KWAME NKRUMAH UNIVERSITY OF SCIENCE AND TECHNOLOGY

DEPARTMENT OF THEORETICAL AND APPLIED BIOLOGY

CLINICAL OUTCOMES AND IMMUNOHAEMATOLOGICAL MARKERS OF PEOPLE LIVING WITH HIV AND AIDS WITH OR WITHOUT *MYCOBACTERIUM TUBERCULOSIS* IN SELECTED ANTI-RETROVIRAL CLINICS IN THE GREATER ACCRA REGION OF GHANA.

JOSHUA OFORI ESSIAM

JULY, 2013

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MPHIL. MICROBIOLOGY

A THESIS SUBMITTED TO THE DEPARTMENT OF THEORETICAL AND APPLIED BIOLOGY, KWAME NKRUMAH UNIVERSITY OF SCIENCE AND TECHNOLOGY, KUMASI, IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE AWARD OF A MASTER OF PHILOSOPHY IN MICROBIOLOGY.

JULY, 2013

DECLARATION

I, Joshua OforiEssiam, certify that this thesis is my original work, and that it has not been presented either in whole or in part to this or any other institution. In instances where references have been made or other people's ideas and views have been cited, full acknowledgement has been made. I therefore, accept full responsibility for any mistakes it may contain.

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ABSTRACT

Tuberculosis (TB) and human immunodeficiency virus (HIV) are two devastating global infectious diseases. The objectives that guided the study were to examine the clinical outcomes, CD4 cells count, Immunohaematological Markers, Erythrocyte Sedimentation Rate of PLWHA with or without TB and also TB results of HIV/ TB coinfected patients at three selected anti- retroviral clinics in the Greater Accra Region of Ghana. A sample size of 544 respondents participated in a case-control study in a 2:1 ratio through a convenience sampling method. Out of which 363 PLWHA with or without TB participated as subjects for the study whilst 181 participated as "healthy controls". The graph pad prism and SPSS 16 version a statistical package for social sciences were used to analyse the data. Findings revealed that there were significant mean differences in all the immunohaematological indices (Haemoglobin level, White blood cells count, Packed cells volume, Platelets count, Erythrocyte Sedimentation Rate, CD4 count) and HIV and TB status ($P < 0.05$). Also, none of the female respondents had a normal ESR (0- 8) mm/hr. Among the TB-HIV coinfected patients, TB was diagnosed in 8 (2.2%) by sputum smear microscopy alone, whilst 13 (3.6%) by sputum culture ($P > 0.05$). There was no case of multi- drug resistance in the TB- sensitivity results. The study concluded that laboratory results of immunohaematological indices, (full blood count, Erythrocyte sedimentation rate, CD4 count) are important in the monitoring and management of TB and HIV infection. The study therefore recommends that immunohaematological indices (CD4 count, FBC and ESR) must be performed routinely to monitor TB and HIV patients on regular basis in order to reduce morbidity and mortality associated with the diseases.

DEDICATION

This study is dedicated pre-eminently to Almighty God and my dear mother Mrs Mary Essiam, affectionately called Eno Mary by her sons and finally to my son David OforiEssiam.

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TABLE OF CONTENTS

PAGE

LIST OF TABLES

LIST OF ACRONYMS

AIDS Acquired immunodeficiency syndrome

ART Antiretroviral therapy

ARV Antiretroviral

DOTS Directly Observed Therapy Short course

ELISA Enzyme-Linked Immunosorbent Assay

HCT HIV counseling and testing

HIV Human immunodeficiency virus

IPT Isoniazid preventive therapy

MDR-TB Multidrug-resistant tuberculosis

STI Sexually transmitted infection

TB Tuberculosis

UN United Nations

UNAIDS Joint United Nations Programme on HIV/AIDS

UNICEF United Nations Children's Fund

WHO World Health Organization

CHAPTER ONE

INTRODUCTION AND BACKGROUND

1.1 BACKGROUND OF THE STUDY

Tuberculosis (TB) and human immunodeficiency virus (HIV) are two devastating global infectious diseases. TB is one of the deadliest diseases of the 20th century and continues to claim millions of lives (WHO, 2008c).The global HIV epidemic also continues to claim many lives, despite the global scale-up of antiretroviral (ARV) therapy.

HIV has resurrected TB as a global health concern, while TB has amplified the mortality from HIV substantially (Dye, 2006). Negative outcomes for co-infected individuals and inadequate services which fail to optimally deal with both epidemics are particularly evident in resource limited settings (Bock*et al.,* 2007). In recognition of the deleterious interaction between these diseases, the World Health Organisation (WHO) has developed guidelines for the collaboration of both modalities of care in the pursuit of a coherent, responsive and adequate model (WHO, 2004). Despite the growing evidence base and the WHO's resounding calls for a stronger connection between TB and HIV care, many of the countries with high negative impact have been slow to implement these recommendations on a wide scale (WHO, 2008a).

In 2008, WHO reported that, an estimated 33.4 million people worldwide were living with HIV, out of which 2.7 million were newly infected. More than 25 million people worldwide have died from HIV since the epidemic began (UNAIDS, 2009). Immune-suppressed HIV-positive individuals are more likely to become co-infected with TB Braitstein(2009) which is a leading cause of death in this population, especially

among those who reside in Sub-Saharan Africa (Moore *et al.*,2007). The dual burden of TB and HIV infection increases the likelihood of death compared with having either disease separately (El-Sony *et al.*, 2002).

Symptom questionnaires provide a quick, cheap and convenient way to identify individuals at a high risk of tuberculosis (TB) disease, termed TB suspects, who then need investigation with more definitive tests such as sputum microscopy, chest radiography and, when available, TB culture (Corbette*et al.*, 2009). Symptom screening for TB has high sensitivity when used to define TB suspects among patients who present themselves to health-care facilities for investigation of ill-health (i.e. passive case-finding) and is a key component of the World Health Organization's DOTS strategy for combating TB. In particular, chronic cough was found to be both highly sensitive and to have a reasonably high positive predictive value for smear-positive TB at the primary health-care level in studies in the pre-HIV era leading up to the development of the DOTS strategy (Corbette*et al.*, 2009).

HIV infection is characterised by CD4+ lymphocyte depletion manifested through the loss of the immune response capacity. The resulting immunodeficit is expressed by the blocking of immune surveillance mechanisms and thus, by the establishment of favourable conditions to the development of opportunistic infections and or malignant processes. In tuberculosis, the immunodeficiency associated with HIV infection makes possible the evolution of a latent infection to a clinically manifest disease. Latent tuberculosis is characterized by the intracellular persistence of some metabolically inactive Tb bacillus forms which are incapable of multiplication. The conversion of these inactive into metabolically active forms capable of multiplication is usually neutralized by immune-surveillance mechanisms. The blocking of such mechanisms in case of CD4+ cell depletion will allow the multiplication of metabolically active Tb bacillus forms, and

the development of a clinically manifest tuberculosis. CD4+ lymphocyte depletion is the result of facilitating antibodies and certain cytokines, and of some autoimmune processes which also affect the non-infected CD4+ cells.

The interaction between tuberculosis (TB) and human immunodeficiency virus (HIV) infection is complex. In the individual patient, HIV infection weakens the immune system and increases the susceptibility to TB. HIV increases the likelihood of reactivation, reinfection and progression of latent TB infection to active disease. It also alters the clinical presentation of TB, complicates the follow up and compromises the response to anti-TB treatment (Harries and Dye, 2006).

In a population, the lifetime risk of developing active TB once infected, in absence of HIV infection, is about 10% (Yassin*et al.,* 2006). However, it increases tenfold in HIV infected individuals. This has resulted in a large increase in the number of TB cases (Datiko*et al.,* 2008). The proportion of smear-negative pulmonary TB (PTB) and extrapulmonary TB (EPTB) is higher among HIV co-infected TB patients (Reid *et al.,* 2006).

1.2 STATEMENT OF THE PROBLEM

The HIV/AIDS pandemic has substantially altered the epidemiology of tuberculosis (WHO, 2008c) the results of various studies have documented that persons coinfected with mycobacterium tuberculosis and HIV have a 5-8% annual risk of developing active TB. Thus coinfected patients have the same probability of developing TB in one year as HIV negative tuberculosis positive patients have in their entire lives (WHO, 2008b). The double impact of TB and HIV is keeping large number of people trapped in poverty and diseases that reinforced each other (UNAIDS, 2009).

In Ghana, the magnitude of HIV is increasing despite progress made in the ART implementation and control programs. As TB and HIV in Ghana are major public health problems, accurate information about the extent and trends of the dual infection is important for effective prevention & control programs. However, there are only limited studies that describe the association between the two diseases so far in (Ghana Ministry of Health/ Ghana Health Service, 2006).

New approaches are needed to tackle the current and impeding disaster of TB/HIV coinfection. The combination will continue unless the detection and treatment of both infections improved simultaneously. Hence an integrated program has greater chance of mitigating the impact of the diseases. This study was therefore undertaken to examine clinical symptoms of the People Living with HIV and AIDS (PLWHA) and also to determine the mean distribution of CD4 count, Full Blood Count and Erythrocyte Sedimentation Rate of the respondents HIV and TB status in order to help physicians to develop a clinical criteria and quickly recognise these cases. The study also investigated the sensitivity of Anti-TB Drugs used in the treatment plan of TB- patients on the National Tuberculosis Program (NTP), Ghana.

1.3 JUSTIFICATION OF THE STUDY

In Ghana, the magnitude of tuberculosis is increasing despite progress made in Directly Observed Therapy Short course (DOTS) implementation, in control programs. These figures are very likely to increase significantly due to spread of HIV infection. However, there are limited studies undertaken in Ghana that would elucidate the association between TB and HIV co-infection (Ministry of Health/ Ghana Health Service, 2006).

The difficulties in diagnosing tuberculosis in HIV infected patients are among the challenges which are facing the national tuberculosis control programmes (Ministry of Health/ Ghana Health Service, 2006). Lack of rapid and effective methods for TB diagnosis is a major problem in developing countries. The study examined the clinical symptoms and laboratory findings of PWLHA with or without TB in order to help physicians to develop a high index of suspicion and quickly recognise these cases.

This study was therefore undertaken to examine clinical symptoms of the PLWHA's and also to determine the CD4 count, Full Blood Count and Erythrocyte Sedimentation Rate of the PLWHA with or without TB in order to help physicians to develop a high index of suspicion and quickly recognise these cases. The study also investigated the sensitivity of Anti-TB Drugs used in the treatment of TB on the National Tuberculosis Program (NTP), Ghana.

Furthermore, the study determined how gender influenced the clinical parameters and inform the care and management of PLWHA with or without pulmonary TB, as part of an overall effort to reduce morbidity and mortality of HIV and TB related death in Ghana.

1.4 STUDY AIMS

The aim of this study is to determine how clinical parameters will inform the care and management of PLWHA with or without pulmonary TB, as part of an overall effort to reduce morbidity and mortality of HIV and TB related death in Ghana.

1.5 SPECIFIC OBJECTIVES

1. To determine the clinical outcomes of the PLWHA's with or without tuberculosis at the selected ART Clinics.

2. To determine the CD4 T cells count of the PLWHA's with or without tuberculosis at the selected ART Clinics.

3. To assess the haematological parameters of the PLWHA's with or without tuberculosis at the selected ART Clinics.

4. To determine the Erythrocyte Sedimentation Rate of the PLWHA's with or without tuberculosis at the selected ART Clinics.

CHAPTER TWO

LITERATURE REVIEW

Globally tuberculosis (TB) is the leading cause of morbidity and mortality among HIV/AIDS patients accounting for about 30% of all death of HIV/AIDS patients (Sharma et al, 2005). Tuberculosis in HIV/AIDS patients is curable provided it is diagnosed accurately and treated promptly, but this need special attention due to the complexity of the diagnosis and treatment involved in tuberculosis and HIV/AIDS coinfection. In Africa and in Ghana tuberculosis is spreading rapidly due to the high prevalence of HIV infection signifying the need of steps to be taken urgently to stop this spread.

Globally, about 11% of new adult cases of tuberculosis are also HIV/AIDS coinfected and in Sub Saharan Africa 31% of new tuberculosis cases are also HIV/AIDS coinfected,(Corbette*et al*., 2003).HIV/AIDS fuels the tuberculosis epidemics in many ways, such as promoting progression to active tuberculosis, increasing the risk of reactivation of latent tuberculosis infection, as well as increasing chance of tuberculosis infection once exposed to tubercle bacilli. Tuberculosis increases the risk of progression from HIV to AIDS (Sharma *et al.,*2005; *Badriet al.,* 2001). World Health Organisation (WHO) recommends inclusion of HIV testing in the algorithm for diagnosis of tuberculosis in countries with adult HIV prevalence rate of> 1% or in settings where the HIV prevalence rate in tuberculosis patients is > 5% (Haileyeus*et al.,* 2007).

2.1 TUBERCULOSIS EPIDEMIOLOGY

Worldwide tuberculosis prevalence has declined by more than 20 per cent but Africa's rates have tripled since 1990 in countries with high HIV prevalence like Ghana, and the figures are still rising across the continent at 3-4 per cent per year (WHO, 2005). Between 1998 and 1999, a 20 percent increase of TB cases was reported in countries severely affected by HIV/AIDS in Africa. This contributed much to the increase of the TB burden globally. About 7-12% of all new tuberculosis cases in adult 15-49 years are also coinfectedwith HIV worldwide, while in Africa 31% of all new tuberculosis cases are also HIV/AIDS coinfected (Sharma*et al.*, 2005; Corbette*et al.,* 2003). The World Health Organization (WHO) in 1993 declared TB a global emergency in recognition of its growing importance as a public health problem. Deaths from TB account for 25% of all avoidable deaths in developing countries. Ghana is estimated to have had 44,733 new cases of TB in 2004 (incidence rate of 206 per 100,000 population), of whom 19,670 were new smear positive cases (92 per 100,000 population). The number of reported TB cases (all forms) gradually increased from 10,386 cases in 1999 to 12,124 in 2005. In 2005, notified smear positive cases totaled 7,505, with a case detection rate of 35 per 100,000 population(Ministry of Health/ Ghana Health Service, 2006).

Treatment success depends on completion of treatment according to national guidelines once a diagnosis of tuberculosis is made. Proper diagnosis and correct treatment of tuberculosis will result in reduction of prevalence, provided that the infectious cases are detected and brought to treatment. However, there are difficulties in achieving the goal of reducing tuberculosis in Ghana due to a number of challenges, in addition to prevailing problems in the control program, the difficulties in diagnosing tuberculosis in HIV/AIDS patients due to unusual clinical picture, increase in extrapulmonary (EPTB) and acid fast bacilli (AFB) smear negative pulmonary disease and atypical findings in chest x ray, all these complicate the tuberculosis diagnosis

(Lucas, 1994). To date, no simple test, apart from smear microscopy that can be used to diagnose TB. Moreover, maintaining quality of smear microscopy in Ghana still need emphasis (Mfinanga*et al.* 2007).

The stigma associated with tuberculosis with its link to HIV/AIDS, poor adherence (associated with high pill burden in case of coinfection), high mortality in HIV/AIDS andtuberculosis coinfected patients and difficulties in integrating tuberculosis and HIV/AIDS in one control program complicate the whole tuberculosis, HIV/AIDS management (Sharma*et al.*, 2005).

2.2 HIV/AIDS EPIDEMIOLOGY

About 1.8 million adults (aged 15-49 years) in Ghana are living with HIV (UNICEF, 2011). The epidemic is spreading in rural areas with less health facilities compared with the urban areas. The spread in rural area is faciltated by poverty, ignorance and lack of information about proper methods of prevention. Although the epidemic is reported to have decrease or stabilised in some areas of Ghana, it is estimated that between 230,000 – 300,000 were living with HIV in 2009 in Ghana (UNICEF, 2011). WHO estimates show that where the HIV prevalence in the general population is high, the prevalence of HIV in tuberculosis patients is also relatively high and *vice versa*. For example, the 1999 World Health Organisation estimates show that in Botswana, with HIV prevalence of 36% in the general population, the prevalence of HIV in tuberculosis patients was 77%. In Sub Saharan Africa with HIV prevalence of 8.7% in the general population, the prevalence in tuberculosis patients was 37% (Corbette*et al.*, 2003).

Efforts to control HIV/AIDS are in progress countrywide through the National AIDS Control Program (NACP) and Ghana Commission for AIDS. The control program includes information, education and communication (IEC) about the prevention of

HIV/AIDS and behaviour change and communication (BCC), emphasis is on abstinence, faithfulness and promotion of safer sex through condom use in high risk groups. Prevention of mother to child transmission of HIV/AIDS (PMTCT) is also promoted by administering anti-retro viral drugs (ARV) during the third trimester or at onset of labour, and by education about breast feeding options. The Government of Ghana initiated the roll out ARV program in October 2004 which aims at scaling up ARV to reach those in need in resource constrained areas. In the roll out ARV program all patients with medical eligibility for ARV are treated free of charge according to Ghananian national policy for HIV/AIDS managements.

In order for the HIV/AIDS patients to start ARV treatment among other screening they should also be screened for tuberculosis before initiation and on the course of treatment with ARV. The World Health Organisation recommends screening of HIV-infected person for TB diseases after HIV diagnosis, before initiation of ARV and during routine follow up care. In this strategy TB, if diagnosed, is treated promptly before starting ARV or for a few days before introduction of ARV to minimise overlapping of the drugs side effects (WHO, 2004c). To achieve the target of treating many HIV/AIDS patients in need of ARV, there is the need to screen those with features or diseases suggesting HIV infection such as tuberculosis and this will help as the entry point to HIV/AIDS care and treatment since tuberculosis patients coinfected with HIV/AIDS are eligible for ARV (WHO, 2004b). The available drugs for treating HIV/AIDS patients can suppress the viral replication, which results in increase in cellular immunity (CD4 T lymphocytes) and improved response and fight against opportunistic infections including tuberculosis. However the drugs do not eradicate the virus from the body of an infected individual. HIV/AIDS patients need tuberculosis prophylaxis using isoniazid (IPT).

However due to difficulties in diagnosing active tuberculosis in HIV/AIDS patients, starting isoniazid preventive therapy may be challenging. Isoniazid, if given to HIV/AIDS patients reduces the increased risk of these patients to develop active tuberculosis(Campos *et al.,* 2003). Isoniazid prophylaxis has a risk of developing resistance due to anti TB mono-therapy in patients with active tuberculosis (Tegbaru*et al.,* 2011).

