TUBERCULOSIS AMONG CLIENTS ATTENDING HIV VOLUNTARY COUNSELING AND TESTING CENTRES IN DAR ES SALAAM

BY

DR. PATRICIA MUNSERI

A dissertation submitted in partial fulfillment of the requirements for the degree of Master of Medicine (Internal Medicine) of the University of Dar es Salaam.

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10th Nov 2004

.....

DR. M. BAKARI
(SUPERVISOR)

.....

PROF. K. PALLANGYO
(SECOND SUPERVISOR)

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ACKNOWLEDGEMENT

It is not possible for a single individual to cover all the aspects that has made this dissertation into being, and I am therefore deeply grateful to all those who have, with such good grace, given their time and energy to supply valuable opinions, facts or even moral support.

Much of any merit this dissertation may have is due to the generosity of my supervisors Dr. Muhammad Bakari and Prof K. Pallangyo for their guidance and patience as they devoted their spare time so as to offer facts and contributions towards this dissertation.

Principally I am grateful to Prof Lyamuya, and Dr. F. Mugusi, who assisted in the initial stages of this dissertation with their opinions and advice.

I would also like to thank Prof A.B.M.Swai, Mr. C. Makwaya, R. Mpembeni, C.Moshiro and Dr. G.Kwesigabo for their assistance in statistical and epidemiological issues.

I am grateful to Prof J. Shao who assisted with material support and encouragement.

I owe many thanks to Prof Kilonzo, Dr. Hogan, and Dr. Mbwambo for kindly allowing me to collect my data at the MHIC and all the counsellors and other staff at the MHIC and the Mnazi Mmoja VCT not forgetting all the clients who agreed to participate in this study.

Much appreciation goes to Prof Matuja, Dr. J Lwakatare and the entire staff of the department of internal medicine who contributed in one way or another to this dissertation.

I also thank NIMR, who facilitated the laboratory aspect of this study and in particular I would like to thank Dr Kundaeli John, Mr. Ngowi and all the other staff who facilitated in one way or another.

Special thanks to Dr Kazema and Dr. Lyimo who assisted in radiological interpretation.

I thank all the staff who worked in the biochemistry and histopathology laboratory not forgetting Dr Mgaya.

I am thankful to Prof Odd Morkve and Dr S.Mfinanga for their contributions to this dissertation.

I remain indebted to my boy friend Dr L. Mwakalukwa who assisted with the follow up of the specimen and patients during my absence while I was in Bergen as well as moral support. I gratefully acknowledge my mother and brother for their moral support and encouragement.

I would also like to thank Prof Lugalla who assisted in sending me references despite the geographical distance.

ABSTRACT

Background: There is an increase in Tuberculosis (TB) among HIV infected individuals and these pose and increased risk of TB transmission. The diagnosis of TB among these individuals' remains a challenge especially in developing countries. Despite the close epidemiological links between TB and HIV the public health responses have been largely separate.

Objectives: To determine the prevalence of TB and develop a means of diagnosis of tuberculosis among HIV infected without using undue laboratory investigations among VCT clients.

Study setting: Two VCT centres located in Dar-es-salaam.

Study design and subjects: A cross-sectional study of 1318 consecutive clients aged 8years and above attending the selected VCT's between 1st November 2002 and 31st January 2003.

Methods: Clinical evaluation was performed to all study subjects. Sputum was sent for Acid alcohol fast bacilli staining (AAFB), culture and sensitivity for Mycobacterium tuberculosis. Aspirates and biopsies were performed from appropriate sites from patients with pleural effusion, ascites and palpable peripheral lymph nodes. The specimens were sent for AAFB staining, culture and histology.

Results: The overall TB prevalence was 101(7.7%), of these 38(2.9%) TB diagnosis was made before reporting to the VCT and these came only for HIV screening, while 63(4.92%) of the remaining 1280 were subsequently diagnosed to have active tuberculosis.

Pulmonary TB was the more prevalent form of disease 82.5% (52/63) compared to the Extra pulmonary TB that was diagnosed in 15.9% (10/63), $p<0.0001$. One subject (1.6%) had both pulmonary and extra-pulmonary tuberculosis.

Overall HIV prevalence was 26.3 %(347/1318).20.2% (70/347) had concomitant tuberculosis.

Following multivariate analysis, factors that could differentiate tuberculosis from those without tuberculosis among HIV infected individuals were night sweats, Cough, lymphadenopathy, previous history of TB, matted lymph nodes, hair changes, crackles, consolidation and pleural effusion. These factors could correctly classify (85.9%) of the HIV infected individuals into those with tuberculosis and no tuberculosis, and a simple clinical algorithm is proposed.

None of the *M.Tuberculosis* isolates was found to be resistant to the tested anti-TB drugs.

Conclusion: It is recommended that TB screening at VCT's be aggressively pursued to allow early diagnosis, prevention of transmission, early institution of anti-TB treatment, and provision of prophylaxis against tuberculosis among HIV infected individuals excluded to have active tuberculosis.

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LIST OF ABBREVITIONS

AFB	Acid Fast Bacilli
AIDS	Acquired Immunodeficiency Syndrome
EPTB	Extra Pulmonary Tuberculosis
FHI	Family Health International
HIV	Human Immunodeficiency Virus
IUATLD	International Union against Tuberculosis and Lung disease
MHIC	Muhimbili Health Information Centre
MTB	Mycobacterium Tuberculosis
MDR	Multidrug resistance
MMC	Muhimbili Medical Centre
NIMR	National Institute of Medical Research
NTLP	National Tuberculosis and leprosy Programme
PPD	Purified protein derivative
PTB	Pulmonary Tuberculosis
TB	Tuberculosis
WHO	World Health Organization
VCT	Voluntary Counselling and Testing

INTRODUCTION AND LITERATURE REVIEW.

HIV epidemiology

HIV/AIDS is the most far reaching and damaging epidemic the world has ever seen. Within a single generation it has grown into an individual and societal tragedy with huge implications for human security for social and political stability and for economic development.

The overwhelming share of the global HIV burden is borne by developing countries, where 95% of HIV infected people live.[1] Of the global total of 36.1 million people living with HIV/AIDS at the end of year 2000, 25.3million (70.1%) were in sub-Saharan Africa, and 5.8million (16.1%) were in South East Asia.[2] Out of 24 countries in the world, with a high adult HIV sero-prevalence rate above 5%, 23 were in sub-Saharan Africa (the other country was Haiti).[1] In 8 countries all in southern Africa, the adult HIV sero-prevalence rate was above 15%.Thus sub-Saharan Africa bears the largest burden of the HIV/AIDS epidemic. However certain countries in other regions are also badly affected by HIV, with an adult HIV sero-prevalence of 1-5% e.g. Guyana, Panama, Surinam and Honduras (The Americas) and Myanmar, Thailand and Cambodia (South East Asia).[1]

The burden of HIV continues to worsen, with an increase in the number of cases with time as was reported by WHO that 40 million people were infected with HIV in the year 2001.[3]And this epidemic had killed more than 3 million people globally in the year 2003.[4]

Southern Africa one of the regions in sub-Saharan Africa with less than 2% of the world's population is badly affected by HIV, having about 30% of the people with HIV/AIDS world wide. [4]

Several surveys have been conducted in Tanzania in attempt to estimate the prevalence of HIV.

