association of Medical Laboratories Sciences,* 4(4): 1-5.

Ti, T., Tun, A., Yaw, O. and Myint, H. (1998). Study of HIV seropositivity among TB patients in five zonal TB centers Myanmar (1995-1997). *International Journal of TB and Lung Diseases* , 2(11), supplement 2. S203.

Tuberculosis in South East Asia- The time to act now-2000, WHO-Regional office for south East Asia, New Delhi.

Telzak, E.E., Chirgwin, K.D., Nelson, E.T., Matts, J.P., Sepkowitz ,K.A., Benson, C.A., Perlman, D.C. and Rl-sadr, W.M.(1999). Predictors of Multi-drug Resistant TB among HIV infected patients and response to specific drugs regimens. Terry Beirn Community Programs for Clinical research on AIDS (CPCRA) and AIDS Clinical Trials Group (ATCG), National Institutes for Health. *Int J Tuberc Lung Dis,* 3(4):337-343.

TB and HIV-the Deadly Duo. WHO Stop TB Program, 2001 and 2002.

UNICEF, (2003). Accelerating the Momentum in the Fight Against HIV/AIDS in South Asia. Overview paper, Kathmandu, Nepal. South Asia Regional Office.

United Nations Development Programme (2003) . *HIV/AIDS and Development in South Asia 2003,* New Delhi, India.

UNICEF/South Asia Regional Office (2001). *The HIV /AIDS Epidemic***,** Kathmandu, Nepal.

Uriz, J., Reparaz, J., castiello, J. and Sola, J. (2005). Tuberculosis in patients with HIV infection, *Anales del sistema sanitario de Navarra* , 30 suppl. 2:131-142.

UNAIDS, *Global Report on HIV/AIDS Epidemic* 2008

Verma, G.K. (2002). Sex workers and the spread of AIDS News you can use HIV/AIDS, p6.

Vajpayee, M., Kanswal, S. and Wig, N. (2003). Spectrum of opportunistic infection and profile of CD_4^+ counts among AIDS patients in North India. Department of Microbiology, All India Institute of Medical Science (AIIMS), New Delhi India.

Von Reyn, C.F. (1999). The significance of bacterium tuberculosis among persons with HIV infection in developing countries. AIDS, 13:2193-95.

World Health Organization. 2003. *Global TB Report 2007,* Geneva

World Health organization/ South Asia regional Office (WHO/SARO). 2001**.** *Beyond 2000: Responding to HIV/AIDS in the New Millennium***,** New Delhi, India.

WHO, Towards Universal Access: Scaling up Priority HIV/AIDS Interventions in the Health Sector, Progress Report 2009.

World Health Organization, (2003). Neglected Global epidemic: three growing threats, The World Health Report, Geneva, WHO.

World Health Organization (1997) Tobacco or Health**,** *A global status report*.
WHO, SERO (1992) Carrying out HIV Sentinel Surveillance

ANNEXES

Questionnaire

General Information

Form No: _____ Date: _____

ART No: _____ OPD No: _____

Name: _____Age/Sex _____

Address: _____

Educational Status _____Occupation:_____

Marital Status: _____ No. Of Children:_____

Other Information

Medical History:_____

_____

_____

Family Health Behavior: _____

_____

_____

_____

Surgical History if any: _____

_____

_____

Prevalence of any diseases

Sl No	To the Victim	✓	To the spouse	✓
1	Tuberculosis		Tuberculosis	
2	Hepatitis		Hepatitis	
3	STDs		STDs	
4	Diarrhea		Diarrhea	
5	Any others		Any others	

First reason or the symptoms for the purpose of this medical visit:

1. Continue diarrhea for more than a month Yes----------No--------
2. Continuous fever and cough Yes----------No--------
3. Blood tinged sputum Yes----------No--------
4. Itching and inflammation of skin Yes----------No--------
5. Genital Warts Yes---------No--------
6. Weight loss more than 10% of body weight Yes---------No----------
7. Loss of Appetite Yes--------No---------

Knowledge of the following :

1. Tuberculosis: Yes---------No--------
2. STDs Yes--------No---------
3. HIV/AIDS Yes---------No--------
4. Reproductive Health Yes---------No--------
5. Opportunistic Infection Yes--------No---------
6. Smoking Yes--------No---------

Mode of Exposure [MOE]

1. Through Family Members
2. Through Friends
3. Through organization
4. Hospital referred
5. Self

Mode of Transmission [MOT]

1. MCT
2. Other heterosexual route
3. IDUs
4. MSM
5. SW
6. Other

Physical observation:

1. Body Weight_____
2. WHO Stage : _____

3. General appearance:_____

Medical Examination

1. CD4 count:_____
2. Hemoglobin:_____
3. RBC count: _____
4. WBC Count:_____
5. STGP: _____
6. VDRL _____
7. Hepatitis: _____
8. Tuberculosis: _____

Knowledge and Attitudes of the disease

Q. Who encouraged you to come for this medical checkup?

_____

Q. How do you know that you have HIV?

_____

Q. Do you know how this disease does get transmitted to you?

_____

Q. Do you have what happens when you are infected with HIV?

_____

Q.Do you know people who are living with HIV / AIDS get TB easily?