2.3 HIV/AIDS AND TUBERCULOSIS COINFECTION

In Sub Saharan Africa, including Ghana, the HIV/AIDS infection contributed significantly to the rising in tuberculosis incidence. People with HIV infection are increasingly infected with TB because HIV weakens their immune system. HIV/AIDS is the most risk factors for the development of tuberculosis (Sonnenberg*et al.,* 2001). Patients with TB infection, coinfected with HIV, have a 20-30 times higher risk of developing tuberculosis diseases during their lives, than TB infected person without HIV infection, (Sharma*et al.,* 2009). In immunocompetent individuals with TB infection the lifetime risk of developing active TB disease is 10% in contrast with TB infected patient coinfected with HIV where the annual risk of developing TB disease is 5-8% (Sharma *et al.,* 2009; Corbette*et al.,* 2003). TB is the commonest opportunistic infection (OI) in HIV/AIDS patients in developing countries (WHO, 2005). Autopsy studies have found disseminated TB in 40-54% of HIV infected people in HIV prevalent countries, many of whom were undiagnosed prior death (WHO, 2005; Haileyeus*et al.,* 2007).

Tuberculosis is the common pre AIDS opportunistic infection and accounts for about 40% of all presentations seen in HIV patients in Haiti (Pape, 2004). Other common presentations are the wasting syndrome, which includes weight loss of more than 10% of normal weight and prolonged fever or diarrhoea. The wasting syndrome is also associated

with TB and more often the symptoms of TB are misattributed to HIV/AIDS (Cahn *et al.*, 2003). TB can occur at any stage of CD4 T cells depletion but it is common during the early stage when the CD4 T cells is relatively normal (Sharma*et al.*, 2005). In the work of Pape(2004), 56% of the TB patients infected with HIV were diagnosed when the CD4 T cells were > 350/microlitre, 23% and 12% of the patients infected with HIV has TB at the CD4 T cell levels of 200 - 350 /micro litre and < 200/microlitre, respectively. The pattern of chest radiography in TB patients coinfected with HIV/AIDS varies diversely, the typical upper-lobe cavitatory picture usually seen in reactivated adult pulmonary tuberculosis (PTB) occurs when the CD4 T cells are still relatively normal. As the CD4 T cells continue to fall with the progression of HIV to AIDS atypical presentations such as pleural effusion, mediastinal and lower lobe consolidation, milliary pattern and hilar lymph node enlargement become more common. Some of these changes are similar to presentations of other opportunistic infections affecting the lungs in HIV/AIDS patients, therefore, making interpretation of radiography for assisting diagnosis of TB difficult(Pape, 2004).

2.4 SPUTUM SMEAR MICROSCOPY AND CULTURE METHOD

Atypical presentation of pulmonary tuberculosis patients coinfected with HIV/AIDS includes smear negative AFB pulmonary tuberculosis. In Ghana, the smear positive record is about 40% and in the rest of the cases, the diagnosis is made clinically with the assistance of the chest radiography. However, the diagnosis of extrapulmonary tuberculosis (EPTB) was mainly clinical and may not be correct. The diagnosis of extrapulmonary tuberculosis is made histologically in areas where these facilities is available; however, in Ghana histology for TB diagnosis is not done routinely; it is done in referral hospitals and at Universities for research purposes. Other author has found that

histological evidence of mycobacterial disease was only found in three quarters of patients that were clinically diagnosed and started on empirical treatment for tuberculous adenitis (Mfinanaga, 2007).

Sputum culture is a more reliable means of diagnosing tuberculosis; however in resource limited setting like Ghana, sputum culture for tuberculosis is not done routinely in Teaching Hospitals and Research Institutions. In referral hospitals and in Universities *Mycobacterium* culture is done mainly for teaching and research purposes. In resource constrained countries the available culture media is Lowenstein Jensen media (LJ media); this media lack sensitivity as compared to the liquid media, though liquid culture media has disadvantages such as high rates of contamination. Also, more complicated logistics are involved during drug susceptibility testing using liquid media as compared to LJ media.

2.5 TUBERCULOSIS DRUGS SUSCEPTIBILITY TEST

Tuberculosis drugs susceptibility testing is important during this era of emergence of *Mycobacterium* species which are resistant to the currently used anti tuberculosis drugs. Drugs susceptibility in TB patients' coinfected with HIV/AIDS is important since HIV/AIDS has been associated with the current emergence ofMultidrug-resistant tuberculosis (MDR-TB) (Campos *et al.,* 2003). There is a need to establish and strengthen the national surveillance for MDR-tuberculosis. However, in Ghana TB drugs susceptibility testing is not done routinely even for the patients referred for sputum culture and sensitivity testing. The reason for this is lack of resources including adequate number of staff, lack of funds for the procurements of reagents and culture media used for the isolation and drugs susceptibility testing.

2.6 CD4 T CELLS COUNT

Immunohaematological indices such as leukocytes, lymphocytes and their subsets such as CD4 T cells and CD8 T cells play a major role in both cellular and humoral types of immunity. CD4 T cells are the lymphocytes sub sets used for monitoring progression of HIV infection, and they are also used as a surrogate marker for the improvement of HIV/AIDS patients after initiation of ARV (WHO, 2005). Furthermore, CD4 T cell levels determine when to start or stop prophylactic drugs for opportunistic infections (Masur, 2002). Management of HIV patients include proper monitoring, irrespective of ARV treatment. This monitoring can be done clinically by means of the WHO clinical staging, but more reliably by measuring CD4 T cells and viral load. In resource limited countries like Ghana, viral load is not determined and the only reliable method for follow up of HIV infected patients is by CD4 T cell counts.

Immunohaematological variations have been reported in various studies, showing association with sex, geographical location, race (Prins, 1999), altitude and diet (Tsegaye*et al.,* 1999). Other reasons for variations are pregnancy, age, exercise, co-morbid conditions and diurnal variation, in addition to variations caused by methodological differences (Malone *et al.,* 1990). Several studies have shown significant variations of CD4 T cells within African populations and in Africans compared with the values established for Europe and North America (Tsegaye*et al.,* 1999). The HIV virus targets and destroys CD4 T cells responsible for the cellular immunity against infections by intracellular microorganisms like *Mycobacterium tuberculosis*. In patients with HIV/AIDS, the CD4 T cells decrease as the HIV viruses targets the CD4 T cells resulting in immunodeficiency which in turn can lead to reactivation of latent tuberculosis or new tuberculosis infection once exposed to *Mycobacterium tuberculosis* (Sharma *et al.,* 2005).

2.7 OVERLAPPING OF SIGNS AND SYMPTOMS BETWEEN HIV/AIDS AND TUBERCULOSIS

Clinical features of HIV/AIDS and tuberculosis are difficult to separate as both diseases present with wasting and persistent fever. In cases of tuberculosis patients coinfected with HIV/AIDS the physician tends to attribute the signs and symptoms of tuberculosis to HIV/AIDS, hence there is under-diagnosing tuberculosis in HIV patients. The non-specific signs and symptoms of HIV/AIDS and its coinfection with tuberculosis make the clinical diagnosis difficult in most cases. The fact that HIV/AIDS also makes the patient susceptible to other opportunistic infections with symptoms similar to tuberculosis are among the difficulties encountered in diagnosing tuberculosis in HIV/AIDS patients.

2.8 DIFFICULTY IN DIAGNOSING TUBERCULOSIS IN HIV INFECTED PATIENT.

In advanced cases of HIV/AIDS, the sputum samples are often AFB negative, yet does not rule out tuberculosis (Sharma et al., 2005. In early stages of HIV infection the sputum may be AFB positive but the proportion of these smear positive cases is small. Chest x-ray in HIV/AIDS coinfection may be atypical and not specific for tuberculosis. It may present only pleural effusion or other atypical radiological findings similar to *Pneumocysticjirovecii*pneumonia and other opportunistic lung infections in individuals with immunodeficiency (Malone et al., 1990).

2.9 COMPLEXITY OF TREATMENT OF TUBERCULOSIS AND HIV/AIDS COINFECTION

Two different diseases with two different modalities of diagnosis and treatment do exist in one patient. Both diseases involve the combination of more than one drug.

Treatment is for life in HIV/AIDS and for a minimum of six month in tuberculosis patients, resulting in high pill burden, many side effects and interaction of drugs. The consequence may be poor adherenceto treatment and loss from follow up (Sharma et al., 2005).

2.10 DIFFICULTIES IN BRINGING THE HIV/AIDS AND TUBERCULOSIS PROGRAMMES TOGETHER

The National Tuberculosis Programme (NTP) and the National AIDS Control Programme (NACP) are coordinated differently. There is a need to have one national program coordinating these activities since the two diseases have common problems which need to be tackled uniformly. However, there are difficulties in coordinating these control programs due to different modes of operation and different policies for the two diseases. This results into a referral of patients from one programme to another within the same hospital even in a health centres. This may create delays in treatment and loss from follow up since patients find it difficult to move from one clinician to another.

2.11 CLINICAL OUTCOMES OF PLWHA WITH OR WITHOUT TB

Research on the pattern of presentation and prevalence of tuberculosis in HIV seropositive patients seen at Benin City, Nigeria by Affusim*et al. (*2011) found that, the commonest type of TB found among HIV coinfected patients was pulmonary TB accounting for 78.6% of cases, while extrapulmonary TB accounted for 21.4%. They reported that the most common presenting symptom of TB among those with TB co-infection was weight loss, accounting for 96.4% of all responses in TB patients. In the non TB co-infected HIV patients, 46 were found to have coughed, 27 had sputum production, and three patients had difficulty with breathing. One patient had haemoptysis,

and three patients had night sweat. Affusim*et al.*(2011) also showed that their results may have probably been due to presence of other co-morbid conditions in the non TB co-infected patients and therefore concluded that the TB co-infected patients generally presented worse clinical cases than the nonTB co-infected patients

Studies by Corbette*et al.*(2009) found that the prevalence of TB symptoms was high in HIV positive participants and the sensitivity of initial symptom screening in these individuals ranged from 47.9% when chronic cough was used to define a TB suspect to 81.3% when any of the five TB symptoms considered was used. Symptom screening was more sensitive than sputum culture on a solid medium, whose sensitivity was 64.6%. They found that the diagnostic performance of symptom screening in HIV- positive participants, as assessed using the Area under the receiving operating characteristic curve (AUC), was significantly and incrementally better when acute cough of less than 2 weeks' duration and weight loss were individually added to the cardinal symptom of chronic cough lasting 2 weeks or more. Broadening the definition of a TB suspect further did not improve diagnostic performance. Nevertheless, Positive Predictive Values (PPV) were high for all symptoms among HIV- positive participants, which supports using a less strict definition of a TB suspect in individuals known to have an HIV infection, even though specificities were suboptimal. In summary, Corbette*et al*. (2009) revealed that even smear-positive TB may be missed by symptom screening in HIV+ TB patients. Although the sensitivity and specificity of symptom screening were similar for HIV+ and HIV− participants, the presence of symptoms in HIV+ participants had a higher PPV and a lower NPV. Although imperfect, three of the symptoms evaluated (i.e. cough, drenching night sweats and weight loss) were independently predictive of TB and their combination had a NPV over 99% in HIV+ participants. This suggested that symptom screening alone may be able to identify, at least in some settings, a subset of patients who are at a low risk

of undiagnosed TB and in whom antiretroviral therapy or isoniazid preventive therapy can be started without further screening.

Studies by Madhi (2000) on HIV-1 co-infection in children hospitalised with tuberculosis in South Africa revealed that clinical features of cough, fever, night sweats, tachypnea and a history of measles disease/immunisation or TB contact were similar between HIV-infected and non-infected children. Although HIV-infected children were equally as likely as non-infected children to have received BCG vaccine, vaccination scars were significantly less common in patients with HIV infection. HIV-infected children with Pulmonary TB were 2.8 times more likely to have a history of chronic weight loss and, as a result, were less likely to be of normal weight for age.

Tegbaru*et al.* (2011) also compared clinical diagnosis and laboratory findings. Correlating the symptoms diagnosed clinically in the suspected TB patients and laboratory results, they found out that, of those suspected patients with dry cough and laboratory results (n=62), cough with sputum (n=73) and those with blood stained sputum (n=18); 39(62.9%), 50(68.5%) and 13(72.2%) of them were confirmed to be TB patients, respectively. Moreover, from those patients with fever (n=71), 43(60.6%) of them were confirmed TB patients. Among those who reported having a contact with a TB patient (n=45), 21 of them had their laboratory results and 18(85.7%) were found to be confirmed TB cases. In individuals with past history of tuberculosis (n=47), 26 had laboratory results and 15(57.7%) of them were confirmed to have TB of which 9 of them were HIV infected.

2.12 CD4 VALUES OF PLWHA WITH OR WITHOUT TB

Tegbaru*et al.* (2011) studied the clinical outcomes and laboratory results of tuberculosis patients with or without HIV infection in two health institutions in Addis

Ababa, Ethiopia. They found that, of the enrolled study subjects, 141(58.2%) of the suspected TB cases had CD4+ T cellcount after 2 months of intensive phase of anti-TB chemotherapy. However, there was no difference in CD4+ T cell number before and after 2months of anti-TB therapy (p=0.20). Similarly, no difference was observed in HIV infectedpatients (130.5 cells/μl versus 144 cells/μl, p=0.50) after therapy.

Affusim*et al.*(2011) reported that the mean CD4 count of the TB co-infected population was 150.6cells/mm^3, while the mean CD4 count of the patients without TB co-infection was 276.4cells/mm^3.Madhi*et al.* (2000) also reported that CD4+ lymphocyte levels were available for 52 (76%) HIV-infected and 78 (84%) non-HIV-infected children. Children with HIV co-infection had significantly decreased CD4+ levels compared with non-HIV-infected children in all age groups. CD4+ lymphocyte counts were severely decreased in 50% (26/52) and 5.1% (4/78) of HIV-infected and noninfected children, respectively ($P < 0.00001$). An additional 34.6% (18/52) of HIV-infected and 10.3% (8/78) of non-infected children had moderately decreased CD4+ lymphocyte counts ($P = 0.0007$). The site of disease (PTB versus EPTB) and nutritional status did not affect CD4+ levels in children with or without HIV co-infection. Also, for both HIV groups, CD4+ levels did not differ in children with culture or microscopic confirmation of disease compared with those diagnosed only by clinical signs or symptoms. The mean CD4+ lymphocyte percentage of HIV-infected children who died (17.8%, standard deviation [SD] 11.0) was not different from that in those who survived

(19.5%, SD 12.0; $P = 0.79$). Tarbarsi*et al*. (2008) showed that the mean total CD4+ T-cell count was 229.15 (SD 199.45) cells/mm^3 with a range of 8–627 cells/mm^3. They also reported that, 50% of the CD4 count was < 200 cells/mm^3, while in 79% it was < 350 cells/mm^3.They also compared the patients with CD4+ counts < 200 and ≥ 200 cells/mm^3, statistical analysis showed significantly more men in the ≥ 200 CD4+ group ($P < 0.05$).

There was also no significant difference in the mortality rate of TB/HIV patients with CD4 counts < 200 and ≥ 200 cells/mm^3.

2.13 FULL BLOOD COUNTS OF PLWHA WITH OR WITHOUT TB

Findings from Jemikalajah and Okogun (2008) in Nigeria revealed that the mean packed cell volume obtained for infected subjects was statistically significant (p=0.0000074) when compared to the control subject's value. They concluded that full blood count is important in the monitoring and management of TB and HIV infection.Laboratory results from Affusim*et al.* (2011) indicated that the range of PCV in the study population was 14% - 56%. The mean PCV in the study population was 32.13 % while the mean WBC of the study population was 5,067.61cells/mm^3.

Audu*et al.*(2004) reported that PCV was significantly lower in all categories of subjects when compared with the controls (p< 0.003). The median PCV levels in HIV subjects co-infected with TB though lowest (32.5%) among all categories of subjects; the value was not significantly different when compared with the level in subjects with HIV infection only. The prevalence of anaemia (13.6%) in HIV infected subjects and subjects co-infected with TB (25%) were not significantly different (p = 0.064), neither was the prevalence of anaemia in TB subjects (21.7%) significantly different from those co-infected with HIV. Audu*et al.*(2004) concluded that co-infection of HIV with TB did not worsen anaemia in the studied subjects. Nwachukwu and Peter (2010),reported that 32 (12. 8%) of patients with*M. tuberculosis* infection had severe anaemia (PCV 26 - 35%) and 5 (2.0%) had normal value (PCV > 36%) whiles 18 (7.2%) with HIV infection had severe anaemia (PCV; 20 -25%), 13 (5.2%) moderate anaemia (PCV; 26 - 35%) and 4 (1.6%) had normal value (PCV > 36%).They further reported that positive significance existed between anemia and *M. tuberculosis* and HIV infections (p < 0.01).

Haematological findings from Tarbarsi*et al.*(2008) indicated that anaemia was detected in 73% of patients while white blood cells counts were normal in 75% (4.0 – 8.0) cells/l. Report from the study also revealed that leucocyte count (cells/l) was 5.797 ± 2.657, Haemoglobin level (g/dl) was 10.5 ± 1.7, PCV (%) was 32.5 ± 5.5 whilst Platelet count was 161.6 ± 88.6(cells/l).

2.14 ERYTHROCYTE SEDIMENTATION RATE VALUES IN PLWHA WITH OR WITHOUT TB

Ukpe and Southern (2006) in South Africa reported that one hundred and fifty-nine of the 202 cases (78%) had their ESR measured, and in 110 (69%) of the 159 cases this was done during the active period of the disease. Of the 110 TB patients who had the ESR measured during active disease, 64 (58%) were males and 46 (42%) were females. The ages of the male patients ranged from 24 to 70 years, and the females from 14 to 64 years. There were 97 cases of pulmonary tuberculosis (PTB) (88%) and 13 of extrapulmonary tuberculosis (EPTB) (12%). ESR values ≥ 100 mm/h were found in84 (76%) of the 110 active TB cases, and values < 100 mm/h in 26 (24%) of the cases.HIV status was known in 88 (80%) of the 110 active TB cases. Seventy-three (83%) of the 88 cases were HIV positive, and 15 (17%) were HIV negative. Fifty-nine (81%) of the 73 HIV-positive cases had ESR values ≥ 100 mm/h and 14 (19%) had values < 100 mm/h. Nine (60%) of the 15 HIV-negative cases had ESR values ≥ 100 mm/h and 6 (40%) had values < 100 mm/h.

Later on, Nwachukwu and Peter (2010) showed the cross - tabulation between*M.tuberculosis*, Human HIV and erythrocyte sedimentation rate (ESR). None of the patients with *M.tuberculosis* and HIV infections had normal erythrocyte

sedimentation rate (3 - 8 mm / hr) whiles 32(12.8%) recorded ESR values > 100 mm/h. There was significant ($p < 0.01$) positive association between *M. tuberculosis* and erythrocyte sedimentation rate (ESR) as well as HIV and erythrocyte sedimentation rate. Studies byTarbarsi*et al.* (2008) revealed that their mean ESR was 69.9 (SD 33.6) mm/h. They further showed that 75% of the cases were> 30 mm/h.