Prevalence of HIV in Tanzania was found to be about 10% in those aged 15 years and above.[5] According to the surveillance report for the year 2002 there were 2.3 million people aged 15 and above living with HIV/AIDS in Tanzania. Most cases of HIV were in the age group 20-49 years with the highest reported cases in the age groups 25-34, among females and 30-39, among males. Surveillance reports among antenatal clinic attendees for the year 2002 revealed an overall prevalence of 9.6%. While the overall prevalence of HIV among blood donors for the same year was 9.7% females had a significantly higher prevalence compared to males. The prevalence among females was 12.3% compared to 9.1% for males. Dar-es-salaam region was found to have the highest AIDS case rate at 235 cases for the year 2002 compared to all other regions[6], and it was found that HIV was the leading cause of death among females aged 15-59years. [7]

HIV flourishes in the context of poverty, ignorance and lack of female autonomy, particularly with regard to their sexual partners. [8]Unlike women in other regions in the world, African women are considerably more likely, at least 1.2 times, to be infected with HIV than men.[9]

Burden of Tuberculosis.

Precise data on the true extent of the TB pandemic are not currently available due to the inadequate surveillance and reporting in many countries. Therefore, data on the impact of TB are achieved indirectly by using the average annual risk of TB infection, the estimated incidence of smear positive TB, case notifications rates, estimated coverage of the population with health care services, and the estimated case fatality rates.[10]Case notification data are often used to assess the burden of tuberculosis. However it is believed that a substantial number of cases of tuberculosis are not detected by the health care systems in most developing countries.[11]

The burden of tuberculosis on mankind has been and continues to be enormous. Tuberculosis persists as a major cause of human mortality and morbidity affecting almost a third of the world's population. Approximately1.7 billion people were believed to be infected with Mycobacterium tuberculosis in 1990[12-14]

It is estimated that eight million new cases of active tuberculosis occur annually and 2.6-2.9 million people die annually from TB-related causes.[15]It is thus estimated that TB accounts for 7% of all avoidable adult deaths worldwide.[16]

In the 1990's it was estimated that 30 million people died as a result of TB, making a strong argument for TB being the most important pathogen in the world today .[17] It is also regarded as being the most frequent cause of death in the world from a single pathogen.[18]

Largely associated with poverty and inadequate health service response, the TB epidemic in sub-Saharan Africa remained at a relatively constant level until the onset of the impact of HIV epidemic in the 1980s. [19] The global prevalence of MTB infection was 32% (1.86 billion people).In 1997; the global case fatality rate was 23% but exceeded 50% in African countries with high HIV rates. Most of the infected people live in Asia, Sub-Saharan Africa and Latin America, where about half of the adult population is infected. These are the same areas where HIV continues to increase steadily. [14,20] It is in these regions where it is estimated that more than 95% of new TB cases and TB-related deaths occur [15]. Thus, HIV has devastating consequences for the already over-burdened tuberculosis programs.

In Brazil one of the countries in Latin America reported to have a high TB prevalence, WHO estimated that there were 122,000 TB cases in 1997, the 13th highest number of cases in a single country worldwide[14]. In the same year the reported prevalence rate of tuberculosis cases in the city of Rio de Janeiro was 174 per 100,000 population, and the rate of new incident cases was 120/100,000.[21,14]

In sub-Saharan Africa the prevalence varies among different countries and ranges from 229-320/100,000 persons per year.[18]For instance **a** study conducted in peri-urban settings in Uganda which involved a sample of 263 households which evaluated 1142 individuals, found 9.2 new cases per 1000 people per year.[22] However this figure was almost five times the estimated national average of two cases per 1000 people per year.[20,23] indicating a disparity in case rates between the poor urban and other parts of the country.[22]

Tuberculosis continues to be among the major public health problems in Tanzania. [24] This country is among the 22 countries with the highest tuberculosis burden in the world.[25, 26]

The number of TB cases has steadily increased from 11,753 in 1983 to about 61,000 in the year 2001 this is more than a five fold increase.[24] The case notification rate of tuberculosis in Tanzania for the year 2000 was 81/100,000. The majority affected were young people aged 25-44 years living in major towns, with a slight male predominance.[26]The case notification rate for Tanzania in the year 2000 was 81/100,000 while in the year 2002 was 186/100,000 and Dar-es-Salaam had the highest case notification rate of 653/100,000 [27]

Clinical features

Clinically, tuberculosis is usually classified as pulmonary or extra- pulmonary. Before the advent of HIV infection, more than 80% of all cases of tuberculosis were limited to the lungs.[28] However; up to two thirds of HIV-infected patients with tuberculosis may have both pulmonary disease and extra pulmonary disease. Early in the course of disease, symptoms and signs are often non-specific and insidious, consisting of fever and night sweats, weight loss, anorexia, generalized malaise, and weakness. However in the majority of cases, cough eventually develops, initially non- productive and subsequently accompanied by production of purulent sputum. Blood stained sputum is frequently documented. Massive haemoptysis may ensue as consequence of the erosion of a fully patent vessel located in the wall of a cavity. Pleuritic chest pain sometimes develops in patients with sub- pleural parenchymal

lesions but can also result from muscle strain due to persistent coughing. Extensive disease may produce dyspnea.[28]

The association between HIV and M.tuberculosis has peculiarities that complicate the treatment and control of both TB and AIDS. These peculiarities include: greater difficulty in diagnosing TB as a result of the presence o f non-specific or atypical types with the appearance of extra-pulmonary and disseminated forms; a smaller number of positive sputum smears and sputum cultures; disappearance or abatement of the cutaneous reaction to purified protein derivative (PPD) of M.tuberculosis and uncharacteristic X-ray images.[29] Some studies have tried to ascertain useful clues toward the diagnosis of smear negative pulmonary tuberculosis and certain factors have been found to be associated with smear negative pulmonary tuberculosis. The factors include age less than 37 years, family contact with TB, never having been married, loss of weight, lack of expectoration, human immunodeficiency virus (HIV) seropositivity and tuberculin reactivity.[30]Other common features accompanying the presentation of TB in an HIV infected individual in Africa are oral candidiasis, generalized lymphadenopathy and recent history of Herpes Zoster. [31- 33.] With associated HIV infection, symptoms of extra-pulmonary tuberculosis are often identical to those without HIV infection. [34] With progression of HIV infection, the occurrence of constitutional symptoms can be misleading, as they can be caused by HIV infection itself. The variety and severity of symptoms will depend on the degree of underlying immunodeficiency.[35]

Burden of tuberculosis and HIV

The recent increases in TB has been closely associated, temporally with the spread of the HIV epidemic through out sub-Saharan Africa.[36]

Because HIV destroys cell-mediated immunity, it is uniquely positioned to be one of the most important determinants of the epidemiology of TB. This has startling effects especially in sub-Saharan Africa where the burden of HIV is high.

HIV is the greatest risk factor for tuberculosis ever known. Infection with HIV leads to both greatly increased rate of reactivation of latent tuberculosis infection[37] and to a greatly enhanced susceptibility to progression to active tuberculosis following new infection.[38-41]

HIV and Tuberculosis are currently the two leading infectious causes of death world wide, responsible for almost four million deaths annually [14]

Tuberculosis is the most important opportunistic infection observed among HIV-infected patients because it occurs frequently, it is transmissible to both HIV-infected and uninfected persons.