_____

Q. Do you like your social exposure as HIV victim? Why?

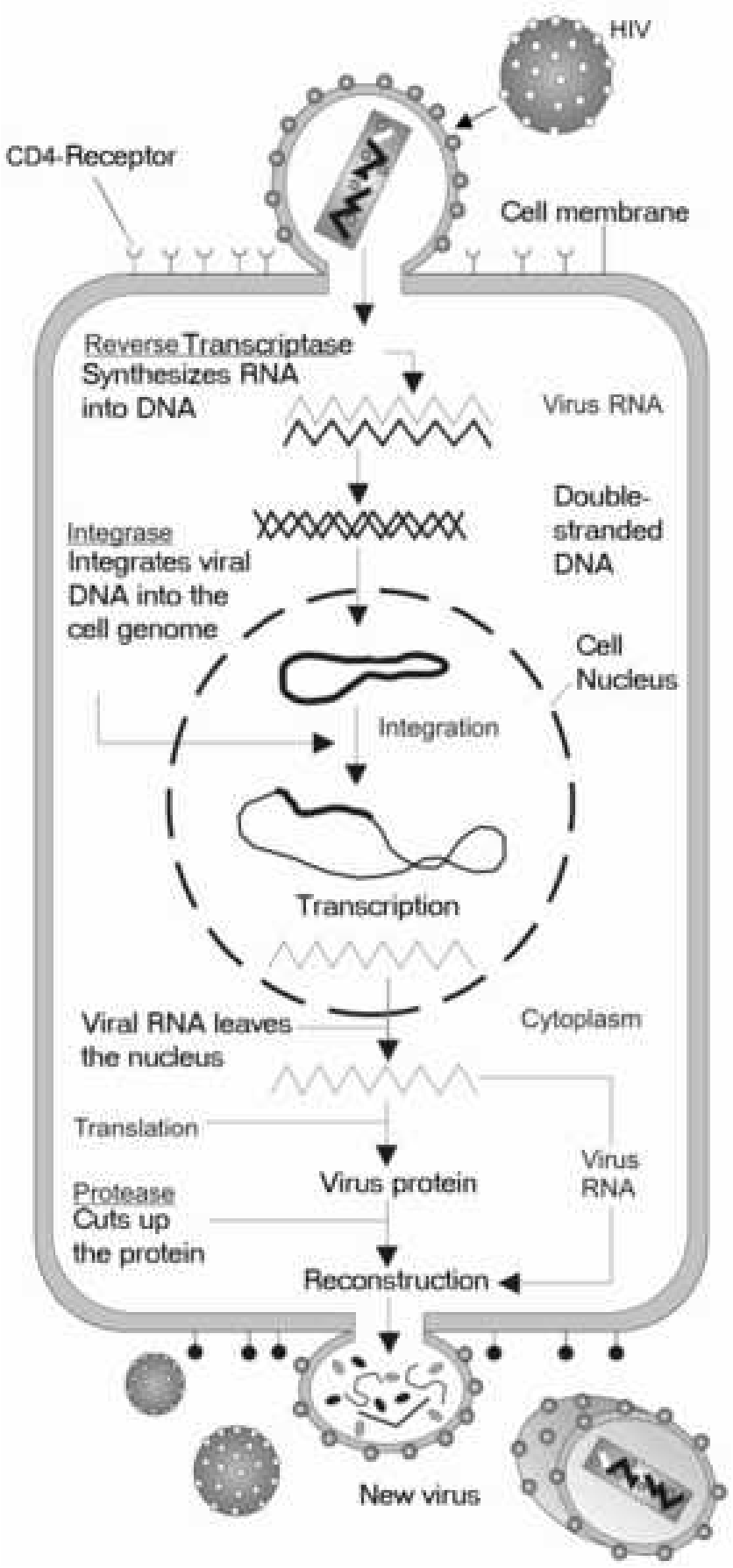
_____

Q. What can be done to prevent and control this epidemic?

_____

Medical Examination made at: _____

Date of Medical Examination: _____ Name and Sig. of the Interviewer


HIV
CD4-Receptor
Cell membrane
Reverse Transcriptase
Synthesizes RNA
into DNA
Virus RNA
Double-
stranded
DNA
Integrase
Integrates viral
DNA into the
cell genome
Cell
Nucleus
Integration
Transcription
Viral RNA leaves
the nucleus
Cytoplasm
Translation
Virus protein
Virus
RNA
Protease
Cuts up
the protein
Reconstruction
New virus