Affusim*et al.* (2011) reported that the mean ESR of their study population was 73.37mm/hr. The range of the ESR in the non- TB co-infected population was 15 – 65mm/hr, while that of the TB co-infected population was 105 – 165mm/hr.

2.15 TB RESULTS OF PLWHA

Tuberculosis (TB) remains one of the most important causes of mortality and morbidity in PLWHA in the world (Cahn, 2003). Tarbarsi*et al.* (2008)in the Islamic Republic of Iran found that a total of 15 patients were enrolled in thestudy made up of 13 males (87%) and 2 females (13%).All were Iranian and resided in urban areasof the Islamic Republic of Iran. The meanage was 36.9 (SD 5.87) years, range 24–46years; 11 weremarried, while 4 were unmarried. The routeof transmission of HIV was intravenousdrug use in 13 (87%, all the male patients)and heterosexual intercourse in 2 (all of thefemale patients).Sputum smear and culture were positive for acid-fast bacilli in 13 (87%) and 9 (60%) patients respectively. In 4 of the cases, the sputum culture was unknown. Antiobiotic sensitivity tests were performed for 9 of them; in 8 patients there was sensitivity to 4 drugs while 1 patient had isolated resistant to rifampicin.

Onubogu*et al.* (2010) indicated that, outof the 1280 patients screened, 318 (24.8%) were positive for AFB. Among these 318 confirmed cases of TB 145 (45.6%) and 173 (54.4%) were male and female respectively, ($p < 0.05$). The age group 21 - 40 years had the highest TB cases while the age group 61 years and above had the lowest TB

cases. The age and sex distribution of TB/HIV co-infected cases observed that 236 of the study population had TB and HIV co-infection and this gave a prevalence rate of 18.4%. Of all the patients diagnosed of TB, 74% (236/318) were HIV positive. The distribution showed that among these 236 co-infected cases, 99 were male and 137 were female, ($p < 0.05$). Also the age group 21 - 40 years had the highest cases of TB/HIV co-infection while the age groups 10 - 20 years and above 60 years had the lowest TB/HIV cases. Correlation between the result of microscopy and culture for the diagnosis of acid-fast bacilli in TB/HIV and TB/non-HIV patients revealed that among the positive cases 175 (55%) were detected by culture alone, 61 (19%) were detected by microscopy alone while 82 (26%) were detected by both culture and microscopy. The difference between the detection for culture and microscopy was statistically significant ($p < 0.05$).

Nwachukwu and Peter (2010) showed that out of the total number 127 (50.8%) were males while 123 (49.2%) were females. There were more patients in the 26 to 35 years age group, 74 (29.6%) while age group 46 years and above have less number of patients 51 (20.4%). The overall prevalence of *M. tuberculosis* was 54 (21.6%) of which 31 (12.4%) were males and 23 (9.2%) were females. There was no significant different at$P = 0.01$ between sex and *M. tuberculosis.* Their study also revealed an overall prevalence of 35 (14.0%) for HIV of which 18 (7.2%) were males and 17 (6.8%) females. There is also no significant association between sex and HIV infection. The prevalence of patients with TB/HIV coinfection was 16 (6.4%) of which 9 (3.6%) were males and 7 (2.8%) were females. The calculated chi-square statistics indicated that there was no association between sex and TB/HIV co-infection.

The age-frequency distribution of*M. tuberculosis* and HIV infections indicated the highest rate of infection for *M.tuberculosis* and HIV was 25 (10%) and 19 (7.6%) respectively, in the age group 26 - 35 years. The least rate of prevalence for TB infection,

2 (0.8%) was in over 56 years age group and for HIV infection, 4 (1.6%), was in 46 - 55 years age groups. There was no significant association between age and TB /HIV co-infection.

Affusim*et al.*(2011) reported that the prevalence of TB in HIV seropositive patients seen at University of Benin Teaching Hospital was 33.9%. A total of 112 patients out of 330 patients had TB. Their study further recommended that since some investigation results were found to be atypical in those with both infections, physicians should be aware of this pattern of presentation and the atypical findings on investigation for early diagnosis and treatment.

2.16 TRANSMISSION OF TB/ HIV

The most common form of disease, caused by *Mycobacterium tuberculosis* is pulmonary tuberculosis. *Mycobacterium tuberculosis* is a genus of Actinobacteria, a non-motile bacillus that grows slowly and, under optimal conditions, reproduces every twenty-four to forty-eight hours (Moulding, 1988). It is an aerobic bacterium requiring high levels of oxygen for growth. It is neither gram- positive nor – negative as the waxy coating on the cell surface makes the bacillus impermeable to gram staining (Moulding, 1988). *M. tuberculosis* was identified in 1882 by Robert Koch (Moulding, 1988) and the genome was sequenced in 1998 (Cole*et al.*, 2002).

Within the lungs, the bacterium is taken up and if not contained by the immune system, is able to grow uncontrollably, resulting in the subsequent development of tuberculosis disease. It can also involve other parts of the body and produces extrapulmonary TB (Houghton, 2002). Tuberculosis is a very contagious, but curable disease. Tuberculosis can also involve non- respiratory sites, occurring in the peripheral lymphatic system, bones and joints, genitourinary system, gastro-intestinal tract, central nervous system,

ocular system and pericardium (Cook & Long, 2007). Non-respiratory tuberculosis disease does not contribute significantly to the rates of tuberculosis transmission however, control of these disease forms is important as transmission may occur if aerosolization of the bacterium occurs during surgical procedures or post-mortem examination (Cook & Long, 2007).

Transmission of the bacterium occurs most commonly through bacterium-infected droplets of moisture expelled in the environment by a respiratory case. For most people who become infected by *M. tuberculosis* and develop primary infection, progression to tuberculosis

disease does not occur.

The human immunodeficiency virus disease is very complex and its natural history can be further complicated by a myriad of factors: mode of transmission, the prevalence of opportunistic infections, the availability of anti-HIV therapy, host genetics, and the viral strain (Deschamps*et al.*, 2000). Infection with HIV causes destruction of the cell-mediated immunity in infected patients, which increases susceptibility to both pulmonary and extrapulmonary TB.

Tuberculosis can also involve non- respiratory sites, occurring in the peripheral lymphatic system, bones and joints, genitourinary system, gastro-intestinal tract, central nervous system, ocular system and pericardium (Cook & Long, 2007). Non-respiratory tuberculosis disease does not contribute significantly to the rates of tuberculosis transmission however, control of these disease forms is important as transmission may occur if aerosolization of the bacterium occurs during surgical procedures or post-mortem examination (Cook & Long, 2007). Transmission of the bacterium occurs most commonly through bacterium-infected droplets of moisture expelled in the environment

by a respiratory case. For most people who become infected by *M. tuberculosis* and develop primary infection, progression to tuberculosis disease does not occur.

An individual with Acquired Immune Deficiency Syndrome (AIDS) has a 110-170 times greater risk of developing TB than a person with no known risk factors and an individual with Human Immunologic Virus (HIV) has a greater risk of 50-110 times than a person with no known risk factors (Menzies& Khan, 2007). Immunologic containment by an individual's immune system is deficient in individuals with HIV whilst TB is has been identified as the most common cause-of-death in HIV infected individuals (Houghton, 2002).

The immune response to the infection is complex and involves both the innate and adaptive immune system (Flynn, 2006). If the organism is successful in reaching the lungs it will begin multiplying within the alveolar macrophages (Flynn, 2006; Long &Schwartzmann, 2007).

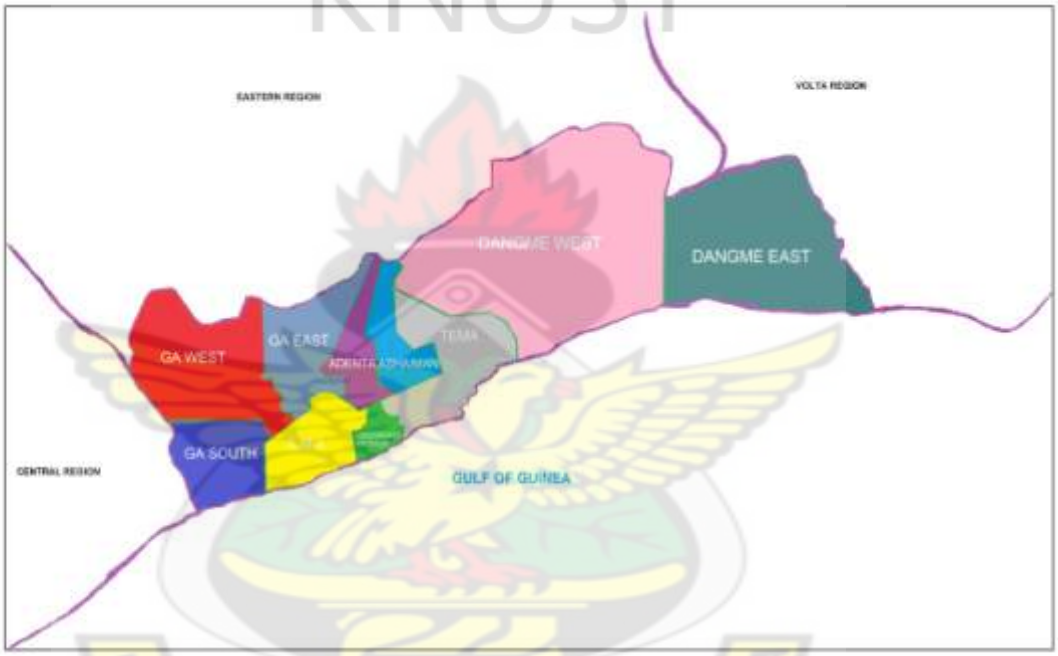
If the innate response is unable to destroy the bacterium, cell-mediated immunity and delayed type hypersensitivity immunity are activated (Long &Schwartzmann, 2007). The subsequent adaptive immune responses include activation of the CD4+ and CD8+ T cells (Flynn, 2006). The inflammatory response includes the formation of granulomas by the host immune system that work to limit the spread of infection. In the majority of infected individuals, the infection is contained and tuberculosis disease does not develop (Long &Schwartzmann, 2007).

CHAPTER THREE

RESEARCH METHODOLOGY

3.1 PROFILE OF STUDY AREA AND POPULATION

The Greater Accra Region is one of the administrative regions of Ghana and it is challenged by problems of assuring quality equitable access to an acceptable quality of primary care and referral services in the context of complex developing country urban and rural settings. There is a wide variation in communities and living standards in the region ranging from reasonably situated high and middle income urban slums and typical deprived rural farming and fishing communities (Ministry of Health/ Ghana Health Service, 2006).



Source:

http://upload.wikimedia.org/wikipedia/commons/9/91/Greater_Accra_districts.jpg

The study was conducted in three hospitals located under three different Municipalities in the Greater Accra region of Ghana. The International Health Care Centre falls under the Ga East Municipal Assembly which is located at the northern part of Greater Accra Region.

The Ga East Municipality is one of the ten (10) districts in the Greater Accra Region and covers a Land Area of 166 sq km. It is boarded on the west by the Ga West Municipal Assembly (GWMA), on the east by the Adenta Municipal Assembly (AdMA), the south by Accra Metropolitan Assembly (AMA) and on the north by the Akwapim South District Assembly.

The University of Ghana Hospital falls under the Ayawaso west a Sub metro of the Accra Metropolitan Assembly. The boundary continues to the road between the University of Professional Studies, Accra (UPSA) and the Accra Teachers Training College (ATRACO), westwards crossing the Accra-Aburi Road to the University of Ghana behind the great Hall to Kisiseman and Christian Village to join the Accra-Nsawam Road at the Achimota Brewery road Junction.
The Ga West Municipal Hospital is located in Ga West Municipal Assembly which was carved out of the erstwhile Ga municipal which was created in 1988 in pursuance of the government decentralization and local government reform policy. In 2004, the Ga Municipality was divided into two with Amasaman the former municipal capital remaining the capital for the newly created Ga West Municipal.The Ga West Municipal is the second largest of the six Municipalities & Districts in Greater Accra Region. With relative stability in fertility rates and the appreciable reduction in death rates nationwide, the general expectation was that the district would record an increase in the population given the availability of land.

3.2 STUDY DESIGN

The study design was a cross-sectional study with the experimental case – control strategy option. This is because experiment is a research that owes much to the natural

sciences. The purpose of an experimental research was to study causal links; whether a change in one independentvariable produces a change in another dependent variable (Hakim, 2000 cited in Saunders *et al.*, 2007). The experiments are concerned with whether there is a link between the two variablesie. thecase - group and a control - group.

3.3 SAMPLE SIZE DETERMINATION

The sample size was composed of a case – control group in a ratio of 2:1. A total sample size of 544 respondents were considered for the study through the convenience sampling method, out of which 363 were PLWHA with or without tuberculosis as case subjects whiles 181 "Healthy persons" as control - subjects for the study. The sample size for the case - subjects was calculated using the formula for single population proportion (Affusim*et al*.,2011).

$$n = \frac{(P)\,(1-p)\,(Z\alpha/2)^2}{d^2}$$

Where n is the sample size, Alpha is the critical value corresponding to 95% confidence interval

(CI), P is the estimated prevalence which was obtained from Ministry of Health/ Ghana Health Service (2006).

n = the desired sample size when the population is greater than 10,000

(Zα/2) = the standard normal deviation usually set at 1.96 (Affusim*et al*.,2011)

d = is the degree of margin of error for which 5% is taken.

Accordingly, using P = 30% or 0.30 with marginal error of 5% and 10% allowance for lost cases.

$$n = \frac{(0.30) \times (0.70) \times (1.96)^2}{(0.05)^2}$$

n = 323

The calculated sample size was 323. This was rounded off to 330, and 10% of this number was added for attrition. Thus, a total sample size of 363 PLWHA's with or without tuberculosis participated in the study as case – subjects.

3.4INCLUSION / EXCLUSION CRITERIA

The inclusion criteria for the study subjects was HIV infected patients 18 years and above, receiving ART treatment at the selected hospitals during the period of the study who gave informed consent to participate in the study. The population group covered during this study was men and women aged 18 and above, who were known PLWHA's attending antiretroviral clinics at the selected ART Hospitals. It is pertinent to mention that those aged 18 - 49 years are the productive work force of any nation while women in this age bracket are the reproductive group and are therefore a good proxy for the general population in the determination of the prevalence of TB, HIV and TB/HIV confection. Patients that were too sick and unable to communicate were excluded from the study.

3.5 DEFINITION OF CASES

Tuberculosis included cases positive for acid fast bacilli by smear microscopy and/or culture and those smear/culture negative patients with clinical and radiological features suggestive of pulmonary tuberculosis and failure to respond to a course of broad spectrum antibiotics. Anaemia was classified as haemoglobin level less than 11.0 g/dl. Immunological status was assessed using CD4 T cells count and immunodeficiency was

defined as CD4 T cells count of less than 500 cells/mm^3. High infection was determined by Erythrocyte Sedimentation Rate (ESR) greater than 100 mm/hr. Nutritional status was assessed using body mass index (BMI). Normal nutritional status was defined as BMI of greater than 18.4 Kg/m^2, mild malnutrition was defined as BMI of 17-18.4kg/m^2, moderate malnutrition as BMI of 16-16.9kg/m^2, severe malnutrition as BMI of less than 16kg/m^2 and malnutrition as BMI of less than 18.3 Kg/m^2.

3.6 "HEALTHY CONTROL" SUBJECTS

This group was recruited from the HIV voluntary counseling and testing (VCT) clinics.

Individuals who tested negative during HIV VCT were counseled about the study and those who agreed were included in the study. Subjects were interviewed, using a structured questionnaire, and screened for symptoms such as fever, cough and weight loss to rule out any recent and/or current infections. Blood slide for malaria; blood sugar and rapid plasma reagin (RPR) test for syphilis were done for all participants, in addition to a physical examination, including measurement of height and weight.

The following categories were excluded from this group: pregnant women, smokers, patients receiving medical treatment and those with history of recent or current chronic alcoholism and moderate and severe malnourishment, patients with malaria, subjects testing positive for HIV antibody (Sharma *et al.*, 2005).

3.7 TUBERCULOSIS DIAGNOSIS AMONG PLWHA

All PLWHA attending care and treatment clinic at the Ga-West Municipal Hospital, International Health Care Center and the University of Ghana Hospital were counseled about the study. Those who agreed were asked to give sputum samples which

were sent to the laboratory for smear microscopy and culture. All patients were able to provide sputum samples, but for those who could not produce sputum spontaneously (53 patients); they were allowed to produced saliva. Front-loaded sputum samples were obtained from each patient. Thus each patient produced two sputum samples within an hour interval.

Tuberculosis diagnosis was made based on the finding of acid-fast bacilli by ZiehlNeelsen (ZN) staining and/or culture and drugs susceptibility testing (Ngowi, 2009). For the smear negative cases the diagnosis was based on the clinical and radiological diagnosis according to the algorithm for diagnosing smear negative tuberculosis (NTB, Ghana, 2006). All newly diagnosed tuberculosis patients during the study period were counseled about the study and those who agreed were asked for sputum samples for repeat microscopy prior to initiation of anti-tuberculosis therapy. Blood was collected in ethylene diamine-tetraacetic acid (EDTA) tubes for HIV tests, full blood cell (FBC) counts, ESR and for CD4 T cell counts.

In Ghana, screening for tuberculosis among PLWHA by using fluorescence microscopy and culture is not done unless there are clinical and radiological features suggesting tuberculosis in these patients.

3.8 RADIOLOGICAL EXAMINATION FOR TB FOR PARTICIPANTS

Results of chest x-ray were collected from individual patient's record. Secondary results for chest x- ray were recorded for all the PLWHA hospital folders irrespective of their TB status. No x-ray was taken from the PLWHA for the purpose of the study. The X-ray was reported as unilateral/bilateral infiltration with/without cavities, infiltrations withhilar lymph node enlargement and unilateral/bilateral pleural effusion.

The radiological findings were used together with clinical information such as chronic cough for more than 2 weeks, weight loss and chronic fever to make the diagnosis of smear/culture negative pulmonary tuberculosis. For the smear/culture positive pulmonary cases, chest X-ray was not considered in making the diagnosis.