In the absence of HIV, only about 10% of the people infected with M.tuberculosis will develop active TB whether from progression of recent infection or reactivation. Half of those who develop active TB are infectious, usually smear positive [42]

HIV infection is the strongest risk factor for progression to active disease from tuberculosis infection, and about 40% of HIV infected people co-infected with M.tuberculosis will develop active TB in their lifetime.[43]

About one third of the 36.1 million people living with HIV worldwide are co-infected with M.tuberculosis and the annual risk of developing tuberculosis ranges from
5-15 %.[2]

The prevalence of MTB/HIV co infection worldwide is 0.18 %.[14] Sixty eight percent (68-70%) of those co-infected live in sub-Saharan Africa. And it was estimated that 7-12% of all new TB cases in adults aged 15-49years were attributable to HIV infection. However the proportion was much greater in the WHO African region (31%) and as a result this region carries the burden of the global epidemic of HIV associated tuberculosis.[44, 45] Twenty-two percent (22%) of co-infected patients live in South East Asia making this region bear a considerable burden as well. [14]
Various studies on tuberculosis/HIV have been conducted in different parts of Africa with various results. Studies done in Kenya and South Africa among HIV patients admitted to hospitals revealed a prevalence of tuberculosis ranging from 27-34%.[46, 47]
In Tanzania, TB case rates nearly doubled in the early 1990s, and nearly two thirds of the increase in the population rate of smear positive cases was thought to be directly attributable to HIV infection.[48]

Another study done in rural Tanzania, among HIV patients presenting with respiratory symptoms, revealed a prevalence of 39%.[49] While taking into consideration TB patients, studies in Uganda and Zambia observed that more than 60% of TB patients were HIV positive [32, 50]

In Brazil 26.7% of sputum smear positive tuberculosis patients had HIV [51]

Surveys done in Tanzania found that, 32% of the patients with TB were HIV infected for the years 1991-1993. This prevalence increased to 44% in the next survey conducted in 1994-1998. [52]

Thus in order to effectively control TB, it is necessary not only to intensify case-finding and decrease diagnostic and treatment delays, but also to implement additional measures to prevent HIV, because HIV has been fuelling the tuberculosis epidemic.[53]

Copathogenicity of TB and HIV Disease

The association of Tuberculosis and HIV infection in sub-Saharan Africa is well documented. [31, 32]

Evidence indicates that the HIV epidemic contributed substantially to the increased numbers of TB cases in the late 1980s and early 1990s.The percentage of persons with TB who are diagnosed with AIDS has been increasing rapidly. HIV induced immunosuppression is an important contributor to the TB epidemic and probably

accounts for a minimum of 30% excess TB cases during the period from 1985 through 1990. [54]

In the developing world, about 50% of HIV seropositive individuals are co-infected with tuberculosis and in resource poor countries, many HIV infected individual die prematurely of tuberculosis.[8]

HIV infection can directly cause an increase in tuberculosis cases because co-infected patients are more likely to experience endogenous reactivation of latent tuberculosis infection or rapidly progress from recent TB infection to disease.[55, 56]

Indirectly, an increase in number of infectious TB-HIV co-infected patients represents a source of potential transmission of Mycobacterium tuberculosis to their contacts, with a possibility of secondary cases of TB infection and disease.[57]

The actual onset of tuberculosis in HIV patients is conflicting. Studies in Africa document that tuberculosis often develops in the earlier stages of HIV infection, [58] [59]While in the industrialized countries as well as in Brazil it was found that the majority of HIV-seropositive pulmonary tuberculosis patients expressed a low CD4 cell count, anergy and atypical chest radiography indicating that tuberculosis occurs late during the disease.[51,60,61]

Several studies have evaluated the infectiousness of tuberculosis patients co-infected with HIV with varying results. Some studies detected higher risk of tuberculosis

transmission by HIV positive index cases to their close contacts,[62] whereas others report low risk or no difference in the risk of tuberculosis infection and disease among contacts.[63 64]

Some studies have shown that tuberculosis accelerates the course of HIV infection and may contribute to the mortality of HIV infected individuals by a one to two fold increase, as described by two cohort-based studies of HIV patients.[65- 67]

Human immunodeficiency virus type 1 (HIV-1) and *M. tuberculosis* are two intracellular pathogens that interact at the population, clinical, and cellular levels. Initial studies of HIV-1 and TB emphasized the impact of HIV-1 on the natural progression of TB, but mounting immunologic and virologic evidence now indicates that the host immune response to *M. tuberculosis* enhances HIV replication and might accelerate the natural progression of HIV infection [8, 68]

The interaction between these two pathogens has important implications for the prevention and treatment of TB among HIV-infected persons. Studies of the immune response in persons with TB disease support the biologic plausibility of co pathogenesis in dually infected persons. The initial interaction between the host immune system and *M. tuberculosis* occurs in the alveolar macrophages that present mycobacterial antigens to antigen-specific CD4+ T cells. [69] These T cells release interferon-gamma, a cytokine that acts at the cellular level to activate macrophages and enhance their ability to contain mycobacterial infection. The activated macrophages also release proinflammatory cytokines, such as tumour necrosis factor

and interleukin (IL)-1, cytokines that enhance viral replication in monocyte cell lines in vitro. [70,71]

The mycobacterium and their products also enhance viral replication by inducing nuclear factor kappa-B, the cellular factor that binds to promoter regions of HIV [72,73]

In communities with high prevalence of HIV the diagnosis of tuberculosis is more challenging. More severely immune-compromised individuals have smear negative disease[74], difficult to diagnose in resource poor settings where sputum smear is the mainstay of detection. The symptoms of tuberculosis and other HIV related lung disease can be very similar resulting in both over diagnosis and under diagnosis thus missing out the opportunity to cure tuberculosis. [75]Thus TB can be easily under diagnosed as well as over diagnosed in HIV infected patients. Atypical or normal X-rays in patients with cough may mislead clinicians not to send sputum specimens for stain and TB culture. When mycobacterial blood cultures are not available or not performed TB diagnosis can be easily missed. This may be a problem especially for Africa.[35]

The only reliable way of diagnosing pulmonary tuberculosis in most sub-Saharan African countries is by finding acid –fast bacilli (AFB) on direct microscopic examinations of sputum. Cultures for Mycobacterium tuberculosis and chest x-rays are not routinely available. In general, positive AFB smears are detected in about 50% of persons with culture positive pulmonary disease.[30,76,

However the tuberculosis and human immunodeficiency virus epidemics in sub-Saharan Africa have been associated with an increase in proportion of smear

negative pulmonary TB cases registered and it is in these areas where such cases are not confirmed by culture.[77, 78,79]

The reasons of this increase in negative sputum smears among patients who are HIV infected who have tuberculosis is due to the effects of increasing immunosuppression reducing pulmonary cavity formation and sputum bacillary load. [31,80,81,82]

However this difference in AFB-smear positivity between HIV-seropositive and seronegative patients was not observed in Tanzania. [83]

Extra-pulmonary involvement is one of the most frequently reported features of TB and has been found to occur in 60-90% of patients dually infected with HIV and tuberculosis.[84]

Prompt initiation of effective antituberculosis treatment increases the probability that a patient with HIV infection who develops TB will be cured of this disease. TB treatment also quickly renders patients non-infectious, with the resulting reduction in the amount of *M. tuberculosis* transmitted to others, and it minimizes the patient's risk of death resulting from TB. [85]

Recurrent tuberculosis appears to be more common in high HIV prevalent settings, this may be due to re-infection which is more common in HIV positive individuals.[86]

A study done by Perriens in Kinshasa Zaire revealed that patients with HIV had a higher overall TB therapy failure rate as compared to those who were HIV negative. HIV patients who had TB were found to have higher relapse rate and higher mortality as compared to those who had TB and were HIV negative.[87]

There is thus an urgent need, particularly where HIV is increasing the prevalence of TB, to ensure that all TB patients have access to effective TB diagnosis and treatment. Failure to ensure the essential basics of case-finding and treatment in countries with severe HIV epidemics will result in an increased burden of TB over the coming decades including increased risk of drug resistance.[88] and an increase in tuberculosis mortality rates in high HIV-prevalent settings. [89] Many studies have demonstrated that the severity of immunodeficiency among TB-HIV patients is a predictor of decreased survival.[51, 85, 90,91]

Tuberculosis prophylaxis among HIV infected individuals

It is estimated that one third of the world's population is latently infected with tubercle bacilli. [14]