3.9 SPUTUM MICROSCOPY AND CULTURE

At the Chest Clinic Laboratory of the Korle-Bu Teaching Hospital,the sputum specimens were decontaminated by modified Petroff's methods using4% sodium hydroxide (NaOH) and then concentrated by centrifugation at 3000 rpm for 15 mimutes. Aftercentrifugation it was examined by fluorescence microscopy and also cultured onto slopes ofLowenstein Jensen (LJ) medium with glycerol (GLJ) and pyruvate (PLJ), and incubated at 37^{o}Cfor 8 weeks. Culture slopes were inspected after 48 hours to detect contamination andthereafter weekly to observe growth. Identified contamination of the culture was removed bysub-culturing the specimen. All positive culture slopes were assessed for *Mycobacteriumtuberculosis* bygrowth rate, acid fastness, colony morphology, pigment production, rate of growth at 25 ^{o}C,growth onto 500 mg/ml Para-Benzoic Acid (PNB), and sensitivity or resistance to the thiophen 2-carboxylic acidhydrazide (TCH 2mg/ml). Smear microscopy were read as follows; 1-9 AFB per 100 scanned fields were recorded in absolute number, 10-99 AFB per 100 scanned fields were reported as (1+), 1-10 AFB per field scanned were reported as (2+) and >10 AFB per field scanned as (3+). Positive culture was quantified as the total number of colony forming units.

3.10 DRUGS SUSCEPTIBILITY TEST

Tuberculosis drug susceptibility testing was done on culture positive specimens. Different LJmedia was prepared, two drug free LJ media, one containing

thiophenecarboxylic acidhydrazide (TCH), one containing para-benzoic acid (PNB) and four containing one of the following drugs: 40microgram/ml of rifampicin, 5microgram/ml of dihydrostreptomycinsulphate, 0.2microgram/ml and 1.0microgram/ml of isoniazid and 2 microgram/ml ofethambutol. On the drug free medium, 10^{-2}*mycobacterium* suspension was inoculated followedby 10^{-4}*mycobacterium* suspension into the drug containing media.

The media containing*mycobacterium* were incubated at 37^{o}C for 4 weeks. The culture was read after 3 and 4 weeks.The results were recorded as follows; Colony growth of 1-19, the colonies were recorded as scanty growth, 20-99 colonies were recorded as (1+), 100-200 as (2+) and >200 colonies as(3+). The proportion of bacilli in inoculums that were resistant to the drug used were calculatedas the ratio of the number of colonies in a drug media to number of colonies in control medium,multiplied by 100. While susceptible isolates were interpreted as colony growth of less than 1%in a drug medium compared to the control tube, resistant isolates were 1% or more colonygrowth in a drug medium.

3.11 QUALITY CONTROL FOR THE SMEAR MICROSCOPY, CULTURE AND DRUG SUSCEPTIBILITY TEST

Laboratory staff of the Chest Clinic Unit of the Korle – Bu Teaching Hospital received proficiency testing in the performance of culture and sensitivity procedures through the National TB Programme prior to the survey. Also, the readings for the smear microscopy, culture and the drug susceptibility testing results for the study were double checked by colleagues and confirmed by the supervisors at the Chest Clinic of the Korle – Bu Teaching Hospital.

3.12 HIV TESTING

HIV test was done using two different rapid antibody tests, First Response HIV-1/2 and OralQuick. Discordant samples were sent to the Public Health and Reference Laboratory Unit of the Korle – Bu Teaching Hospital for confirmatory test using both ELISA. Standard Operating Procedure for OraQuick Rapid HIV-1/2 Antibody Test detects antibodies to HIV-1 and HIV-2 in 20 minutes.

Step 1- Samples were collected by swabbing between the teeth and upper and lower gum once.

Step 2- The devicewas inserted into the buffer.

Step 3- Reading took place between 20and 40 minutes.

Results were depicted as follows:

Non-Reactive: Line in the C Zone

Preliminary Positive: Line in the C and T Zones (Ministry of Health/ Ghana Health Service, 2006)

3.13 FULL BLOOD CELL COUNTS

Complete blood cell counts were done using Sysmex Kx-21 (Sysmex Corporation; Japan). The machine automatically dilutes a whole-blood sample, lyses, counts and gives a printout result of absolute numbers of leucocytes (expressed as number of cells × [10^9] per litre), erythrocytes (number of cells × [10^{12}] per litre), platelets (number of cells × [10^9] per litre), lymphocytes (number of cells × [10^9] per litre), mononuclear cells (number of cells × [10^9] per litre), granulocytes (number of cells × [10^9] per litre) and haemoglobin (grams per decilitre).The quality and accuracy of the technique was done every 24hours through quality control whilst the quality and accuracy

of the analyser was assessed every quarterly through a routine maintenance checks by the Sysmex agent in Ghana, (Narmaka Modern Medicals Limited).

3.14 CD4 T CELL COUNTS

CD4 T cells were analyzed using a BD FACSCount flow cytometer (Becton DickinsonImmunocytometry Systems, San Jose, California, USA.) with two monoclonal antibodies (CD4 andCD8; Becton Dickinson Immunocytometry Systems). Exactly, 100 µl of whole blood wasmixed and incubated at room temperature for 20 min with 10 µl of aCD4 and aCD8. Redblood cells were then lysed by adding 2 ml of fluorescence-activated cell sorter lysingsolution (Becton Dickinson Immunocytometry Systems). The sample was then analyzed withthe FACSCounts's Cell Quest software (Becton Dickinson Immunocytometry Systems). TheFACSCount was calibrated with fluorescent beads (CaliBrite; Becton DickinsonImmunocytometry Systems) and Auto-Comp software (Becton Dickinson ImmunocytometrySystems) weekly. By using quality control (Multicheck; Becton Dickinson ImmunocytometrySystems), the accuracy of the technique was assessed every 3 months.

3.15QUESTIONNAIRE ADMINISTRAION

After the patients were examined by the physicians, the nurses assistedby interviewed and filled the information obtained from the patients onto the questionnaire. Completed questionnaires were coded by numbers and double entered in a computer software Excel sheet. Data quality was assured by cross-checking and data cleaning. During data cleaning and cross checking missing information were obtained by going back to the questionnaire and when necessary reviewing the patients on the next visit to the clinics. The data was transferred to SPSS version 16 and Graph Pad Prism 5 for

analysis. The data were also stored in an external hard drive as a backup.All information obtained from the patients were recorded in questionnaire and kept in a hardcover file. Only the researcher and staffs working with HIV/AIDS and tuberculosis care and treatment had an access to the files.

3.16INFORMED CONSENT

Oral informed consent was obtained from the patientsprior to enrolment. For those below the age of 18 years permission was sought from parents or caretakers. For the newly diagnosed tuberculosis patients counseling for HIV test was done and those who gave consent were tested for HIV. Tuberculosis, and other opportunistic infections in HIV/AIDS patients and HIV/AIDS diagnosis and treatment are given free of charge according to policy for HIV/AIDS and tuberculosis management by the National AIDS Control Programme (NACP).

3.17 STUDY VARIABLES

a. Dependent

HIV sero-status (HIV positive) with TB status (positive, negative)

b. Independent

The independent variables include socio-demographic variables (age, sex, religion), socio economic variable (occupation, marital status), clinical symptoms (fever, weight loss, cough, blood in sputum), clinical signs (rashes, lymphadenopaty, oral candidiasis, herpes zoster, hepatomegaly, splinomegaly).

3.18 STATISTICAL ANALYSIS

Completed questionnaires were coded by numbers and entered in a computer software Excel. Cross-checking and data cleaning was done. The data was then

transferred to Statistical Package for Social Sciences version 16 (SPSS Inc, Chicago, USA) and Graph Pad prism 5 for analysis. Chi square test was used to test for differences in proportions. Student t test was used to test for differences in means between 2 or more groups. All statistical tests were considered significant if the two sided P-value (p) was <0.05.

CHAPTER FOUR

RESULTS

4.1 BACKGROUND DEMOGRAPHIC AND BASELINE INFORMATION OF THE RESPONDENTS

Findings from Table 1 showed that a total of 544 respondents were recruited in the study. Out of which 363 PLWHA with or without TB participated as subjects for the study. Out of the 363 subject cases, 350 were HIV^+/ TB^- and 13 were HIV^+/ TB^+. The remaining 181 respondents participated in the study as "healthy controls" (HIV^-/ TB^-) giving a ratio of 2:1 case – control study.

Among the TB-HIV coinfected, eight of them were males while the remaining five were females. Among the PLWHA without TB, 112 (32.0%) of them were males while the remaining 238 (68.0%) were females. Also, among the "healthy control" group, 72 (39.8%) of them were males while the remaining 109 (60.8%) were females.

Majority of the respondents were Christians followed by Muslims. The average ages of the HIV+/ TB+ was 32.42 years, HIV+/ TB- was 33.21 years while HIV-/ TB- was 31.09 years. Five of the HIV+/ TB- were single while eight were married. Among the PLWHA without TB, 151 were single, 150 were married, 37 were either widows or widowers and 12 were divorced. The educational background of the respondents showed that majority have had primary to post secondary education. One hundred and fifty eight of the PLWHA without TB were businessmen/ businesswomen whist 162 of the HIV+/ TB- participants were unemployed.

Table 1: Demographic and Baseline information of Participants

VARIABLE	HIV+/ TB+	HIV+/TB-	HIV-/TB-
MEAN AGE (YEARS)	32.42 ± 11.24	33.21 ± 19.32	31.09 ± 18.18
MARITAL STATUS	n (%)	n (%)	n (%)
SINGLE	5 (38.5)	151 (43.1)	121 (66.9)
MARRIED	8(61.5)	150 (42.9)	35 (19.3)
WIDOW/ WIDOWER	-	37 (10.6)	9 (5.0)
DIVORCED	-	12 (3.4)	16 (8.8)
RELIGION			
CHRISTIAN	6 (42.2)	226 (64.6)	149 (82.3)
MUSLIM	7 (53.8)	112 (32.0)	15 (8.3)
OTHER	-	12 (3.4)	17 (9.4)
GENDER			
MALE	8 (61.5)	112 (32.0)	72 (39.8)
FEMALE	5 (38.5)	238 (68.0)	109 (60.2)
EDUCATION			

NO SCHOOLING	4 (30.8)	60 (17.1)	18 (9.9)
UP TO PRIMARY	1 (7.7)	85 (24.3)	45 (24.9)
UP TO JSS	2 (15.4)	136 (38.9)	21 (11.6)
POST SECONDARY AND BEYOND	6 (46.2)	69 (46.2)	97 (53.6)
OCCUPATION			
STUDENT	-	-	56 (30.9)
BUSINESSMAN/ WOMAN	4 (30.8)	158 (45.1)	37 (20.4)
GOVERNMENT	-	9 (2.6)	62 (34.3)
LABOURER	-	21 (6.0)	-
UNEMPLOYED	9 (69.2)	162 (46.3)	26 (14.4)

Percentages are in parenthesis ( )

Table 1 represents demographic and baseline characteristics of respondents. The mean age distribution revealed that the TB-HIV coinfected had 32.42 ± 11.24 years. PLWHA without TB had 33.21 ± 19.32 years whilst the healthy control subjects had a mean age of 31.09 ± 18.18 years. With regard to the marital status of the respondents, 5 (38.5%) HIV+/TB+, 151 (43.1%) HIV+/TB- and 12 (66.9%) HIV-/TB-, were single. Among the married respondents 8(11.5%), 150 (42.9%) and 35 (19.3%) were HIV+/TB+, HIV+/TB- and HIV-/TB- respectively. With respect to widows/ widowers, 37 (10.6%)

and 9 (5.0%) were HIV+/TB- and HIV-/ TB- respectively. Also, with the divorced, 12 (3.4%) and 16 (8.8%) were HIV+/TB- and HIV-/TB-respectively.

Religious status of the respondents showed that 6 (42.2%) of the HIV+/TB+, 226 (64.6%) of the HIV+/TB- and 149 (82.3%) of the HIV-/TB- were Christians. Among those who were Muslims, 7 (53.8%) were HIV+/TB+, 112 (32.0%) were HIV+/TB- and 15 (8.30%) were HIV-/TB-. With regard to those who were neither Christians nor Muslims, 12 (3.4%) were HIV+/TB- and 17 (9.4%) were HIV-/TB-.

With respect to the gender of the respondents, 8 (61.5%) HIV+/TB+, 112 (32.0%) HIV+/TB- and 72 (39.8%) HIV- / TB- were males. Among the females 5 (38.5%) were HIV+/ TB+, 238 (68.0%) were HIV+/TB- and 109 (60.2%) were HIV-/ TB-.

Also, the educational status of the respondents indicated that, 40 (30.8%) HIV+/TB+, 60 (17.1%) HIV+/TB- and 18 (9.90%) HIV-/TB- had no schooling. Among those who had schooling up to primary 1 (7.7%), 85 (24.3%) and 45 (24.9%) were HIV+/TB=, HIV+/TB- and HIV-/TB- respectively. Two (15.4%) HIV+/TB+, 136 (38.9%) HIV+/TB- and 21 (11.6%) HIV-/TB- had schooling up to JSS. With respect to those who had post secondary education and above, 6 (46.2%) were HIV+/TB+, 69 (46.2%) were HIV+/TB- and 97 (53.6%) were HIV-/TB-.

Concerning the occupational status of the respondents, 56 (30.90%) students were HIV-/TB-. Among the business men/ women, 4 (30.5%) were HIV+/TB+, 158 (45.1%) were HIV+/TB- and 37 (20.4%) were HIV-/TB-. Among the government workers, 9 (2.60%) and 62 (34.3%) were HIV+/TB- and HIV-/TB- respectively. Also with the unemployed 9 (69.2%), 162 (46.3%) and 26 (14.40%) were HIV+/TB+, HIV+/TB- and HIV-/TB-. There were 21 (6.0%) respondents who were HIV+/TB-.

4.2 DISTRIBUTION OF CLINICAL OUTCOMES AND HIV AND TB STATUS OF RESPONDENTS

Section 4.2, shows the distribution of clinical outcomes of the respondents by their HIV and TB status.

Table 2: HIV and TB Status, Cough with Sputum, Blood in Sputum and Dry cough in Participants

HIV AND TB	COUGH WITH SPUTUM	BLOOD IN	DRY

STATUS			SPUTUM		COUGH	
	YES (%)	NO (%)	YES (%)	NO (%)	YES (%)	NO (%)
HIV+/ TB+	12 (92.3)	1 (7.7)	10 (76.9)	3 (23.1)	13 (100.0)	0 (0.0)
HIV+/ TB-	39 (11.1)	311 (88.9)	15 (4.3)	335 (95.7)	138 (39.4)	212 (60.6)
HIV-/TB-	0 (0.0)	181 (100.0)	0 (0.0)	181 (100.0)	16 (8.8)	165 (91.2)
TOTAL	51 (14.4)	493 (90.6)	25 (4.6)	519 (95.6)	167 (30.7)	377 (69.3)
CHI SQUARE	$\chi 2(1) = 68.380$, P = 0.000		$\chi 2$ (1) = 103.129, P= 0.000		$\chi 2(1) = 18.930$, P= 0.000	

Table 2shows that a total of 51 (14.4%) coughed with sputum production. Twelve (92.3%) out of the 13 TB/HIV coinfected persons produced sputum after coughing. Also, 138 (39.4%) of the PLWHA without TB infection produced sputum whilst 212 (60.6%) did not. Further results showed that none of the healthy controls reported of sputum production. The chi square test indicated that there was a significant relationship between HIV and TB status and coughing with sputum production.

Results from the table also indicated that 10 (76.9%) of the TB/HIV coinfected reported blood in sputum, whilst 15 (4.3%) of the PLWHA without TB infection also reported of blood in sputum. The Chi - square test showed that a significant relationship exist between the HIV and TB status and blood in sputum.

Results from the table further showed, that 167 (30.7%) of the respondents had dry cough, whilst 377 (69.3%) did not have. The results further indicated that all the TB-/ HIV- coinfected participants reported dry cough whilst 138 (39.4%) of the PLWHA without TB had dry cough. 14 (8.8%) out of the 181 persons who participated as healthy controls reported dry cough. Chi- square results indicated that there was a significant relationship between the HIV and TB status and dry cough.

Table 3: Occurrence of Short Breath, Chest pain and Joint pains in HIV and TB individuals

HIV AND TB STATUS	SHORT BREATH		CHEST PAIN		JOINT PAINS	
	YES (%)	NO (%)	YES (%)	NO (%)	YES (%)	NO (%)
HIV+/ TB+	11 (84.6)	2 (15.4)	12 (92.3)	1 (7.7)	9 (69.2)	4 (30.8)
HIV+/ TB-	17 (4.9)	333 (95.7)	17 (4.9)	333 (95.1)	251 (71.7)	99 (28.3)
HIV-/TB-	12	169	15	166	9	172

	(14.4)	(93.4)	(8.3)	(91.7)	(5.0)	(95.0)
TOTAL	40 (7.4)	504 (92.6)	44 (8.1)	500 (91.9)	269 (49.4)	275 (50.6)
CHI-SQUARE	$\chi 2$ (1) = 112.012, P= 0.000		$\chi 2$(1) = 130.406, P = 0.000		$\chi 2$ (1) = 0.038, P = 0.845	

Table 3 shows that 40 (7.4%) of the respondents indicated shortness of breath whilst 504 (92.6%) did not have short breath. Results further indicated that 11 (84.6%) of the TB/ HIV coinfected participants showed shortness of breath whilst 12 (14.4%) out of the 181 healthy participants in the study also presented shortness of breath. The Chi - square testshowed a significant relationship between the HIV and TB status and shortness of breath.

Findings from the study, revealed that 44 (8.1%) had chest pain whilst 500 (91.9%) did not reported of chest pain. The results further indicated that 12 (92.3%) of the TB/ HIV coinfected participants had chest pains whilst 17 (4.9%) of the PLWHA without TB also reported of chest pains. Fifteen persons (8.3%) of the healthy controls reported of chest pains.

Chi - square test revealed that a significant relationship exists between the HIV and TB status and chest pains.

Table 3 shows that 269(49.4%) of the participants complained of bone or joint pain. Out of these were 9(69.2%) of the respondents with TB- HIV coinfection,

251(71.7%) of the PLWHA without TB and 9 (5.0%) of the healthy controls. There was no significant relationship between the HIV and TB status and bone or joint pain.

Table 4: HIV and TB Status and Fever, Night Sweat and Loss of Appetite

HIV AND TB STATUS	FEVER		NIGHT SWEAT		LOSS OF APPETITE	
	YES (%)	NO (%)	YES (%)	NO (%)	YES (%)	NO (%)
HIV+/ TB+	13 (100.0)	0 (0.0)	11 (84.6)	2 (15.4)	12 (92.3)	1 (7.7)
HIV+/ TB-	286	64	237	113	261	89

	(81.7)	(18.3)	(67.7)	(32.3)	(74.6)	(25.4)
HIV-/TB-	29 (16.0)	152 (84.0)	17 (8.9)	164 (91.1)	25 (13.8)	156 (86.2)
TOTAL	328 (60.3)	216 (39.7)	254 (46.7)	290 (53.3)	298 (54.8)	246 (45.2)
CHI SQUARE	$\chi 2$ (1) = 2.886, P= 0.089		$\chi 2$ (1) = 1.654, P= 0.198		$\chi 2$ (1) = 2.115, P = 0.146	

Table 4 shows that majority 328 (60.3%) of the respondents reported of fever whilst 216 (39.7%) did not have fever. All the TB/ HIV participants and 286 (81.7%) of the PLWHA without TB infection reported of fever.In addition, 29 (16.0%) of the healthy controls also reported fever. Computed Chi - square test showed that there was no significant relationship between HIV and TB status of respondents and fever.

Results from the table, show that 254 (46.7%) of the participants had night sweat whilst 290 (53.3%) did not. The results further indicated that 11 (84.6%) of the TB/ HIV coinfected persons, 237 (67.7%) of the PLWHA without TB and 17 (8.9%) of the healthy controls also reported of night sweat. The $\chi 2$ test showed that there was no significant relationship between the HIV and TB status and night sweat.

Results from table 4 also, indicates that 298 (54.8%) of the respondents reported of loss of appetite whilst 246(45.2%) did not. Further results showed that 12(92.3%) of the TB- HIV coinfected, 261(74.6%) of the PLWHA without TB and 25(13.8%) of the

healthy controls also reported of loss of appetite. The computed Chi-Square tests showed that there was no significant relationship between the HIV and TB status of the respondents and loss of appetite.

Table 5: HIV and TB Status and Skin Rash, Diarrhoea, Tiredness

HIV AND TB STATUS	SKIN RASH		DIARRHOEA		TIREDNESS	
	YES (%)	NO (%)	YES (%)	NO (%)	YES (%)	NO (%)
HIV+/ TB+	5 (38.5)	8 (61.5)	11 (84.6)	2 (15.4)	12 (92.3)	1 (7.7)
HIV+/ TB-	32 (9.1)	318 (90.9)	31 (8.9)	319 (91.1)	251 (71.7)	99 (28.3)
HIV-/TB-	4 (2.2)	177 (97.8)	18 (9.9)	163 (90.1)	39 (21.5)	142 (78.5)
TOTAL	41 (7.2)	503 (92.8)	60 (11.0)	484 (89.0)	302 (55.5)	242 (44.5)
CHI-SQUARE	$\chi 2(1) = 11.770$, P = 0.001		$\chi 2$ (1) = 70.311, P = 0.000		$\chi 2$ (1) = 2.663, P= 0.103	

Results from Table 5, revealed that 41(7.2%) of the respondents had skin rashes whilst 503(92.8%) did not have. The analysis further revealed that 5(38.5) of the TB-HIV coinfected, 32(9.1%) of the PLWHA and 4 (2.2%) of the healthy controls had skin rashes. The computed Chi-Square results showed that there was a significant relationship between the HIV and TB status of the respondents and skin rashes.

Findings from this study, shows that 11(84.6%) of the TB –HIV coinfected persons, 31(8.9%) of the PLWHA without TB and 18(9.9%) of the healthy controls reported of diarrhoea. A total of 60(11.0%) of the participants reported of diarrhoea whilst 484(89.0%) did not have diarrhea. The Chi- square test showed significant relationship between the HIV and TB status and diarrhea disease.

Data from table 5, indicates that 302 (55.5%) of the participants reported of tiredness whilst 242 (44.5%) did not. Detailed results revealed that 12 (92.3%) of the TB/ HIV coinfected, 251 (71.7%) of the PLWHA without TB and 39 (21.5%) of the healthy controls reported of tiredness. The Chi - square testshowed there were no significant relationship between the HIV and TB status of respondents and tiredness.

Table 6: HIV and TB Status and Weight Loss in Participants

HIV AND TB STATUS	WEIGHT LOSS		TOTAL
	YES (%)	NO (%)	
HIV+/ TB+	11 (84.6)	2 (15.4)	13 (100)

HIV+/ TB-	176 (50.3)	174 (49.7)	350 (100)
HIV-/TB-	7 (3.9)	174 (96.1)	181 (100)
TOTAL	194 (35.7)	350 (64.3)	544 (100%)

$\chi 2$ (1) = 5.914, P = 0.015

Table 6, shows that 194 (35.7%) of the respondents reported of weight loss while 350 (64.3%) did not. Also, 11(84.6%) of the TB- HIV coinfected persons, 176 (50.3%) of PLWHA without TB and 7(3.9%) of the healthy controls reported weight losses. A significant relationship between HIV and TB status and weight loss existed when the Chi - square was applied.

Table7: HIV and TB Status and Swelling around the Neck or Inguinal Region

HIV AND TB STATUS	SWELLING AROUND THE NECK OR INGUINAL REGION		TOTAL
	YES (%)	NO (%)	
HIV+/ TB+	6	7	13

	(46.2)	(53.8)	(100)
HIV+/ TB-	0 (0.0)	350 (100.0)	350 (100)
HIV-/TB-	0 (0.0)	181 (100)	181 (100)
TOTAL	6 (1.1)	538 (98.9)	544 (100%)

$\chi 2$ (1) = 164.253, P = 0.000

Table 7, shows that 6(1.1%) of the respondents had swellings around the neck whilst 538(98.9%) did not. Analysis revealed that 6(46.2%) of the TB –HIV coinfected individuals had the swellings around the neck whilst none of the PLWHA without TB and the healthy controls had such a symptom. However, there was a significant relationship between the HIV and TB status of the respondents and having swellings around the neck or inguinal region.

Table 8: HIV and TB Status and X- ray Findings of Participants

HIV AND TB STATUS	X- RAY FINDINGS			TOTAL
	UNLIKELY	PROBABLE	MOST PROBABLE	
HIV+/ TB+	1 (7.7%)	7 (53.8%)	5 (38.5%)	13 (100%)
HIV+/ TB-	327 (93.4%)	23 (6.6%)	0 (0%)	350 (100%)
HIV-/TB-	181 (100%)	0 (0%)	0 (0%)	181 (100%)
TOTAL	328 (90.4%)	30 (8.3%)	5 (1.3%)	544 (100%)

$\chi 2$ (1) = 5.914, P = 0.015

Results from Table 8, show that 5(1.3%) of the total participants had chest x –ray findings that were most probable akin to TB infection. Thirty (8.3%) of respondents showed symptom akin to TB infection of their chest x-ray films whilst 328(90.4%) of the respondents had chest x- ray films that were free from TB infection. There was a significant relationship between the HIV and TB status of the respondents and chest x – ray findings.

Table 9: Body Mass Index of Subjects of Participants

SUBJECTS	BODY MASS INDEX (kg/m^2)	TOTAL NUMBER OF SUBJECTS
HIV + / TB +	21.6	13
HIV + / TB -	23.8	350
HIV - / TB -	24.9	181

Table 9, shows that the body mass index of patients without TB was 23.8 kg/m^2, while the BMI of patients with TB co infection was 21.6 kg/ m^2 (T - test = 5.104, p value < 0.001). T-test results revealed a significant difference between the mean BMIs and HIV and TB status of the respondents.

4.3 DISTRIBUTION OF BASELINE DATA OF IMMUNOHAEMATOLOGICAL MARKERS OF RESPONDENTS

This section shows the distribution of baseline immunohaematological markers, this including HIV and TB status of the respondents.

Table 10: Baseline Data of Immunohaematological Markers of Respondents

IMMUNOHAEMAT-OLOGICAL VARIABLES	HIV^+/TB^+ MEAN ± SD	HIV^-/TB^+ MEAN± SD	HIV^-/TB^- MEAN ± SD	P - VALUE
HAEMOGLOBIN LEVEL (g/dl)	9.69 ±3.812	10.70 ±2.307	12.41 ±2.451	0.000
WHITE BLOOD CELLS (x 10^9/l)	4.90 ± 2.154	5.91 ± 2.432	6.92 ± 3.124	0.000
PACKED CELL VOLUME (%)	32.31 $^{\pm}$ 4.813	34.1 $^{\pm}$ 4.367	36.92 $^{\pm}$ 4.211	0.000
PLATELETS COUNT (x 10^9/l)	163.29 ± 65.110	195.16 ± 88.710	240.07 ± 99.42	0.000

EYTHROCYTE SEDIMENTATION RATE (mm/hr)	115.13 ±11.820	102.51 ±17.350	10.03 ±8.495	0.000
CD 4 COUNT (Cells/mm^3)	264.42 ± 76.02	375.31 ±297.640	748.04 ± 281.100	0.000

Results from Table 10, show someimmunohaematological markers of the respondents. Findings reveal that there were significant differences between the mean distribution of the haemoglobin levels, white blood cells, packed cell volume, platelets count, erythrocyte sedimentation rate and CD4 count of respondents and their HIV and TB status ($p < 0.05$).

4.4 DISTRIBUTION OF GENDER AND IMMUNOHAEMATOLOGICAL MARKERS AND THE HIV AND TB STATUS OF THE RESPONDENTS.

This part of the study outlines the distribution of gender, immunohaematological markers and the HIV and TB status of the respondents.

Table 11: HIV and TB Status and Gender and Haemoglobin levels

HIV AND TB STATUS	HAEMOGLOBIN LEVELS (g/dl)		TOTAL
	<11.0	11.0 – 17.0	
HIV+/ TB+			
MALES	6 (75.0)	2 (25.0)	8 (100)
FEMALES	5 (100.0)	0 (0.0)	5 (100)
HIV+/ TB-			
MALES	43 (38.4)	69 (61.6)	112 (100)
FEMALES	130 (54.6)	108 (45.4)	238 (100)
HIV-/TB-			
MALES	7 (9.7)	65 (90.3)	72 (100)
FEMALES	18 (16.5)	91 (83.5)	109 (100)

$\chi 2$ (1) = 1.477, df= 543, P = 0.224

Results from Table 11, show that among respondents who were coinfected with HIV and TB, 6 (75.0%) males and 5 (100.0%) had haemoglobin levels less than 11.0g/dl, also among the coinfected respondents, who had haemoglobin levels ranging from 11.0 – 17.0g/dl, there were 2 (25.0%) were males, whilst there were no females.

Secondly among respondents who were HIV positive and TB negative, 43 (38.4%) males and 130 (54.6%) females had haemoglobin levels less than 11.0g/dl; 69

(61.6%) males and 108 (45.4%) had haemoglobin levels ranging from 11.0 – 17.0g/dl. Thirdly, among the healthy controls, 7 (9.7%) males and 18 (16.5%) females had haemoglobin levels less than 11.0g/dl and 91 (83.5%) females had their haemoglobin levels ranging from 11.0 to 17.0g/dl.

Table 12: HIV and TB Status and Gender and White Blood Cells Count

HIV AND TB STATUS	WHITE BLOOD CELLS COUNT (x 10^9/l)			TOTAL
	< 4.0	4.0 - 8.0	>8.0	
HIV+/ TB+				
MALES	2 (25.0)	6 (75.0)	0 (0.0)	8 (100)
FEMALES	0 (0.0)	5 (100.0)	0 (0.0)	5 (100)
HIV+/TB-				
MALES	39 (34.8)	55 (49.1)	18 (16.1)	112 (100)
FEMALES	77 (32.4)	142(59.7)	19 (8.0)	238 (100)
HIV-/TB-				
MALES	5 (6.9)	38 (52.8)	29 (40.3)	72 (100)
FEMALES	12 (11.0)	87 (79.8)	10 (9.2)	109 (100)

$\chi 2$ (1) =1.562, P =0.315

Table 12, shows that among the TB-HIV coinfected respondents who had WBC count less than 4.0 x 10^9/l, 2 (25.0%) were males, whilst none were females. 6 (75.0%) males and 5 (100%) females had WBC ranging from (4.0 - 8.0) x 10^9/l and none of the respondents had WBC greater than 8.0 x 10^9/l.

Secondly, with respect to respondents who were HIV+/TB-, 39 (34.8%) males and 77 (32.4%) had WBC less than 4.0 x 10^9/l, while 55 (49.1%) males and 142 (59.7%) females had WBC ranging from (4.0 - 8.0) x 10^9/l.

Thirdly, among the healthy controls 5 (6.9%) males and 12 (11.0%) had WBC less than 4.0 x 10^9/l, among those who had WBC ranging between (4.0 - 8.0) x 10^9/l, there were 38 (52.8%) males and 87 (79.8%) females. Chi-squared test indicated no significant relationship between HIV-TB status and gender and white blood cells count.

Table 13: HIV and TB Status and Gender and Packed Cells Volume results

HIV AND TB STATUS AND GENDER	PACKED CELL VOLUME RESULTS (%)				TOTAL
	10.0 – 19.9	20.0 – 29.99	30.0 – 39.9	40.0 – 49.9	
HIV+/ TB+					
MALES	2 (25.0)	5 (62.5)	1 (12.5)	0 (0.0)	8 (100)
FEMALES	2 (40.0)	3 (60.0)	0 (0.0)	0 (0.0)	5 (100)
HIV+/ TB-					

MALES	0 (0.0)	2 (1.8)	74 (66.1)	36 (32.1)	112 (100)
FEMALES	5 (2.1)	25 (10.5)	152 (63.9)	56 (23.5)	238 (100)
HIV-/ TB-					
MALES	0 (0.0)	5 (6.9)	37 (51.4)	30 (41.7)	72 (100)
FEMALES	0 (0.0)	5 (4.6)	94 (86.2)	10 (9.2)	109 (100)

$\chi 2$ (2) =2.860, P =0.239

Results from Table13, indicates that among the HIV+/TB+, 2 (25.0%) males and 2 (40.0%) females had PCV ranging from (10.0 – 19.9) %, 5 (62.5%) males and 3 (60.0%) females had their PCV to be between (20.0 – 29.9) %, 1 (12.5) males and no female had PCV ranging from (30.0 – 39.9) %. No respondent had PCV ranging from (40.0 – 49.9) %. Furthermore, among the participants who were HIV+/TB-, 5 (2.1%) and no male had PCV of 10 - 19.9, 2 (1.8%) males and 25 (10.5%) females had PCV between (20.0 – 29.9)%. With respect to those with PCV of (30.0 – 39.9) %, 74 (66.1%) were males and 152 (63.9%) were females. 36 (32.1%) males and 56 (23.5%) had PCV of (40.0 – 49.9) %.

Finally, out of 281 healthy subjects, none had PCV of (10.0 – 19.9) %, 5 (6.9%) males and 5 (4.6%) females had PCV of (20.0 – 29.9) %. Considering subjects with PCV of (30.0 – 39.9) %, 37 (51.4%) males and 94 (86.2%) females fell within this category and 30 (41.7%) males and 10 (9.2%) had PCV of (40.0 – 49.9). Computed Chi-square test showed that there was no significant relationship between HIV-TB status and gender and packed cell volume.

Table 14: HIV and TB Status and Gender and Platelets Count

HIV AND TB STATUS	PLATELET COUNT (x 10^9/l)			TOTAL
	< 140	140– 400	>400	
HIV+/ TB+				

MALES	5 (62.5)	3 (37.5)	0 (0.0)	8 (100)
FEMALES	2 (40.0)	3 (60.0)	0 (0.0)	5 (100)
HIV+/ TB-				
MALES	22 (19.6)	84 (75.0)	6 (5.4)	112 (100)
FEMALES	44 (18.5)	190 (79.8)	4 (1.7)	238 (100)
HIV-/ TB-				
MALES	5 (6.9)	67 (93.1)	0 (0.0)	72 (100)
FEMALES	7 (6.4)	100 (91.7)	2 (1.8)	109 (100)

$\chi 2$ (1) = 0.124, P = 0.725

Results from Table 14, show that, among the HIV+/TB+, 5 (62.5%) males and 2 (4.0.0%) had platelets count less than 140 x 10^9/l, 3 (37.5%) and 3 (60.0%) had platelets count ranging from 140 – 400 x 10^9/l; no coinfected respondents had platelets count greater than 400 x 10^9/l. With respect to subjects who were HIV+/ TB+ with platelets count less than 140 x 10^9/l, there were 22 (19.6%) males and 44 (18.5%) females. 54 (75.0%) males and 190 (79.8%) had platelets count ranging from 140 to 400 x 10^9/l, Among respondents who were HIV+/ TB-, with platelets count greater than 400 x 10^9/l, there were 6 (5.4%) males and 4 (1.7%) females.

Lastly, among the healthy controls, 5 (6.9%) males and 7 (6.4%) females had platelets count less than 140 x 10^9/l, 67 (93.1%) males and 100 (91.7%) females had

platelets count ranging from 140 – 400 x 10^9/l; with respect to those who had platelets count greater than 400 x 10^9/l, there were 2 (1.8%) males and no females. The chi-square test showed that there was no significant relationship between HIV - TB and gender and platelets count.

Table 15: HIV and TB Status and Gender and Erythrocyte Sedimentation Rate

HIV AND TB STATUS	ERYTHROCYTE SEDIMENTATION RATE (mm/hr)				TOTAL
	0 – 8	9 – 50	51– 100	>100	
HIV+/ TB+					
MALES	0 (0.0)	0 (0.0)	0 (0.0)	8 (100.0)	8 (100)
FEMALES	0 (0.0)	0 (0.0)	0(0.0)	5 (100.0)	5 (100)
HIV+/ TB-					
MALES	1 (0.9)	12 (10.7)	8 (7.1)	91 (81.3)	112 (100)
FEMALES	0 (0.0)	2 (0.8)	60 (25.2)	176 (73.9)	238 (100)
HIV-/ TB-					
MALES	68 (94.4)	4 (5.6)	0 (0.0)	0 (0.0)	72 (100)
FEMALES	86 (78.9)	23 (21.1)	0 (0.0)	0 (0.0)	109 (100)

$\chi 2$ (1) = 0.133, P = 0.715

Table15,summarises results of Erythrocyte sedimentation rate. Among the coinfected subjects, no subjects (males or females) had ESR ranging from 0 -8 mm/hr, 9 – 50 mm/hr and 51 – 100 mm/hr; however 8 (100%) males and 5 (100%) females had ESR greater than 100 mm/hr. With respect to the HIV+/ TB- subjects, 1 (0.9%) males and no females had ESR ranging from0 – 8 mm/hr, 12 (10.7%) males and 2 (0.8%) females had ESR of 51 – 100 mm/hr and 91 (81.3%) males and 176 (73.9%) females had ESR greater than 100 mm/hr.

Thirdly, among the healthy controls who had ESR of 0 – 8 mm/hr, there were 68 (94.4%) males and 86 (78.9%) females, among those who had ESR ranging from 9 – 50 mm/hr there were 4 (5.6%) and 23 (21.1%) females, none of the subjects had ESR results of 51 – 100 mm/hr and results greater than 100 mm/hr. Chi-square analysis show that there was no significant relationship between HIV- TB and gender and erythrocyte sedimentation rate.