Despite this enormous and increasing global burden of tuberculosis, there is still no reliable test to confirm active M.tuberculosis infection in culture negative cases, or to detect latent infection in asymptomatic individuals, because the tuberculin skin test is of limited sensitivity and specificity.[92,93] An increasing proportion of tuberculosis infection occurs in individuals with HIV infection, this is the group in which active tuberculosis is more difficult to diagnose.[64]

Detection of latent tuberculosis infection in HIV infected patients is a diagnostic challenge, as it has been appreciated that the sensitivity of tuberculin skin testing may be depressed in patients with critical illness. Treatment of latent tuberculosis infection decreases the short term risk of developing active tuberculosis by

approximately one half in PPD-positive individuals.[94]Treatment of latent tuberculosis infection requires adequate resources to exclude active tuberculosis before beginning preventive therapy. Multi drug regimens for treatment of latent tuberculosis infection offer an additional safeguard against the inadvertent use of mono-therapy in persons with occult active tuberculosis not identified during screening. In industrialized nations HIV seropositive individuals can be offered skin testing for tuberculosis and isoniazid prophylaxis, but this approach is neither practicable nor affordable in most developing countries.[95]

Another unresolved question is the durability of the efficacy of preventive therapy. Prior to HIV, it was possible to give a limited course of preventive therapy and still demonstrate an effect many years later.[96]

However several studies have shown that the efficacy of 6 months prophylaxis with isoniazid waned over the next couple of years. [94,97]

Prophylaxis against tuberculosis is not dependent on CD4+ lymphocyte count and is recommended in any person who is suspected of being infected with both *M.tuberculosis* and HIV in whom active tuberculosis has been excluded.[98,99]The Tanzanian National guidelines recommend isoniazid tablets in a dose of 5mg/kg(max 300mg)to be taken daily for at least six months .(This contradicts the above statement that the effect of six month prophylaxis with Isoniazid wanes off in a couple of years).Thus the question becomes how long should one be kept on prophylaxis ?

Recent analysis of isoniazid therapy in Bethel, Alaska revealed that maximal efficacy from isoniazid therapy occurred after 9 months, with no additional benefit associated with longer therapy. [96]

Prophylaxis with isoniazid has documented efficacy in reducing the 2year risk of active disease in HIV infected patients who have latent tuberculosis from 24-30% to 4-5%. Other recent studies have shown that short course rifampicin plus pyrazinamide (for 2months) is as effective as isoniazid for 12 months.[100]

Drug resistance to anti TB

The problem of drug resistant tuberculosis is increasing world-wide [88]

Drug resistance with its associated increased morbidity and mortality enormously complicates TB control and increases its costs. [101]

Several studies have been done to determine the prevalence of multi-drug resistant tuberculosis, A study done in Thailand in the mid 1990s found a prevalence (MDR) of 3.8 %.[102] The prevalence of primary and acquired MDR-TB in a survey in Brazil was 0.9% and 5.4%, respecitively.[88]

Globally, the association between new HIV epidemics and the emergence of TB drug resistance is less than clear.[103,104]

However certain studies have demonstrated that HIV infected patients have a higher incidence of drug resistant tuberculosis isolated than non HIV infected patients, there

have been several reports of increased risk of rifampicin resistance among HIV positive patients.[105]

There have also been outbreaks of both sensitive and drug resistant tuberculosis within HIV positive communities indicating the potential for nosocomial transmission.[106,107]

The presence of multi-drug resistant TB could increase the mortality among HIV-seropositive pulmonary tuberculosis patients. High case fatality rates among hospitalized HIV-seropositive patients with multi-drug resistant TB have been described.[108,109]In the Zaire study, TB patients co-infected with HIV had an almost twofold higher post treatment relapse rate than patients not infected with HIV who received the same TB treatment regimen; however, the authors did not investigate whether the relapses were the result of a recurrence of disease with the same strain of *M. tuberculosis* or re-infection (new disease) with a different strain.[110]

Directly observed therapy, regarded as the best strategy for ensuring adherence and limiting drug resistant tuberculosis is thus recommended for all patients with HIV infection.[111]

Primary mycobacterial drug resistance is the presence of resistant strains of *M. tuberculosis* in a patient who, in response to direct questioning, denies having had anti-TB treatment for more than a month and, in countries where adequate documentation is available, no evidence of such history exists. Recent investigation shows that prevalence of resistance to any drug ranges form 2% (Czech Republic) to

41% (Dominican Republic), with a median value of 10.4%. Primary resistance to isoniazid, rifampicin, streptomycin and Ethambutol was found in a median of 0.2% of the cases (range 0 to 4.6%) [112]

Among the African countries surveyed, the prevalence of drug resistance was generally low, despite high rates of HIV co-infection .The low level of multi-drug resistance in particular may be due to the relatively late introduction of rifampin and the unavailability of antituberculosis drugs outside national programs. However, resistance to isoniazid was found in almost 10% of cases, and multi-drug resistance was present in 5.3% of new cases in Ivory Coast.[88]

Moreover some countries with high incidences of tuberculosis including Democratic Republic of Congo, Ethiopia and Nigeria have not been surveyed, thus more data are needed to produce a balanced picture of drug resistance in Africa.[113]

HIV voluntary counselling and testing centres

HIV voluntary counselling and testing (VCT) is usually done at special centres where a person chooses to undergo HIV/AIDS counselling so that, that person can make an informed decision whether to be tested for HIV. Ideas to establish VCT in the developing world started in 1997 following encouraging results from a multi-centre, multi-country study conducted by Family Health International (FHI), the joint United Nations Program on HIV/AIDS (UNAIDS) and the World Health Organization (WHO) in collaboration with researchers from Tanzania, USA, Kenya

and Trinidad. [114]The key to the FHI strategy is providing affordable, accessible and sustainable VCT services that offer valuable information, skills and support to individuals or couples. Such services enable individuals to recognize and reduce their risk behaviours, protect their sexual partners, plan for the future, and seek treatment for opportunistic infections and anti-retroviral therapy when available.

Models of VCT's

There are several models of VCT services delivery.

The choice of model depends upon a program's goal, cost effectiveness, sustainability and affordability, confidentiality and convenience to the client.

Models that have been utilized to date include: -

(i.) Stand alone (direct sites /free standing sites)

These are not associated with an existing medical institution and usually have staff fully devoted to VCT.

(ii) Integrated.

In these a VCT service package is an integral part of other ongoing, usually public sector, health care services such as; hospitals, sexually transmitted disease clinics, tuberculosis clinics, family planning clinics or antenatal care settings.

(iii.) Non-Governmental organization (NGO)

In this model the NGO either integrates VCT into its other established activities or provides VCT services as its only activity.

(iv.) Private Sector Model.

(v.) Public Sector /NGO partnership model -An NGO provides VCT in a public sector facility where both parties contribute to the management of the VCT services.

(vi.) Mobile /Outreach model

In this model, the services are offered through a " mobile unit" van or caravan offering services at designated places These are temporary VCT facilities which are placed outside their sites to serve rural or remote areas or "hard to reach" groups such as injecting drugs users, sex workers, street kids who have no fixed address.[115]

Potential role of HIV VCT's in TB diagnosis.

Voluntary counselling and testing (VCT) is one of the few potentially effective and affordable methods for reducing the transmission of HIV in developing countries.[116, 117] It is an essential service for both prevention and treatment of HIV, TB as well as other opportunistic infections. Voluntary counselling and testing centres can link Tuberculosis and HIV programs and the WHO is coordinating the ProTEST Initiative which is the promotion of voluntary HIV testing as an entry point for access to the core interventions of intensified TB case finding and preventive therapy. [118,119]

PROBLEM STATEMENT.