Table 16: HIV and TB Status and Gender and CD4 Count

HIV AND TB STATUS	CD4 COUNT RESULTS (Cells/mm^3)				TOTAL
	< 200	200 - < 350	350 - < 500	500 AND ABOVE	
HIV+/ TB+					
MALES	6 (75.0)	2 (25.0)	0 (0.0)	0 (0.0)	8 (100)
FEMALES	4 (80.0)	1 (20.0)	0 (0.0)	0 (0.0)	5 (100)
HIV+/ TB-					

MALES	52 (46.4)	3 (2.7)	52 (46.4)	5 (4.5)	112 (100)
FEMALES	25 (10.5)	126 (52.9)	83 (34.9)	4 (1.7)	238 (100)
HIV-/ TB-					
MALES	0 (0.0)	0 (0.0)	5 (6.9)	67 (93.1)	72 (100)
FEMALES	0 (0.0)	0 (0.0)	12 (11.0)	97 (89.0)	109 (100)

$\chi 2$ (1) = 0.043, P = 0.835

Results from Table 4.16, show that with respect to the HIV+/TB+, 6 (75.0%) males and 4 (80.0%) females had CD4 count less than 200 cells/mm^3, 2 (25.0%) males and 1 (20.0%) males and 1 (20.0%) females had CD4 between 200 and 350 cells/mm^3, none of the subjects had CD4 count of 350 - <500 cells/mm^3 and 500 cells/mm^3 and above.

Secondly, 52 (46.4%) males and 25 (10.5%) females had CD4 less than 200, 3 (2.7%) males and 126 (52.9%) females had CD4 between 200 and 350, 52 (42.4%) males and 83 (34.9%) females had CD4 between 350 and 500 cells/mm^3 and 5 (4.5%) males and 4 (1.7%) females had CD4 count above 500 cells/mm^3. The results further revealed that none of the subjects had CD4 counts of less than 200 and 200 - < 350 cells/mm^3. However 5 (6.9%) males and 12 (11.09%) females had CD4 350 - < 500 cells/mm^3 and 67 (93.1%) males and 97 (89.0%) females had CD4 count greater than 500. cells/mm^3. The calculated chi-square shows that there was no significant relationship between HIV-TB and gender and CD4 count.

4.5 DISTRIBUTION OF IMMUNOHAEMATOLOGICAL MARKERS AND HIV AND TB STRATIFICATION OF RESPONDENTS

This aspect of the study presents the immunohaematological markers of the PLWHA by their HIV and TB status.

Table 17: HB and TB Status and Haemoglobin Levels

HIV AND TB STATUS	HAEMOGLOGIN LEVELS (g/dl)		TOTAL
	<11.0	11.0 – 17.0	
HIV+/ TB+	11 (84.6)	2 (15.4)	13 (100)
HIV+/TB-	173 (49.4)	177 (50.6)	350 (100)
HIV-/TB-	7 (3.9)	174 (96.1)	181 (100)
TOTAL	191 (35.1)	353 (64.9)	544 (100%)

t = 30.304, df = 543, P = 0.000

Results from Table17, show that out of a total 13 coinfected subjects, 11 (84.6%) had HB levels less than 11.0 g/dl, while, 2 (15.4 %) had HB between (11.0 – 17.0) g/dl. Among the HIV+/TB- subjects 173 (49.4%) and 177 (50.6%) subjects had HB of <11.0 g/dl and (11.0 – 17.0) g/dl respectively. The results also indicates that among the

HIV-/TB- , 7 (3.9%) had HB of 11.0 g/dl, while 174 (96.1%) had HB of (11.0 – 17.0) g/dl. The t-test shows that there was significant difference between the means of haemoglobin levels and HIV-TB status of respondents.

Table 18: HIV and TB Status and WBC Status

HIV AND TB STATUS	WHITE BLOOD CELLS COUNT (x 10^9/l)			TOTAL
	< 4.0	4.0 – 8.0	> 8.0	
HIV+/TB+	2 (15.4)	11 (84.6)	0 (0.0)	13 (100)
HIV+/TB-	116 (33.1)	197 (56.3)	37 (10.6)	350 (100)
HIV-/TB-	17 (9.4)	125 (69.1)	39 (21.5)	181 (100)
TOTAL	135 (24.8)	333 (61.2)	76 (14.0)	544 (100%)

t = 14.004, df = 543, P = 0.000

Table 18, shows that out of 544 in total, 2 (15.4%) and 11 (84.6%) coinfected participants had WBC count of < 4.0 and (4.0 – 8.0) respectively. The results also revealed that among the 350 HIV+/TB- participants 116 (33.1%), 197 (56.3%) and 37

(10.6%) had WBC count of < 4.0, (4.0 – 8.0) and >8.0 respectively. With respect to the 181 healthy controls, 17 (9.4%), 125 (69.1%), 39 (21.5%) had white blood cells count of < 4.0, (4.0 – 8.0) and >8.0 respectively. T-test results show that there were significant mean differences between HIV-TB and white blood cells.

Table 19: HIV and TB Status and Packed Cell Volume

HIV AND TB STATUS	PACKED CELL VOLUME (%)				TOTAL
	10.0 – 19.9	20.0 – 29.9	30.0 – 39.9	40.0 – 49.9	
HIV+/TB+	0 (0.0)	10 (76.9)	2 (15.4)	1 (7.7)	13 (100)
HIV+/TB-	9 (2.6)	25 (7.1)	225 (64.3)	91 (26.0)	350 (100)
HIV-/TB-	0 (0.0)	10 (5.5)	131 (72.4)	40 (22.1)	181 (100)

TOTAL	9 (1.7)	45 (8.3)	358 (65.8)	132 (24.3)	544 (100%)

t = 25.211, df = 543, P = 0.000

Results from Table19, shows that among the coinfected participants 10 (76.9%), 2 (15.4%) and 1 (7.7%) had PCV values of (20.0 – 29.9) %, (30.0 – 39.9) %, and (40.0 – 49.9) % respectively. Among the HIV+/TB-, 9(2.6%), 25 (7.1%), 225(64.3%) and 91 (26.0%) had PCV count of (10.0 – 19.9) %, (20.0 – 29.9) %, (30.0 – 39.9) %, and (40.0 – 49.9) % respectively. With respect to the healthy controls 10 (5.5%), 131 (72.4%) and 40 (22.1%) had PCV count of (20.0 – 29.9) %, (30.0 – 39.9) %, and (40.0 – 49.9) % respectively. The t-test showed a significant mean difference between HIV-TB and packed cell volume statusof the respondents.

Table 20: HIV and TB Status and Platelets Count

HIV AND TB STATUS	PLATELET COUNT (x 10^9/l)			TOTAL
	< 140	140– 400	> 400	

HIV+/TB+	6 (46.2)	7 (53.8)	0 (0.0)	13 (100)
HIV+/TB-	67 (19.1)	273 (78.0)	10 (2.9)	350 (100)
HIV-/TB-	12 (6.6)	167 (92.3)	2 (1.1)	181 (100)
TOTAL	85 (15.6)	447 (82.2)	12 (2.2)	544 (100%)

t= 17.66, df = 543, P = 0.000

Table 20, show that among the coinfected participants 6 (46.2%) and 7 (53.8%) had platelet count of < 140 x 10^9/l and (140 - 400) x 10^9/l. Within the HIV+/TB-, 67 (`19.1%), 273 (78.0%) and 10 (2.9%) had platelet count of < 140 x 10^9/l, (140 – 400) x 10^9/l and > 400 x 10^9/l respectively. Further results shows that 12 (6.6%), 167 (92.3%) and 2 (1.1%) of the healthy participants have platelets count of < 140 x 10^9/l, (140 – 400) x 10^9/l and > 400 x 10^9/l respectively. T-test showed that there was a significant difference between the means of their platelet counts and their HIV and TB status.

Table 21: HIV and TB Status and Erythrocyte Sedimentation Rate

HIV AND TB STATUS	ERYTHROCYTE SEDIMENTATION RATE (mm/hr)				TOTAL
	0 – 8	9 – 50	51 - 100	>100	
HIV+/ TB+	0 (0.0)	0 (0.0)	0 (0.0)	13 (100)	13 (100)
HIV+/ TB-	1 (0.3)	0 (0.0)	80 (22.9)	269 (76.9)	350 (100)
HIV-/TB -	154 (85.1)	27 (14.9)	0 (0.0)	0 (0.0)	181 (100)
TOTAL	155 (28.5)	27 (5.0)	80 (14.7)	282 (51.8)	544 (100%)

t = 7.685, df = 543, P = 0.000

Table 21, indicates that all the 13 TB-HIV coinfected had > 100 mm/hr respectively. With respect to the 350 HIV+/TB- participants 1 (0.3%), 80 (22.9%) and 269 (76.9%) had ESR results of (0 -8) mm/hr, (51 – 100) mm/hr and >100 mm/hr respectively.

Among the healthy controls 154 (28.5%) and 27 (14.9%) of the participants had ESR results of (0 -8) mm/hr and (9 – 50) mm/hr. T-test showed that there was significant mean difference between the HIV and TB status and ESR results.

Table 22: HIV and TB Status and CD4 Count

HIV AND TB STATUS	CD4 COUNT (cells/mm^3)				TOTAL
	< 200	200 - < 350	350 - < 500	500 AND ABOVE	
HIV+/TB+	10 (76.9)	3 (23.1)	0 (0.0)	0 (0.0)	13 (100)
HIV+/ TB-	77 (22.0)	129 (36.9)	135 (38.6)	9 (2.6)	350 (100)
HIV-/ TB-	0 (0.0)	0 (0.0)	6 (3.3)	175 (96.7)	181 (100)

TOTAL	87 (16.0)	132 (24.3)	141 (25.9)	184 (33.8)	544 (100%)

t = 14.474, df = 543, P = 0.000

Results in Table 22, shows that among the participants who were HIV+/TB+; 10 (76.9%), had CD4 count less than 200 cells/mm^3, 3 (23.1%) had CD4 count ranging from (200 - < 350) cells/mm^3. Among the HIV+/TB- 77 (22.0%) and 129 (36.9%) had CD4 count of < 200 cells/mm^3 and (200 - < 350) cells/mm^3 respectively. Also 135 (38.6%) and 9 (2.6%) subjects had CD4 count of (350 - <500) cells/mm^3 and > 500. cells/mm^3. Further results shows that 6 (3.3%) and 184 (33.8%) participants had CD4 count of (350 - < 500) cells/mm^3 and > 500 cells/mm^3 respectively. T-test showed that a significant difference existed between the mean of CD4 count and HIV and TB status.

Table 23: CD4 Count of PLWHA Subjects with their Stratified Ages

AGE OF SUBJECTS	CD4 COUNT RESULTS (Cells/ mm^3)				TOTAL
	< 200	200 - < 350	350 - <500	≥ 500	

18- 27	4 (4.6)	37 (42.5)	46 (52.9)	0	87
28- 37	28 (16.6)	80 (47.3)	57 (33.7)	4 (2.4)	169
38- 47	55 (82.1)	0	12 (17.9)	0	67
48- 57	0	13 (43.3)	17 (56.7)	0	30
58 – 67	0	2 (20.0)	3 (30.0)	5 (50.0)	10
TOTAL	87 (24)	132 (36.3)	135 (37.2)	9 (2.5)	363 100%

$\chi 2$ (12) = 265.358, P = 0.000

Table 23, shows CD4 results of the respondents. 87 (24.0%) had CD4 count of less than 200 cell/mm^3, 132 (36.4%) had CD4 count between 200 but less cells than 350 cell/mm^3. Also 135 (37.2%) had CD4 count of 350 but less than 500 whilst 9 (2.5%) of the respondents had CD4 count of 500 and above in the cells/ mm^3. It was also observed that 28 (16.6%) of the respondents between the ages of 28 – 37 years and 55 (82.1%) of the respondents between the ages of 38 – 47 years had CD4 count of less than 200 cells /mm^3, whiles none within the ages of 18 – 27 years, 38 – 47 years and 48 – 57 had CD4 count of 500 and above. A significant relationship existed between the ages of the PLWHA and their CD4 counts.

Table 24: Sputum Smear Microscopy and Culture Results of the PLWHA Subjects with their Stratified Age

AGE OF SUBJECTS	SPUTUM SMEAR MICROSCOPY		SPUTUM CULTURE	
	AFB PRESENT (%)	NEGATIVE (%)	MYCOBATERIUM ISOLATED (%)	NO GROWTH (%)
18- 27	0	87 (100)	0	87 (100)
28- 37	6 (3.6)	163 (96.4)	9 (5.3)	160 (94.7)
38- 47	2 (3.0)	65 (97)	4 (6.0)	63 (94.0)
48- 57	0	30 (100)	0	30 (100)
58- 67	0	10 (100)	0	10 (100)
TOTAL	8 (2.2)	355 (97.8)	13 (3.6)	350 (96.4)
CHI SQUARE RESULTS	$\chi 2$ (4) = 4.473, P = 0.346		$\chi 2$ (4) =7.313, P = 0.120	

Results from Table 24 show that 8 (2.2%) had AFB whilst 355 (97.8%) did not have AFB. Those within the age groups 18 – 27, 48 – 57 and 58 years and above did not have AFB , whilst those within the age group 28 – 37 years and 38 - 47, 6 (36.0%) and2

(3.0%) respectively had AFB. The Chi- square test indicated that there was no significant relationship between the age of PLWHA and AFB in sputum smear.

Table 24 also shows that 13 (3.6%) had mycobacterium isolates whilst 350 (96.4%) had no isolates for mycobacterium. The results further indicated that out of 363 subject, those who fell under the age groups of 18 – 27 , 48 – 57 year and 58 years and above showed no infection with mycobacterium isolates, whilst 9 (5.3%), 4 (6.0%) of the age groups 28 – 37, 38 - 47 had mycobacterium isolates. The Chi - square testindicated that there was no significant relationship between the ages of PLWHA and mycobacterium in sputum cultures.

Table 25: TB Sensitivity Results for the PLWHA Subjects with their Ages

AGE OF SUBJECTS (YEARS)	SENSITIVITY RESULTS		TOTAL
	SENSITIVE TO ISONIAZIDE ETHAMBUTOL STREPTOMYCIN AND RIFAMPICIN (%)	NIL (%)	
18- 27	0	87 (100)	87
28- 37	9 (5.3)	160 (94.7)	169
38- 47	4	63	67

	(6)	(94)	
48- 57	0	30 (100)	30
58- 67	0	10 (100)	10
TOTAL	13 (3.6)	350 (96.4)	363 100%)

$\chi 2$ (4) = 7.313, P = 0.120

Results from Table 25, show that 13 (3.6%) of the subjects were sensitive to isoniazide, ethambutol, streptomycin and rifampicin whilst 350 (96.4%) indicated no *M. tuberculosis* growth hence sensitivity was not carried out for this group. The chi – square testindicated that there was no significant relationship between the age of PLWHA and sensitivity to isoniazide, ethambutol, streptomycin and rifampicin.

CHAPTER FIVE

DISCUSSION OF RESULTS

5.1 CLINICAL OUTCOMES OF PLWHA WITH OR WITHOUT TB

As HIV infection progresses and immunity declines, patients become more susceptible to infections. These include TB, pneumonia, recurrent fungal infections of the skin and oropharynx, and herpes zoster. These infections can occur at any stage of progression of HIV infection and immunosuppression. Some patients may develop constitutional symptoms (unexplained fever and weight loss), previously known as

"AIDS-related complex" (ARC). Some patients develop chronic diarrhoea with weight loss, often known as "slim disease". Certain specific HIV-related diseases occur predominantly with severe immunosuppression. These include certain opportunistic infections (e.g. cryptococcal meningitis) and certain tumours (e.g. Kaposi sarcoma). At this late stage, unless patients receive specific therapy for HIV infection, they usually die in less than 2 years. This late stage is sometimes known as "full-blown AIDS".

WHO has developed a clinical staging system (originally for prognosis), based on clinical criteria.The definition of symptoms, signs and diseases is according to clinical judgement. Clinical condition or performance score, whichever is the higher, determines whether a patient is at clinical stage 1, 2, 3 or 4. Clinical stage is important as a criterion for starting antiretroviral (ARV) therapy.

HIV probably increases susceptibility to infection with *M. tuberculosis.* HIV increases the risk of progression of *M. tuberculosis* infection to TBdisease. This risk increases with increasing immunosuppression. HIVincreases not only the risk but also the rate of progression of recent or latent *M. tuberculosis* infection to disease. Chest x-ray changes in TB/HIV patients reflect the degree of immunocompromise. In mild immunocompromise, the appearance is often classical (with cavitation and upper lobe infiltrates). In severe immunocompromise, the appearance is often atypical (Affusim*et al.*, 2011).

The clinical findings from the study revealed that dry cough ($p<0.000$), cough with sputum ($p<0.000$), blood in sputum ($p<0.000$), shortness of breath ($p<0.000$), chest pain

($p<0.000$), weight loss ($p<0.015$), swelling around the neck or inguinal ($p<0.000$), diarrhea

($p<0.000$), skin rashes ($p<0.001$), and x-ray findings ($p<0.015$), implying that a significant relationship exist between the HIV and TB status of the study respondents and the afore mentioned clinical symptoms.

However, the study observed that there was no significant relationship between fever, night sweat, tiredness, loss of appetite, joint pain and the HIV and TB status of respondents

($p>0.05$). Further details revealed that all the TB –HIV coinfected, 138(39.4%) of the PLWHA without TB and 16(8.8%) of the healthy controls had dry cough. Also, all the TB – HIV coinfected, 286(81.7%) PLWHA without TB and 29 (16.0%) of the healthy controls reported of fever infection.These data findings are in agreement with the findings of Affusim*et al.*(2011), Madhi*et al.*(2000), Corbette*et al.* (2008) and Tegbaru*et al.* (2011) who also reported dry cough, night sweat, fever, weight loss, cough with sputum and blood stained sputum in infected patients.

Using chest x-ray as a diagnostic tool, the study observed that out of the 13 HIV/TB co – infected patients, 1 (7.7%) showed unlikely, 7(53.8%) showed probably, whilst 5 (38.5%) indicated most probable for TB infection or patches. Out of the 350 PLWHA without TB, 327 (93.4%) showed unlikelihood of TB infection. Whilst 23 (6.6%) revealed likelihood of a TB infection in their x- ray film. These findings agree with the results of Tegbaru*et al.*(2011) who confirmed that chest X-ray results were indicating TB to be very likely in 86.2% of the smear positives and 89.0% of the confirmed (smear and culture positive) TB cases. Other findings revealed that the body mass index of patients without TB was 23.8 kg/m^2, while the BMI of patients with TB Co infection was 21.6 kg/ m^2(T-test = 5.104, p value < 0.001). There was a significant

relationship between low BMI and TB co infection as collaborated by the results of Affusim*et al.* (2011).