HIV/AIDS poses one of the greatest challenges globally. It is associated with a number of opportunistic infections, tuberculosis being one of its major infection, accounting for about a third of all the HIV infected people worldwide.[1] Sub-Saharan Africa carries the overwhelming burden of this co-infection by harbouring 68% of the share. HIV fuels the Tuberculosis epidemic by promoting the progression of active tuberculosis, both in people with recently acquired and with latent *M.tuberculosis* infection.[120, 45,121] HIV increases the rate of recurrent tuberculosis which may be due to either endogenous reactivation (true relapse) or exogenous re-infection. Thus the increase in tuberculosis cases among people living with HIV/AIDS pose an increase risk of tuberculosis transmission to the general community whether HIV infected or not. On the other hand Tuberculosis appears to increase the rate of HIV progression[122] and has become the leading cause of death among people living with HIV/AIDS accounting for a third of all AIDS deaths worldwide. Diagnosis of tuberculosis in HIV infected individuals has become more difficult because of the increased frequency of sputum smear negative, extra-pulmonary and bacteremic cases. Moreover chest radiography in patients with tuberculosis especially in the era of HIV is uncharacteristic with loss of the typical pattern seen before the HIV era and therefore is not always diagnostic. The disappearance of cutaneous reaction to PPD has also added to the difficulty in diagnosing tuberculosis in HIV infected individuals. Despite the close epidemiological links, between HIV and Tuberculosis, the public health responses have largely been separate. Tuberculosis programs have focused on TB case finding and treatment, with little attention to HIV/AIDS interventions, despite the fact that

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TB is the leading cause of HIV related morbidity and mortality, and HIV/ AIDS programs have generally paid little attention to TB despite the fact that TB is the commonest opportunist infection among HIV infected individuals.

RATIONALE.

Voluntary counselling and testing centres offer facilities for individuals interested in knowing their serostatus hence screening of patients/clients for HIV. Voluntary counselling and testing centres can link TB and HIV program activities. It is a good entry point for screening and diagnosing tuberculosis, the most common opportunistic infection associated with HIV infection. People attending a centre of HIV screening can thus benefit from TB screening, those found to have Tuberculosis will benefit early identification and treatment of tuberculosis thus reducing the complications of untreated tuberculosis and limiting the spread of the disease to others seeking HIV testing as well as close contacts, while treating tuberculosis in those who are HIV infected reduces the rate of HIV progression. And those HIV patients without active tuberculosis have an opportunity to be offered preventive therapy against tuberculosis. So this study aims at determining the prevalence of Tuberculosis among individuals attending voluntary counselling and testing centres so as to plan for intervention strategies.

BROAD OBJECTIVE.

To determine the magnitude of tuberculosis, clinical characteristics and Anti-TB drug resistance pattern among clients attending HIV voluntary counselling and testing centres.

SPECIFIC OBJECTIVES.

1. To determine the prevalence of tuberculosis (pulmonary & extra-pulmonary) among Clients attending voluntary counselling and testing centres.

2. To determine the prevalence of HIV among clients attending voluntary counselling and testing centres.

3. To determine the proportion of tuberculosis patients among clients who have HIV.

4. To establish a simple clinical algorithm of identifying HIV infected patients who are Suitable for Isoniazid prophylaxis.

5. To determine the clinical characteristics of patients with tuberculosis diagnosed at and who attend voluntary counselling and testing sites.

6. To describe the pattern of primary resistance to anti TB drugs among patients with Tuberculosis in relation to their HIV status.

HYPOTHESIS

Some of the clients seeking HIV screening at VCT's have active tuberculosis necessitating the need for TB screening among all VCT attendees.

METHODOLOGY.

STUDY DESIGN AND STUDY SITE

This was a Descriptive cross-sectional study which was conducted at the Muhimbili health information centre (MHIC) and Mnazi Moja VCT. The MHIC and Mnazi Mmoja VCT's are stand alone voluntary counselling and testing centres located within Muhimbili National Hospital grounds and Mnazi Mmoja in Ilala district Dar-es-salaam respectively. They were selected on the basis of convenience.

The MHIC VCT covers 0.32% of the total Dar-es-salaam population of approximately 3.5 million. Of the clients accessing the VCT 2%, 21.3% and 18.6% are from Kinondoni, Ilala, and Temeke respectively the remaining clients come from neighbouring districts.

The centre developed five years ago and it is continuously expanded as new linkages are developed aimed at care and support this include behavioural change, acceptance of HIV serostatus and syndromic management of sexually transmitted infections. It offers confidential and anonymous client oriented quality VCT service across the genders and various age groups including youth. Services are offered for 1000 T.sh and for those who are unable to pay are offered the service for free.

Inclusion criteria

Consecutive Individuals attending the selected voluntary counselling and testing centres from 1st November 2002 to 31st of January 2003 aged 8 years and above were seen by the author and enrolled into the study. The age 8 was used as an inclusion in this study as at this age individuals can follow instructions on how to produce a proper sample of sputum for testing.

Exclusion criteria

Individuals who were on Transit (those who weren't available within 2 months from day of enrolment) were excluded from the study.

Sampling of study subjects: Consecutive clients who attended the selected VCT's were enrolled in to the study if they fulfilled the inclusion criteria

Sample Size Determination

Was obtained from the formula for calculating sample size.

$$N=\frac{P(1-P)Z^2}{d^2}$$

Where N is the minimum sample size.

P is the prevalence of tuberculosis among clients attending a VCT in Haiti 6%

Z is the standard deviation of 1.96 at 95% confidence interval.

d is the desired degree of accuracy = 0.013

$$N = \frac{0.06(1-0.06)\ 1.96 \times 1.96}{0.013 \times 0.013}$$

N= 1282

This gave a minimum of 1282 clients who were to be screened; however in this study 1318 subjects were recruited into the study

Data collection.

Socio-demographic and clinical data.

All consenting individuals were interviewed by the investigator whereby personal particulars, a detailed history and physical examination was done and the details were filled into a structured questionnaire.(appendix A) A venous blood sample was obtained from the median vein which was tested for HIV. Sputum was obtained using the spot morning spot method recommended by the National Tuberculosis and leprosy program giving a total of three samples for each individual with cough. Lymph node biopsy performed to all easily accessible lymph nodes and those which were inaccessible aspiration was done, pleural and peritoneal biopsies were also done after aspiration of fluid.

HIV Serology.

Screening was done by Capillus HIV1/HIV2 (Cambridge diagnostics) and reactive samples were confirmed by Determine (Abbott). A sample was considered seronegative if it was non-reactive at screening, and seropositive when reactive on both assays. Discordant samples were confirmed by Western Blot.

Microscopy for determination of AFB's

Three sputum samples, and tissues samples as well as aspirates were subjected to Ziehl- Nielsen's stain to observe for the presence of Acid-fast bacilli (AFB).

Radiography.

Patients had to undergo postero-anterior chest radiographs and the radiographs were interpreted by two independent Radiologists. In case of disagreement a third Radiologist opinion was needed.

Pleural and Peritoneal biopsies

Pleural and Peritoneal biopsies were done to patients with pleural effusion or ascites. The procedure was performed aseptically after pleural or peritoneal fluid aspiration under local anaesthesia using 2% lignocaine, among the study participants who had pleural effusion or ascites. A blind biopsy was performed using Abrams' biopsy needle. Several tissue specimens were taken at different angles by repeated insertion of the needle Specimens were then put in sterile saline or in 50 ml of peritoneal or pleural fluid for acid fast bacilli and culture for M. tuberculosis. Tissue for histological examination was put in 10% formol saline. Pleural and Peritoneal fluid was also taken for biochemistry examination in order to check for protein and sugar levels so as to ascertain whether the fluid was an exudate or a transudate. Patients who required biopsies were admitted in the ward were these procedures were done and they were then kept over night for observation after the procedure.

Lymph node biopsy and Aspiration

Excision biopsy was performed to one of the easily accessible palpable peripheral lymph nodes which was done aseptically under local anaesthesia using 2% lignocaine. The excised lymph node was cut through the midline and was examined macroscopically for caseation and there after a smear was made on a glass slide for Ziehl- Nielsen's staining to observe for the presence of Acid fast bacilli. A piece of the lymph node specimen was put in sterile normal saline for mycobacterium culture and another piece was put in formalin for histology. Lymph node aspiration was done to lymph nodes that were not easily accessible under sterile technique using a 23 G needle and a 10 ml syringe at different angles the aspirate was then smeared on a glass slide and observed for the presence of acid fast bacilli after staining with Ziehl- Nielsen's stain

Cultures for *M.tuberculosis* and Determination of resistance to anti-TB

Sputum and crushed tissues from lymph nodes, pleura and peritoneum were cultured on Lowenstein Jensen media for 8 weeks.

Resistance patterns was ascertained by the Resistance ratio method[123] that is done on Lowenstein Jensen Media incorporated with specific drugs to be tested for (Rifampicin, Isoniazid Streptomycin and Ethambutol) in a wide range concentration. An inoculum (standard inoculum) prepared from primary Lowenstein Jensen slopes containing growth of *M.tuberculosis*, which are less than two weeks old, was

inoculated on the drug incorporated Lowenstein Jensen slopes which was incubated at 37 ^{0} C.

A definitive reading was made at 4 weeks and strains were not reported as sensitive earlier however, if growth occurred after 2 weeks, strains were regarded as resistant. The resistance ratio is the minimal concentration of the drug inhibiting growth of the test strain divided by the minimal concentration inhibiting a standard sensitive strain in the same set of test.

Diagnosis of Pulmonary Tuberculosis

Was based upon the definition of NTLP which defines PTB in the presence of two of following;

(i) Symptoms of tuberculosis, (cough, fever, night sweats for more than 3 weeks.)

(ii) AFB visible by direct Ziehl-Nielsen staining of sputum specimen, or *M.tuberculosis* cultured from sputum in Lowenstein- Jensen media .

(iii) Chest radiograph independently interpreted as highly suggestive of tuberculosis.

(iv) For patents with culture negative tuberculosis, a clinical response to antituberculosis medications.

Diagnosis of Extra pulmonary TB

Defined as presence of two of the following;

(i) Symptoms of tuberculosis (evening fevers, night sweats, involuntary loss of body weight cough for more than 3 weeks, pleuritic chest pain, difficulty in breathing, presence of lymph nodes, abdominal distension and signs pleural effusion, ascites, with matted lymph nodes.

(ii) Presence of acid fast bacilli (AFB) visible by direct Ziehl- Nielsen staining of respective tissues samples or fluid or *M.tuberculosis* cultured from the tissues or fluid in Lowenstein-Jensen media.

(iii) Histological diagnosis- presence of caseaous necrosis with granuloma formation.

(iv) Aspirated fluid with a high protein content > 30g/L (Exudate).

Exclusion of TB

Symptoms signs and simple laboratory test were used as parameters to discriminate HIV patients with tuberculosis from those without tuberculosis. Subjects who were excluded as having TB were referred to the HIV clinic at MNH for further available care including prophylaxis and management of opportunistic infections.

Treatment

Patients who were found to have pulmonary tuberculosis were commenced on Standard anti-tuberculosis treatment according to the Tanzania national tuberculosis and leprosy guidelines which consisted of Rifampicin 10 mg/kg/day, Isoniazid 5 mg/kg/day, Pyrazinamide 30 mg/kg/day and Ethambutol 15 mg/kg/day for two months. Patients who had an extra-pulmonary form of tuberculosis were treated with and intermittent regimen which consisted of the same medications above give thrice weekly for two month under supervision. This was then followed by a continuation phase which consisted of Isoniazid and Ethambutol for six months. Those with cough who were found to be AFB negative were prescribed broad spectrum antibiotics (amoxyllin 500mg 8hourly) for two weeks, if they still had cough repeat sputum

smears and chest radiographs were then done as per National guidelines and were commenced on antituberculosis drugs. Patients who were found to have positive cultures for *M.tuberculosis* in whom smears were initially negative were also commenced on antituberculosis medications when they came for follow up of the culture results. HIV positive patients in whom tuberculosis was excluded were referred to the HIV clinic for further management.

DEFINITION OF TERMS.

Pulmonary tuberculosis-Tuberculosis that affects lungs.

Extra-pulmonary tuberculosis- affecting organs other than the lungs, such as pleura, lymph nodes, peritoneum, pericardium spine and joints.

Easily accessible lymph node- Are superficially located lymph nodes that are not nearby large blood vessels and are not too deep seated.

Exudate- Fluid with a protein content of greater then 30gm/L

Transudate- Fluid with a protein content of less then 30gm/l

Primary drug resistance – is the presence of resistant strains of M.tuberculosis in a newly diagnosed patient who has never received TB drugs or has received them for less than one month of treatment.

Growth of MTB on culture was defined as 20 or more colonies of *M.tuberculosis*

Positive Chest Radiographs – Predominant parenchymal lesions

Presence of cavitations

Presence of hilar lymphadenopathy.

Pleural effusions

ETHICAL CONSIDERATION.

Ethical clearance for carrying out this research was obtained from the Muhimbili University College of health sciences higher degrees and publication ethical committee

Informed consent for participation in the study was obtained from the individual respondents.

Where by the participants were given a patient information sheet(Appendix B) to read and understand what the study is all about, those who could not read were read out the form, and there after they were given the opportunity to ask questions which were answered by the investigator. The respondents who agreed to participate in the study were then required to give their consent by signing the form and for those who could not sign thumbs print were required. For those who were below 18 years their parents or guardians gave written informed consent, and the child gave oral assent.

DATA ANALYSIS.

Data was computerized and analysis was done using a specially designed computer statistical package EPI INFO version 6 and Statistical Package for Social Sciences software.

Comparison of proportions was tested using the Chi-square test and fisher's exact test was adopted when the expected value in a cell was less than five. Logistic regression and multivariate analysis were used to show how several dependent variables vary together.Discriminant analysis was used to find out variables that were diagnostic for tuberculosis among HIV patients and ultimately to develop a simple

clinical algorithm for diagnosing TB in HIV. Differences were considered statistically significant if p values were less than 0.05.

RESULTS

During the study period, a total of 1,735 clients attended the study sites of these 1,318 subjects fulfilled the inclusion criteria and consented to participate in the study. The rest 417 clients were not included, 337 (81%) did not consent and 80(19%) did not meet the inclusion criteria. Among those who did not meet the inclusion criteria, 12(15%) were below 8years of age and the remaining 68(85%) were not able to be available for follow up.

A higher proportion of attendees were women 696/1318 (52.8%), compared to men 622/1318 (47.2%), p-value 0.04. The overall mean age of the study subjects was 30.7 with a range (8-80) years, and by sex the mean age for males was 32.1 with a range of (8-80) while that of females was 29 with a range of (8-65) years. As shown in table 1, a larger proportion, 50.6% (668/1318) of study participants who attended the VCT's were from Kinondoni district.

Majority of the study subjects 54% (712/1318) were single and 684/1318 (51.9%) had attained at least a secondary level of education. Most of the subjects 835/1318 (63.4%) involved a working to earn an income.

Table 1 also shows that 836/1318 (63.4%) of study participants who sought HIV screening voluntarily were self referrals while the rest were referred. Not shown in the table are reasons why the subjects sought HIV screening. Among the reasons for attending VCT for majority of subjects (49.5%) who were self referred was fear of being HIV infected, as either their spouse tested positive for HIV, or recent death of a spouse or biological parents suspected to be due to HIV. Others reasons were, a promiscuous spouse, unprotected sex or having multiple sexual partners. Illness of a

child, spouse or other wives of the spouse was another reason. Some (34.4%) of the attendees were curious about the health status '(just to find out if I am infected or not)'. One hundred and thirty five subjects (16.1%) tested for HIV because of recurrent illness.