5.2 CD4 VALUES OF PLWHA WITH OR WITHOUT TB

HIV infects cells that have the CD4 antigen molecules on their surface. These cells are principally the helper subset of T-lymphocytes, which are central to cell-mediated immunity(Tegbaru*et al.,* 2011). They are called CD4+ T-lymphocytes. In recent years it has also been discovered that HIV needs other molecules, called chemokines, on the cell surface to gain entry into the cell (Affusim*et al.,* 2011). Patients who do not have some of these specific chemokines (for example, CCR5) are more resistant to HIV infection. Others, who have molecular changes in these chemokine receptors, progress more slowly to AIDS. The critical abnormality resulting from HIV infection is a progressive decline in the number of CD4+ T-lymphocytes.

These cells are the most important cells in the cell-mediated immune response. In addition the surviving CD4+ T-lymphocytes do not perform their functions as well as they did before infection. Progressive HIV infection therefore causes progressive decline in immunity. The CD4 count serves as the major laboratory indicator of immune function in patients who have HIV infection. It is one of the key factors in deciding whether to initiate ART and prophylaxis for opportunistic infections and it is the strongest predictor of subsequent disease progression and survival (Tegbaru*et al.,* 2011). Patients who initiate therapy with a low CD4 count or at older age may have a blunted increase in their count despite virologic suppression. As HIV infection progresses, CD4+ T-lymphocytes decline in number and function. These cells play an important role in the body's defence against tubercle bacilli. Thus, the immune system becomes less able to prevent the growth

and local spread of *M. tuberculosis.* Disseminated and extrapulmonary disease is more common (Affusim*et al.,* 2011).

The mean CD4 count results of the study participants indicated that the TB - HIV coinfected respondents had 264.42 ± 76.020 cells /mm^3, the PLWHA without TB had 375.31 ± 297.640 cells /mm^3 whilst the healthy control group also recorded 748.04 ± 281.100 cells /mm^3. The mean difference among the HIV and TB status of the study respondents were significant ($p<0.000$). However, there was no significant relationship between the gender, CD4 count results and HIV and TB status of the respondents ($\chi 2$ (1) = 0.043, P = 0.835). Detailed findings of this study revealed that among the HIV+/TB+, 6 (75.0%) males and 4 (80.0%) females had CD4 count less than 200 cells/mm^3, 2 (25.0%) males and 1 (20.0%) males and 1 (20.0%) females had CD4 between 200 and 350 cells/mm^3, none of the subjects had CD4 count of 350 - <500 cells/mm^3 and 500 cells/mm^3 and above. Also, 52 (46.4%) males and 25 (10.5%) females had CD4 less than 200, 3 (2.7%) males and 126 (52.9%) females had CD4 between 200 and 350 cells/mm^3, 52 (42.4%) males and 83 (34.9%) females had CD4 between 350 and 500 cells/mm^3 and 5 (4.5%) males and 4 (1.7%) females had CD4 count above 500 cells/mm^3. The results further revealed that none of the subjects had CD4 counts of less than 200 and 200 - < 350 cells/mm^3. However 5 (6.9%) males and 12 (11.09%) females had CD4 350 - < 500 cells/mm^3 and 67 (93.1%) males and 97 (89.0%)females had CD4 count greater than 500. cells/mm^3.

These findings were consistent with the report of Tarbarsi*et al.*(2008) and that the statistical analysis also showed more men in the category of ≥ 200 CD4 group (p = 0.05). Findings in this study contrast with the report of Tegbaru*et al.* (2011) and Affusim*et al.*(2011). Meanwhile, there were some similarities between the present results and the

findings of Madhi*et al.* (2000) but differed in sense that the respondents for this study were 18 years and above while respondents in the workMadhi*et al.* (2000) were all children.

5.3 IMMUNOHAEMATOLOGICAL MARKERS AND TB AND HIV STATUS

The reduction in the number of circulating cells is a common complication of infection with human immunodeficiency virus (HIV) and Tuberculosis (TB), and in the course of the disease, more than 70% of the patients developed anaemia that frequently required transfusion (Jemikalajah and Okogun, 2008). The most commonly employed haematological indices include; packed cell volume, platelets count and total white blood cells count (Affusim*et al.,* 2011). Neutropenia, lymphopenia and thrombocytopenia are common features, indicating that more than one haemopoietic lineage may be impaired. Dysfunction of the bone marrow has been suggested as a possible mechanism and the degree of cytopenia often reflects severity of the disease (Tarbarsi*et al.,* 2008). Reports also indicate that as HIV disease progress, the prevalence and severity of anaemia increase. Anaemia has been found to significantly enhance progression to HIV/AIDS and lead to an increase risk of death in patients with HIV (Nwachukwu and Peter, 2010). However, TB may occur in some patients with haematological disease by coincidence or more probably arise as a result of opportunistic infection due to debility or to impaired immunological response to infection, which characterizes the disease of the reticuloendothelial system.

Findings from the study indicated that there were significant mean differences between all immunohaematological markers (haemoglobin levels, white blood cells

count, packed cell volume and platelets count) tested and the TB and HIV status of the participants ($p<0.000$).

The mean haemoglobin levels reported that the TB-HIV coinfected had (9.69 ± 3.812) g/dl, the PLWHA without TB had (10.70 ± 2.307) g/dl whilst the healthy control subjects had (12.41 ± 2.451) g/dl. Mean findings from the white blood cell count revealed that the TB-HIV coinfected had (4.90 ± 2.154) x 10^9/l, PLWHA without TB had (5.91 ± 2.432) x 10^9/l whilst the healthy control subjects reported (6.92 ± 3.124) x 10^9/l.

Packed cell volume measures the percentage of blood volume taken up by the red blood cells. Very low readings for packed cell volume can indicate anemia. With anemia, the cells do not get enough oxygen to function normally. People with anemia feel tired all the time and might look pale. Mean finding from the packed cell volume from the study showed that the HIV^+/TB^+ had (32.31 ± 4.813) %, HIV^+/TB^- had (34.1 ± 4.367) % whilst the HIV^-/TB^- recorded (36.31 ± 4.211) %.

Platelets help stop bleeding by forming clots and scabs. Thrombocytopenia may lead to internal bleeding or could cause one to bruise easily. Mean platelets count from the study indicated that the HIV^+/TB^+ had (163.29 ± 65.110) x 10^9/l, the HIV^+/TB^- had (195.16 ± 88.710) x 10^9/l whilst the healthy control also had (240.07 ± 99.42 x 10^9/l.

Interestingly, findings of this study by and large agreed with of Affusim*et al.*,(2011), Audu*et al.* (2004), Nwachukwu and Peter (2010) and finally with Tarbarsi*et al.*(2008). The differences in the white blood cells count to the infections according to gender may be hormonal but the end results are often similar. The PCV controls show that females were more prone to blood loss, implying higher strain on their erythropoietic activities, secondary to regulate menstrual flow. When this is considered against the backdrop of a relatively poor nutritional status, the debilitating effect HIV and TB

infection would be better understood. This study therefore underscore the need for routine haematological investigations such as Haemoglobin estimation, PCV estimation, WBC count, and Platelet count as a monitoring tool to enable proper care and management of HIV and TB patients as concluded byAffusim*et al.,* (2011).

5.4 ERYTHROCYTE SEDIMENTATION RATE VALUES IN PLWHA WITH OR WITHOUT TB

Ukpe and Southern (2006) reported without substantiatingevidence, that very high erythrocyte sedimentation rate (ESR)values (≥ 100 mm/h) are associated with tuberculosis (TB),Hodgkin's disease, multiple myeloma and chronic infectiveor inflammatory conditions. Interestingly, there are currently nostudies examining extreme ESR elevation in the Ghanaian population with high prevalence of HIV/AIDS. The ESR is a blood test measuring the rate of fall of red blood cells in a column of anticoagulated blood in 1 hour, with the units expressed in millimetres per hour (mm/h).

In clinical practice it is commonly utilised as a nonspecific test for a wide range of pathological conditions such as acute or chronic infections, systemic inflammatory conditions and neoplastic conditions (Levay and Retief, 2005). The ESR is usually elevated in such conditions, and infections, collagen diseases, metastatic malignant tumours and renal disease are said to be the leading causes of elevated values ≥ 100 mm/h (Levay and Vilijoen, 2002). The ESR test is commonly carried out as a nonspecific test during the initial diagnostic work-up for TB, which is a chronic bacterial infection. Some previous studies have documented ESR values associated with the infection (Ukpe and Southern, 2006;Affusim*et al.,* 2011; Tarbarsi*et al.,* 2008 andNwachukwu and Peter, 2010).

Meanwhile, the mean ESR findings from the study revealed that the HIV^+/TB^+ had (115.13 ± 11.820) mm/hr, the HIV^+/TB^- had (102.51 ±17.350) mm/hr whilst the HIV^-/TB^- had (10.03 ± 8.495) mm/hr. This may be due to delayed diagnosis of TB in the HIV subjects. In view of this, some of the HIV subjects may have developed Immune Reconstitution Inflammatory Syndrome (IRIS) which is most often times associated with HIV/TB coinfected patients at the onset of Anti-Retroviral Therapy (Corbettee*et al.*, 2009). This also supports the fact that delayed diagnosis of HIV is a major problem in Ghana and therefore efforts must be intensified to improve surveillance strategy to detect HIV cases in their early stages of sero-conversion. Further ESR result indicated that there was no significant relationship between the HIV and TB status and gender and their ESR readings (p=0.715). Also it was observed that all the HIV^+/TB^+ respondents had ESR values of >100 mm/hr whilst majority of the healthy control respondents had 0-8 mm/hr. Detailed results revealed that all the 13 TB-HIV coinfected had > 100 mm/hr respectively. With respect to the 350 HIV+/TB- participants, 1 (0.3%), 80 (22.9%) and 269 (76.9%) had ESR results of (0 -8) mm/hr, (51 – 100) mm/hr and >100 mm/hr respectively. Among the healthy controls 154 (28.5%) and 27 (14.9%) of the participants had ESR results of (0 -8) mm/hr and (9 – 50) mm/hr. T-test analysis shows that there was significant mean difference between the HIV and TB status and ESR results (p< 0.000).

Results from the study agreed with the findings of Ukpe and Southern (2006),Tarbarsi*et al.* (2008), Nwachukwu and Peter (2010). Findings of the study were in line with that of Affusim*et al.*(2011) which concluded that markedly elevated ESR remained a constant useful finding in making a diagnosis of TB. The mean erythrocyte sedimentation rate (ESR) of TB co-infected patients was significantly higher than that of those without TB infection. Though the ESR was raised in HIV infection, it was extremely raised in TB co-infection. This is expected, because ESR which is mildly

raised in most inflammatory conditions is grossly increased in TB infection. This is similar to what was reported by Affusim*et al.*(2011).

5.5 TB RESULTS OF THE CO-INFECTED

Mycobacteria are "acid- and alcohol-fast bacilli" (AFB) often shortened to "acid-fast bacilli" (AFB). The waxy coat of mycobacteria retains an aniline dye (e.g. carbolfuchsin) even after decolorization with acid and alcohol.Use of this stain to detect TB bacilli requires a special fluorescence microscope. The fluorochrome stain is phenolic auramine or auraminerhodamine. After acid-alcohol decolorization and a methylene blue counterstain, the bacilli fluoresce bright yellow against a dark background. The advantage of this method is that smears can be scanned quickly under low magnification. It is important to check fluorochrome stain-positive smears using the Z-N stain. When *M. tuberculosis* is cultured from clinical specimens (e.g. sputum, lymph node aspirate, and cerebrospinal fluid) this provides the gold standard for the definitive diagnosis of TB. Tubercle bacilli that have grown in culture can also be tested *in vitro* for sensitivity to anti-TB drugs. The usual culture medium is Löwenstein Jensen, although liquid culture media and automated systems (e.g. Bactec) can also be used in more sophisticated laboratories.

M. tuberculosis is a slow-growing organism, and it often takes between 6 and 8 weeks before cultures become positive(Tarbarsi et al., 2008). Culture results may therefore not be helpful in making a rapid individual diagnosis, although they can be helpful retrospectively. There is also the need for considerable laboratory infrastructure and laboratory skills in order to sustain a mycobacterial culture facility. Most developing countries have one or two mycobacterial reference centres where cultures and drug

sensitivity analysis can be performed. However, most hospitals will not have TB culture facilities readily available.

Results from the study showed that 8 (2.2%) of the PLWA had Acid Fast Bacilli through sputum smear microscopy whilst 355 (97.8%) did not have AFB. Further results indicated that within the age groups 18 – 27, 48 – 57 and 58 years and above did not have AFB , whilst those within the age group 28 – 37 years and 38 - 47 , 6 (36%) and 2 (3%) respectively had AFB. The chi- square results indicates that there was no significant relationship between the age of PLWHA and AFB in sputum smear. Also, findings indicated that 13 (3.6%) had *Mycobacterium* isolated through culture whilst 350 (96.4%) had no isolates for mycobacterium. The results further indicates that out of 363 subject, those who fell under the age groups of 18 – 27 , 48 – 57 year and 58 years and above showed no mycobacterium isolates, whilst 9 (5.3%), 4 (6%) of the age groups 28 – 37, 38 - 47 had mycobacterium isolates. The Chi - square testindicate that there was no significant relationship between the age of PLWHA and mycobacterium in sputum cultures. Meanwhile, 13 (3.6%) of the subjects were sensitive to isoniazide, ethambutol, streptomycin and rifampicin whilst 350 (96.4%) had no growth. The chi – square results indicates that there was no significant relationship between the age of PLWHA and sensitivity to isoniazide, ethambutol, streptomycin and rifampicin.

From the present study, it could be inferred that TB/HIV co-infection was commonest among age 28 – 37 years. The TB/HIV co-infection was common among the men than the women and this could be attributed to the differences in social life styles. This study also found that sputum culture 13(3.6%) was more sensitive than sputum smear microscopy 8(2.2%).

This finding did not agree with the report of Tarbarsi*et al.* (2008) who observed that sputum smear and culture were sensitive for acid-fast bacilli in 13 (87%) and 9 (60%)

patients respectively due to high rate of contamination among the culture samples. Other researchers such asOnubogu*et al.*(2010),Nwachukwu and Peter (2010) andAffusim*et al.*(2011) also reported that TB culture was more sensitive compared to sputum smear microscopy.

CHAPTER SIX

CONCLUSION ANDRECOMMENDATIONS

6.1 CONCLUSION

Based on the findings that emerged from the study, the following conclusions were made.

1. There were significant mean differences between all the immunohaematologicalmarkers (Haemoglobin level, White blood cells count, Packed cells volume, Platelets count, Erythrocyte Sedimentation Rate, CD4 count) and HIV and TB status of the study participants($p< 0.00$).
2. All the TB-HIV coinfected respondents had ESR value of greater than 100mm/hr.
3. None of the females of the PLWHA respondents had a normal ESR (0- 8) mm/hr.
4. There were significant relationships between TB and HIV status of the respondents and clinical symptoms (dry cough, chest pain, cough with sputum, blood in sputum, shortness of breath, weight loss, swelling around the neck and diarrheoa ($p< 0.05$).
5. The highest rate of infection for infection for both *M. tuberculosis* and HIV was among the age group 28 – 37 years.
6. Among the coinfected patients, TB was diagnosed in 8 (2.2%) by sputum smear microscopy alone, whilst 13 (3.6%) by sputum culture. The higher yield of TB cases by culture alone compared to microscopy alone further confirms the higher sensitivity of culture for TB case detection among TB/ HIV coinfected patients.
7. There was no case of multi- drug resistance in the TB- sensitivity results.

In summary, the clinical symptoms and immunohaematological markers, (Full Blood Count, Erythrocyte Sedimentation Rate, CD4 count) were important and could be used in the monitoring and management of TB and HIV coinfection.

6.2 RECOMMENDATIONS

The study therefore recommends that immunohaematological indices (CD4 count, FBC and ESR) must be performed routinely to monitor TB and HIV patients on regular basis in order to reduce morbidity and mortality associated with the diseases. Future research should be conducted to identify strains of MTB in order to help prevent MDR cases among HIV patients. This study investigated two separate diseases and the interaction between them, but the absence of existing measurement instruments in Ghana was a major limitation of the study.

REFERENCES

Affussim, C., Kesieme E and Abah, V. O. (2011). The Pattern of Presentaion of Tuberculosis in

HIV seropositive Patients Seen at Benin City, Nigeria. Ambrose Alli University, Ekpoma.

Audu, R. A., Akanmu, A. S., Efienemokwu, C., Musa, A. Z., Lemoha, E., Odunaike, M. I.,

Funso- Adebayo, E. O., Meshack, E., and Idigbe, E. O. (2004). Changes in Serum Proteins and Creatinine Levels in HIV Infected Nigerians. Nigerian *Journal of Health and Biomedical Sciences.* 3(2): 69-72.

Audu, R. A., Akanmu, A. S., Efienemokwu, C., Dele, A. Z, Lemoha, E., Odunaike, M. I, and Idigbe, E. O., (2004). Impact of Tuberculosis Co-infection on The Level of PCV in HIV Infected Patients. *Nigerian Quarterly Journal of Hospital Medicine.* 14(2): 115- 117.

Badri, M., Ehrlich, R., Wood, R. and Maartens, G. (2001). Initiating Co-trimoxazole Prophylaxis in HIV-Infected Patients in Africa: An Evaluation of the Provisional WHO/UNAIDS Recommendations. *AIDS*. Vol. 15, 1143 – 1148.

Bock, N.N., Jensen, P.A., Miller, B, &Nardell, E. (2007). Tuberculosis infection control in resource-limited settings in the era of expanding HIV care and treatment. The Journal of Infectious Diseases 196(Suppl 1), S108–S113.

Braitstein, P. (2006). Mortality of HIV-1-Infected Patients in the First year of Antiretroviral Therapy: Comparison between Low Income and High-Income Countries. *Lancet* 367:817–824.

Cahn, P., Perez, H., Ben, G. (2003). Tuberculosis and HIV: a partnership against the most vulnerable. J IntAssocPhysicians AIDS Care (Chic Ill);2:106–23. [PubMed]

Campos, P. E., Chiappe, M., Carcamo, C., Garcia, P., Buendia, C., Segura, P. (2003).*STI Prevalence among Female Sex Workers from 24 Peruvian Cities*. Paperpresented at the 8th World STI/AIDS Congress/40th IUSTI World General Assembly/XIV Pan American STI/AIDS Congress, Punta del Este, Uruguay.