Another group involved referred clients 482/1318 (36.6%), who were referred by Priests, Embassy's, Schools or some Employers because their HIV status was needed as a prerequisite for studying abroad, employment, travel or for getting married.

Table 1: Baseline characteristics of study population.

	Males (%) n=622 (47.2%)	**Females (%)** n=696 (52.8%)	p-value for trend
Age:(yrs)			<0.0001
8-15	8 (1.3)	14 (2.0)	
16-25	136(21.9)	234(33.6)	
26-35	283(45.5)	298(42.8)	
36-45	133(21.4)	118(17.0)	
46-55	47 (7.60)	30 (4.30)	
56+	15 (2.40)	2 (0.30)	
Education			0.003
None	15 (2.4)	31 (4.5)	
Primary	277(44.5)	311(44.7)	
secondary	285(45.8)	331(47.6)	
University	45 (7.2)	23 (3.30)	
Address			0.485
Kinondoni	307(49.4)	361(52.2)	
Ilala	172(27.7)	196(28.4)	
Temeke	135(21.7)	128(18.5)	
Others	8 (1.3)	11 (1.6)	
Reason for VCT attendance			0.274
Self referral	385(61.9)	451(64.8)	
Referred	237(38.1)	245(35.2)	
Marital status			<0.0001
Single	357(57.4)	355(51.0)	
Monogamous	168(27.0)	163(23.4)	
Polygamous	21 (3.4)	22 (3.16)	
Cohabiting	41 (6.59)	64 (9.20)	
Divorced	17 (2.7)	40 (5.75)	
Widowed	18 (2.9)	52 (7.47)	
Occupation			<0.0001
Employed	486(77.9)	379(54.5)	
Unemployed	117(18.8)	304(43.6)	
Peasants	20 (3.2)	13 (1.9)	

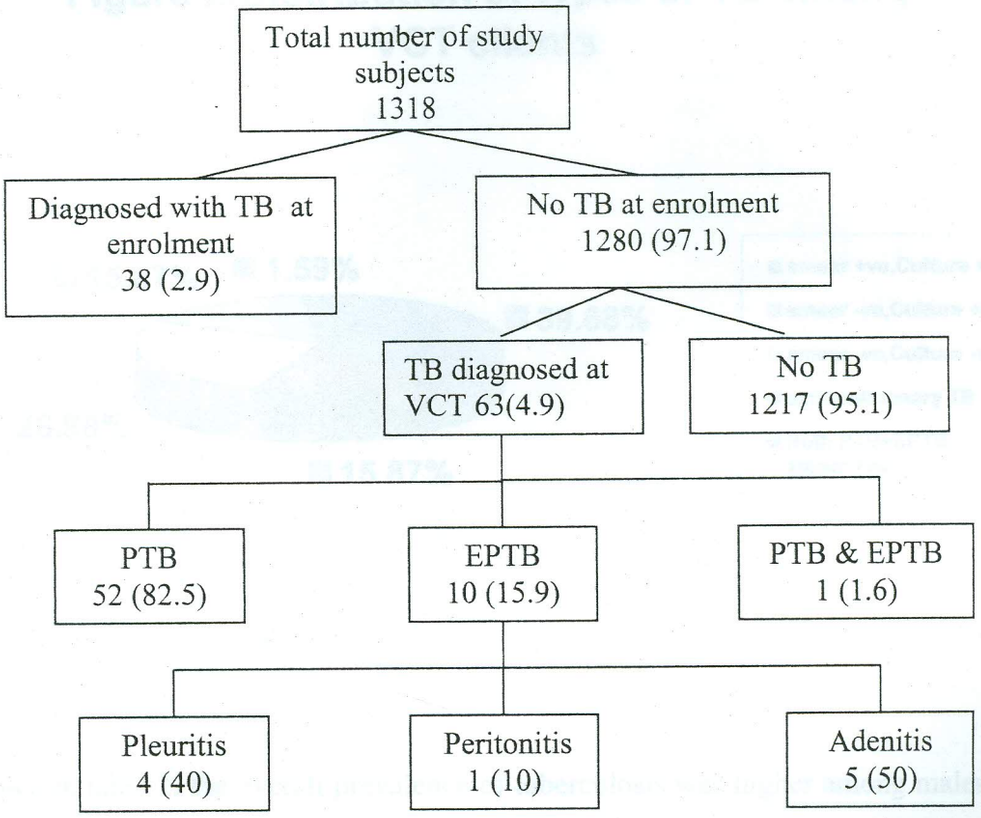
Prevalence of tuberculosis

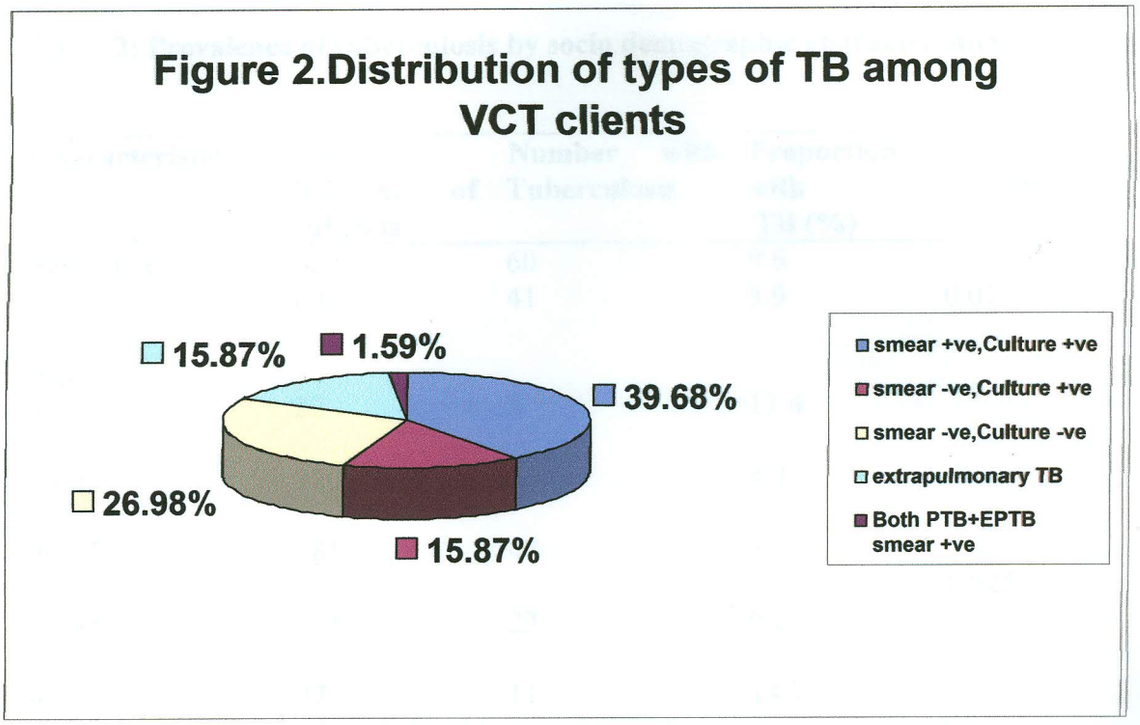
Among the study subjects, 101 (7.7%) had a diagnosis of TB. Of these, 37.6% (38/101) were diagnosed to have TB prior to visiting the VCT's and had come only to have their HIV sero-status checked.