Cook, V. & Long, R. (2007). Nonrespiratory tuberculosis. In Long, R. & Ellis, E. (Eds) *Canadian Tuberculosis Standards 6th Ed.* Public Health Agency of Canada.

Cole, J., Pryor, M., Medigue, C. & Cole, S. (2002). Re-annotation of the genome sequence of *Mycobacterium tuberculosis* H37RV. *Microbiology, 148(1),* 2967-2973.

Corbette, E. L., Zerai, A., Cheung, B. Y., Bandason, T., Dauya, E., Munyati, S. S., Butterworth, Rusikaniko, S., Churchyard, G. J., Mungofa, S., Hayes, R. J. and Mason P. R. (2009).*Bull World Health Organ*. 88: 13- 21.

Corbette, E. L., Watt, C. J., Walker, N., Maher, D., Williams, B. G. (2003). The Growing Burden of *Tuberculosis*: Global Trends and Interaction with the HIV Epidemic. Arch. Int. Med., 163: 1009–1021.

Datiko, D. G., Yassin, M. A., Chekol , L.T, Kabeto, L. E., Lindtjørn, B. (2008). The Rate of TB-HIV Co-infection Depends on the Prevalence of HIV Infection in a Community. *BMC Public Health*, 8: 266. doi: 10.1186/1471-2458-8-266.

Deschamps, M., Fitzgerald, D., Pape, J., & Johnson, W. (2000). HIV infection in Haiti: natural history and disease progression. *AIDS, 14*(16), 2515-2521.

Dye, C. 2006.Global epidemiology of tuberculosis. Lancet 367:938-940.

El-Sony ,A. I., Khamis, A. H., Enarson, D. A, Baraka, O., Mustafa, S. A, Bjune, G. (2002). Treatment Results of DOTS in 1797 Sudanese Tuberculosis Patients with or without HIV Co-infection. *International. Journal of .Tuberculosis. Lung Diseases.*,6: 1058–1066.

Ghana Health Service. Implementation of TB/HIV collaborative activities in Ghana: technical policy and guidelines Accra. http://www.ghanahealthservice.org/tb_publications.php.

Haileyeus, M. H, O'Brien, R., Nunn, P. (2007**).**Diagnosis of Smear-Negative Pulmonary Tuberculosis in a People with HIV infection or AIDS in Resource -Coinstrained Settings: Informing Urgent Policy Changes. *Lancet Public Health* 2007,369(9578)**:**2042-2049

Harries, A. D. & Dye, C. (2006).Tuberculosis. Annals of Tropical Medicine and Parasitology, 100, 415–431.

Houghton, M. (2002).*Tuberculosis: definitions, synonyms and much more from Answers.com* [On-line].Retrieved June 16, 2005.http://www.answers.com/topic/tuberculosis

Jemikalajah, J. S. S. D. and Okogun, G. A., (2009). Health Point Prevalence of HIV and Pulmonary Tuberculosis among Patients in Various Parts of Delta State, Nigeria.*Saudi Med Journal*.30(3); 387 -391.

Long, R. &Shwartzman, K. (2007).Transmission and pathogenesis of tuberculosis. In Long, R. & Ellis, E. (Eds) *Canadian Tuberculosis Standards 6th Ed.* Public Health Agency of Canada.

Lucas S., Nelson, A. M., (1994). Tuberculosis: pathogenesis, protection, and control. Washington, DC: ASM Press. Pathogenesis of tuberculosis in human immunodeficiency virus-infected people; pp. 503–13.

Madhi, S. A., Huebner, R. E., Doedens, L., Aduc, T., Wesley, D., Cooper, P. A., (2000). HIV- 1 Co- infection in Children Hospitalised with Tuberculosis in South Africa. International *Journal of Tuberculosis Lung Diseases*. 4 (5): 448- 454

Masur, H., Kaplan, J. E., and Holmes, K. K. (2002). Guidelines for Preventing Opportunistic Infections among HIV-Infected Persons Recommendations of the U.S. Public Health Service and the Infectious Diseases Society of America.*Annals of Internal Medicine*, 137(5 Pt 2), 435_78.

Mfinanga, S.G., Egwaga, S. M., Chode, T.M., Matee, M. I., Ngowi, P. E., Lwilla, F., Cobelens, F. G. J. (2007). Low specificity of HIV – testing on sputum kept at ambient temperatures for 4 – 7 days: A blinded comparism. BMC Clinical Pathology; 7:8.

Ministry of Health/ Ghana Health Service (2006). Technical and Policy Guidelines for TB-HIV Collaboration in Ghana.Draft.

Moore, D., Liechty, C., Ekwaru, P., Were, W., Mwima, G., Solberg, P., Rutherford, G., and Mermin, J. (2007).Prevalence, Incidence and Mortality Associated with Tuberculosis in HIV-Infected Patients Initiating Antiretroviral Therapy in Rural Uganda. AIDS; 21(6):713-719.

Moulding, T. (1988).Pathogenesis, pathophysiology, and immunology.In Schlossberg, D. (Ed). Tuberculosis, 2nd Ed. New York: Springer-Verlag, Inc.

Nwachukwu, E. and Peter, G, A. (2010). Prevalence of *Mycobacterium Tuberculosis* and Human Immunodeficiency Virus (HIV) Infections in Umuahia, Abia state, Nigeria,*African Journal of Microbiology Research* Vol. 4(14) pp. 1486-1490.

Onubogu, C. C, Kunle-Ope, C. N, Onyejepu, N, Nwokoye, N. N, Raheem, T. Y., Igbasi, U.T., Tochukwu, N. E, Omoloye, R. M, Ejezie, C. O, Musa, A. Z, Odunukwe, N. N, Onwujekwe, D. I. and Idigbe, E. O. (2010).Prevalence of Tuberculosis and Human Immunodeficiency Virus (TB/HIV) Co-infections amongst Patients with Bronchopulmonary Disorders in Lagos.*African journal of microbiology research*. pp. 1904 – 1908

Pape, J.W. (2004). Tuberculosis and HIV in the Caribbean: approaches to diagnosis, treatment,
and prophylaxis.*Top HIV Med* 2004, **12:**144-9. PubMed Abstract | Publisher Full Text

Prins, J. M., (1999).Immuno-activation with Anti-CD3 and Recombinant Human IL-2 in HIV-1-
Infected Patients on Potent Antiretroviral Therapy..*AIDS.*13:2405–10.

Reid, A., Scano, F., Getahun, H., et al. (2006). Towards universal access to HIV prevention,
treatment, care and support: the role of tuberculosis/HIV collaboration. Lancet Infect Dis. 2006;6:483–95. doi: 10.1016/S1473-3099(06)70549-7. [PubMed] [Cross Ref]

Saunders, M., Lewis, P., Thornhill, A., Research Methods for Business Students. Financial
Times/Prentice Hall, 2007 - Business & Economics – p. 62.

Sharma, S. K, Mohan, A., and Kadhiravan, T. (2005).HIV-TB Co-infection: Epidemiology,
Diagnosis & Management.*Indian Journal of Med Research*, 12:550-67.

Sonnenberg, P., Murray, J., Glynn, J. R., Shearer, S., Kambashi, B. and Godfrey-Faussett, P.
(2001).HIV-1 and recurrence, relapse, and reinfection of tuberculosis after cure: a cohort study in South African mineworkers.*Lancet.*358(9294):1687-93.

Tabarsi, P., Mirasaeidi, S. M., Amiri, M., Mansouri, S. D., Masjedi, M. R.andVelayati, A. A.
(2008) Clinical and Laboratory Profile of Patients with Tuberculosis/ Coinfection at a National Referral Centre: A Case Series. National Research Institute of Tuberculosis and Lung Diseases.

Tegbaru, B., Messele, T., Hailu E., Meless, H., Girma, M., Girmachew, F., Demissie, D.,
Lemma, E., Gebeyehu, G. E., Van Baarle, D., WorlayDawit.(2011) Clinical Outcomes and Laboratory Results of Tuberculosis Patients with or without HIV Infection in Two Health Intitutions in Addis Ababa, Ethiopia.Ethiopian Health and Nutrition Research Institute.

Ukpe, I. S and Southern, L. (2006) Erythrocyte Sedimentation Rate values in Active
Tuberculosis With and Without HIV Co-infection.*Sam. Journal*.

UNAIDS 2009. AIDS epidemic update: November 2009.UNAIDS, Geneva, Switzerland.

World Health Organisation (2008a) New Laboratory Diagnostic Tools for Tuberculosis Control.
Geneva, World Health Organization.

World Health Organisation (2008b) Molecular Line Probe Assays for Rapid Screening of

Patients at Risk of Multidrug-Resistant Tuberculosis (MDR-TB) - *Policy Statement*. Geneva, World Health Organization. http://www.who.int/tb/features_archive/policy_statement.pdf

World Health Organization (2008c), Strategic and Technical Advisory Group for *Tuberculosis*.

World health organization (2005) TB/HIVresearch priorities in resource-limited settings.
Report of an expert consultation 14–15 February 2005 Geneva, Switzerland.who/htm/tb/2005.355.

Yassin, M. A., Takele, L., Gebresenbet, S., Girma, E., Lera, M., Lendebo, E., Cuevas, L. E:
(2006) HIV and Tuberculosis Coinfection in the Southern Region of Ethiopia: A Prospective Epidemiological Study. *Scand Journal of Infectious Diseases* ;36:670-673.

APPENDIX

DEPARTMENT OF THEORETICAL AND APPLIED BIOLOGY - KNUST

QUESTIONNAIRE

Dear Respondent,

I am a student of the Kwame Nkrumah University of Science and Technology conducting research into TB infection among HIV infected individuals at selected ART Clinics in the Greater Accra Region of Ghana. The research is purely for academic purposes and any information obtained from individuals shall remain private and confidential. You are kindly requested to carefully read each questions in the questionnaire and make the appropriate response(s) as would apply to you. THANK YOU.

INSTRUCTIONS

Please tick as appropriate

1. Gender of respondent

(a) Male [ ] (b) Female [ ]

2. Age group of respondents

(a) 18-27 yrs [ ] (b). 28-37 yrs [ ]

(c). 38 – 47 yrs [ ] (d). 48 – 57 yrs [ ]

(e). 58 – 67 yrs [ ] (f). 68 yrs and above [ ]

3. Marital status of respondent

(a) Single [ ] (b) Married [ ]

(c) Widowed [ ] (d) Divorced [ ] (e) others (specify) ----------

4. Religion

(a) Christian [ ] (b) Moslem [ ] (c) Traditional [ ] (d) Others (specify) ----------

5. Educational status:

(a) No schooling [ ] (b) Primary [ ] (c) JSS [ ] (d) SSS [ ] (f) Degree/Diploma/Post-Secondary Education [ ]

6. Please indicate your occupation

(a) Farmer [ ] (b) Student [ ] (c) Business man/woman [ ]

(d) House wife [ ] (e) Government employee [ ] (f) Unemployed [ ]

(g) Daily labourer [ ] (h) others (specify) ----------

Please indicate whether or not if you have experienced the following conditions within the last six months.

7. Dry cough? Yes [ ] No [ ]

8. Cough with sputum? Yes [ ] No [ ]

9. Blood in sputum? Yes [ ] No [ ]

10. Chest pains? Yes [ ] No [ ]

11. Short breath? Yes [ ] No [ ]

12. Fever? Yes [ ] No [ ]

13. Night sweat? Yes [ ] No [ ]

14. Tiredness? Yes [ ] No [ ]

15. Weight loss? Yes [ ] No [ ]

16. Loss of appetite? Yes [ ] No [ ]

17. Swelling around the neck, inguinal region? Yes [ ] No [ ]

18. Diarrhoea? Yes [ ] No [ ]

19. Skin rashes? Yes [ ] No [ ]

Thank you

GLOSSARY

Acid-Fast Bacilli (AFB): Microorganisms that are distinguished by their retention of specific stains even after being rinsed with an acid solution. The majority of AFB in patient specimens are mycobacteria. The term, mycobacteria, includes *Mycobacterium tuberculosis* complex as well as non-*tuberculous mycobacteria* (NTM). A positive nucleic acid amplification (NAA) or culture result is needed to differentiate *M. tuberculosis* from the others.

Acquired Immunity: Immunity that develops during a person's lifetime. There are two types of acquired immunity: active immunity and passive immunity.

Acquired Immunodeficiency Syndrome (AIDS): A disease of the immune system due to infection with HIV. HIV destroys the CD4 T lymphocytes (CD4 cells) of the immune system, leaving the body vulnerable to life-threatening infections and cancers. Acquired immunodeficiency syndrome (AIDS) is the most advanced stage of HIV infection.

Acute HIV Infection: Early stage of HIV infection that extends approximately 2 to 4 weeksfrom initial infection until the body produces enough HIV antibodies to be detected by an HIV antibody test. Because the virus is replicatingrapidly, HIV is highly infectious during this stage of infection.

Antigen: Any substance that is foreign to the body and triggers an immuneresponse. Antigens include bacteria, viruses, and allergens, such as pollen.

Antiretroviral (ARV): A drug used to prevent a retrovirus, such as HIV, from replicating.The term primarily refers to antiretroviral (ARV) HIV drugs.

Antiretroviral Therapy (ART): Treatment with drugs that inhibit the ability of retroviruses (such as HIV) to multiply in the body. The antiretroviral therapy recommended for HIV infection is referred to as highly active antiretroviral therapy

(HAART), which uses a combination of medications to attack HIV at different points in its life cycle.

CD4 Count: ALSO KNOWN AS: CD4 Cell Count, CD4 T Lymphocyte Count**.** A laboratory test that measures the number of CD4 T lymphocytes (CD4 cells) in a sample of blood. In people with HIV, the CD4 count is the most important laboratory indicator of immune function and the strongest predictor of HIV progression. The CD4 count is one of the factors used to determine when to start antiretroviral therapy (ART). The CD4 count is also used to monitor response to ART.

Coinfection: When a person has two or more infections at the same time. Forexample, a person infected with HIV may be coinfected with tuberculosis (TB).

Dyspnea: Difficult or labored breathing or shortness of breath.

Eligibility Criteria: Also known as: Exclusion/Inclusion Criteria, Inclusion/Exclusion CriteriaFactors used to determine whether a person is eligible (inclusioncriteria) or not eligible (exclusion criteria) to participate in a clinical trial.Eligibility criteria may include disease type and stage, other medicalconditions, previous treatment history, age, and gender.

Extra-pulmonary TB: TB disease that occurs in places other than the lungs, such as the lymph nodes, the pleura, the brain, the kidneys, or the bones; most types of extrapulmonary TB are not infectious.

Full Blood Count (FBC): A blood test that measures the following components in a sample of blood: red blood cells, white blood cells, platelets, and hemoglobin. A full blood count (FBC) with differential also measures the levels of the five types of white blood cells found in blood: neutrophils, lymphocytes, monocytes, eosinophils, and basophils. The FBC is used to assess overall health and to diagnose and guide treatment of numerous diseases.

HIV-1: One of the two types of HIV, the virus that causes AIDS. AIDS is themost advanced stage of HIV infection. HIV-1 is transmitted throughdirect contact with HIV-infected body fluids, such as blood, semen, andgenital secretions, or from an HIV-infected mother to her child duringpregnancy, delivery, or breastfeeding (through breast milk). HIV-1 isresponsible for the majority of HIV infections worldwide.

HIV-2: One of the two types of HIV, the virus that causes AIDS. AIDS is the most advanced stage of HIV infection. HIV-2 infection is endemic toWest Africa. Like HIV-1, HIV-2 is transmitted through direct contactwith HIV-infected body fluids, such as blood, semen, and genitalsecretions, or from an HIV-infected mother to her child duringpregnancy, delivery, or breastfeeding (through breast milk). HIV-2infection generally takes longer to progress to symptomatic HIV/AIDSand has a lower mortality rate than HIV-1 infection.

Human Immunodeficiency Virus (HIV): The virus that causes AIDS, which is the most advanced stage of HIVinfection. HIV is a retrovirus that occurs as two types: HIV-1 and HIV-2.Both types are transmitted through direct contact with HIV-infected body fluids, such as blood, semen, and genital secretions, or from an HIV-infected mother to her child during pregnancy, birth, or breastfeeding (through breast milk).

Immune Reconstitution Inflammatory Syndrome (IRIS): In HIV infection, an exaggerated inflammatory reaction to a disease causingmicroorganism that sometimes occurs when the immunesystem begins to recover following treatment with antiretroviral (ARV)drugs. Immune reconstitution inflammatory syndrome (IRIS) occurs intwo forms: "unmasking" IRIS refers to the flare-up of an underlying,previously undiagnosed infection soon after antiretroviral therapy (ART)is started; "paradoxical" IRIS refers to the worsening of a previouslytreated infection after ART is started. IRIS can be mild or life-threatening.

Latent Tuberculosis Infection: When a person is infected with Mycobacterium tuberculosis, but theimmune system prevents the bacteria from growing. Because thebacteria are inactive, the person does not feel sick and does nothave any symptoms of tuberculosis (TB). A person with latent TBinfection cannot spread TB to others. Without treatment, latent TBinfection can advance to TB disease, especially in people withweakened immune systems.

Multidrug-resistant tuberculosis (MDR-TB): MDR-TB is a specific form of drug-resistant tuberculosis, due to a bacillus resistant to at least isoniazid and rifampicin, the two most powerful anti-tuberculosis drugs.

Mycobacterium tuberculosis: The bacterium that causes tuberculosis (TB). Mycobacteriumtuberculosis usually infects the lungs, but it can also infect other partsof the body, such as the kidneys, spine, and brain. M. tuberculosis isspread when a person with an active infection coughs, sneezes, speaks,or sings, and then a person nearby breathes in the bacteria.

Prevalence: The number or proportion of people with a particular disease orcondition in a given population and at a specific time.

Seroconversion: When an HIV-infected person converts from HIV negative to HIV positiveby blood testing. Shortly after infection with HIV, the body begins to produce HIV antibodies. It takes the body a while to produce enough antibodies to be detected by an HIV antibody test- usually 10 to 14 days but sometimes up to 6 months. When HIV antibodies in the blood reach a detectable level, the HIV-infected person seroconverts. In other words, the person's antibody test goes from HIV negative to HIV positive.

Tuberculosis Disease: The active form of tuberculosis (TB) infection. During TB disease, the bacteria multiply, become active, and make the person sick. A person with TB disease of the lungs can spread TB to others. TB disease primarily affects the lungs, but it can also affect other parts of the body, such as the kidneys, spine, and brain, and it can be fatal. Symptoms include a bad cough that lasts 3 weeks or longer, chest pain, coughing up blood or sputum, weakness, fatigue, loss of appetite, weight loss, fever, chills, and sweating at night. In people with HIV, TB disease is an AIDS-defining condition.