The remaining 63 subjects were ultimately diagnosed to have active tuberculosis at the VCT. They thus comprised of 4.9% of all subjects screened for TB at the VCT, (figure 1). Among these 82.5%, (52/63) had pulmonary tuberculosis of whom 25 (48.1%) were smear positive, 10 (19.2%) were smear negative but culture positive and the remaining 17 (32.7%) were diagnosed on the basis of a combination of abnormal CXR, suggestive history and response to anti TB therapy (figure 2).

On the other hand extra-pulmonary tuberculosis was diagnosed in 15.9% (10/63) of subjects with TB. Among these 5/10(50%) had lymphadenitis, 4/10 (40%) had pleuritis, and 1/10(10%) had peritonitis. One subject, 1.6%, had both pulmonary and extra-pulmonary tuberculosis.

Figure 1. Flow chart of study participants





As shown in table 2, the overall prevalence of tuberculosis was higher among males (9.6%) as compared to females 5.2%, p-value <0.001. Furthermore, there was a statistically significant difference in prevalence of tuberculosis among the different age groups, with the 46-55 years group having the highest prevalence of 14.3%, while the age group 16-25 years had the least prevalence of 4.3%, p-value=0.025. There was a statistically significant difference in the prevalence of TB in relation to the level of education. Subjects with no formal education or with Primary school level of education had a higher prevalence of TB, accounting for 15.2% and 12.8% respectively, whereas those with secondary school and university levels of education had TB prevalence of 2.9% and 1.5% respectively Table 2.

Table 2: Prevalence of tuberculosis by socio demographic characteristics

Characteristic	Total Number of subjects	Number with Tuberculosis	Proportion with TB (%)	P-value
Sex: Male	622	60	9.6	
Females	696	41	5.9	0.01
Age:(yrs)				
8-15	22	3	13.6	
16-25	370	16	4.3	
26-35	581	47	8.1	
36-45	251	23	9.2	0.025
46-55	77	11	14.3	
56+	17	1	5.9	
Education				
None	46	7	15.2	
primary	588	75	12.8	0.0001
secondary	616	18	2.9	
university	68	1	1.5	
Address				
Kinondoni	668	39	5.8	
Ilala	368	38	10.3	0.05
Temeke	263	23	8.7	
Others	19	1	5.3	
Smoking	85	16	18.8	0.0001
Alcohol intake	347	19	5.5	0.07

Prevalence of HIV

The overall HIV prevalence was 26.3% (347/1318) (95%CI 23.98-28.81) p< 0.001

It was found that females had a higher HIV prevalence (30.6%) compared to males (21.5%), p value <0.001

The overall mean age for those with HIV infection among the subjects was 33.5 (SD 9.3) years. However HIV infected men had higher mean age of 35.9 (SD10.4) years, compared to women whose mean age was 32(SD 8.2) years, p<0.0001.

There was a statistically significant difference in HIV prevalence among the different age groups with the age group 36-45 years having the highest prevalence of 42.2%. While the age group 16-25 years had the least prevalence of 14.9%, p value<0.0001

A statistically significant difference was noted in HIV prevalence when related to marital status. Widows had a higher prevalence of HIV accounting for 61.4% followed by those involved in polygamous marriage, and those divorced, with HIV prevalence of 53.5% and 45.6% respectively. On the other hand, study subjects who were single and those involved in a monogamous marriage accounted for the least prevalence of 32.3% and 32.9% respectively, (p-value <0.0001).

The prevalence of HIV was also noted to significantly differ in relation to the level of education attained by the subjects. Participants with no formal education had the highest prevalence of 15.2% while those with a university level education accounted for the least figure of 1.5%, table 3.

Table 3. Prevalence of HIV-1 by socio-demographic characteristics

Characteristic	Number with HIV	%	Total N	P-Value
Sex: Male	134	21.5	622	<0.0001
Females	213	30.6	696	
Age:(yrs)				
8-15	9	40.9	22	
16-25	55	14.9	370	
26-35	141	24.3	581	<0.0001
36-45	106	42.2	251	
46-55	32	41.6	77	
56+	4	23.5	17	
Education				
None	7	15.2	46	
Primary	75	12.8	588	<0.0001
Secondary	18	2.9	616	
University	1	1.5	68	
Address				
Kinondoni	163	24.2	668	
Ilala	105	28.5	368	0.24
Temeke	76	28.9	263	
Others	3	15.8	19	
Marital status				
Single	112	15.7	712	
Monogamous	109	32.9	331	0.0001
Polygamous	23	53.4	43	
Cohabiting	34	32.4	105	
Divorced	26	45.6	57	
Widowed	43	61.4	70	
Occupation				
Civil Servant	71	20.2	351	
Related to Entertainment	11	34.4	32	
Students	13	11.4	114	<0.0001
Unemployed	13	31.7	41	
Business	131	28.4	462	
Peasant	13	39.4	33	
Drivers	16	31.4	51	
Others				
Housewife house girls	79	44.1	179	

TB/HIV co-infection

As shown in table 4, among the 347 participants who tested positive for HIV, 70 (20.2%) had a diagnosis of TB. On the other hand among the 101 who had tuberculosis 70 (69.3%) tested positive for HIV.

More females 36/70 (51.4%) accounted for this co-infection compared to males 34/70 (48.6%) however this difference was not statistically significant, p = 0.7. It was also found that most of the study subjects with this co-infection were least educated, predominantly with a primary level of education 56/70(80%) p-value <0.0001

Table 4. Distribution of tuberculosis in relation to HIV status

HIV	TUBERCULOSIS		TOTAL
	POSITIVE	NEGATIVE	
POSITIVE	70 (20.2)	277 (79.8)	347 (26.3)
NEGATIVE	31 (3.2)	940 (96.8)	971 (73.7)
TOTAL	101 (7.7)	1217 (92.3)	1318

X^2 test, p-value <0.001

Presenting symptoms of the study participants

The frequency of symptoms among the study participants in relation to TB status were as shown in table 5. Compared to those with no TB, a higher proportion of subjects with a diagnosis of TB presented with fevers, night sweats, weight loss cough, haemoptysis, lymph node swelling pleurisy, difficulty in breathing abdominal distension and a history of previous tuberculosis. These findings do not differ from what is generally known about tuberculosis.

Table 5. Frequency of symptoms among study subjects in relation to tuberculosis status.

Symptom	Number with tuberculosis n=101 (%)	Number without tuberculosis n=1217	P-value
Fevers	60 (59.0)	69 (5.7)	0.0001
Night sweats	58 (57.4)	37 (3.0)	0.0001
Weight loss	63 (62.4)	84 (6.9)	0.0001
Dry cough	15 (14.9)	27 (2.2)	0.0001
Productive cough	60 (59.4)	49 (4.0)	0.0001
Haemoptysis	5 (4.9)	3 (0.2)	0.0001
Lymph node	8 (7.9)	6 (0.4)	<0.0001
Pleurisy	8 (7.9)	8 (0.6)	<0.0001
Non pleuritic pain	3 (2.9)	2 (0.16)	0.004
Dyspnea	7 (6.9)	2 (0.16)	<0.0001
Abdominal distension	3 (2.9)	0 (0.00)	0.0004
Previous history of TB	32 (31.7)	74 (6.08)	0.0001

Physical signs of the study participants

The commonest signs seen among patients with tuberculosis which significantly differed from those who did not have tuberculosis were cervical lymph node enlargement which was noted in 12.9% of the patients with tuberculosis, hair changes (33.7%), pallor (31.7%), oral candidiasis (23.8%) crackles (39.6%) signs of lung consolidation (18.8%) and pleural effusion (6.9%). Table 6

Table 6: **Frequency of signs among study subjects in relation to tuberculosis status**

Sign	Number with Tuberculosis n=101 (%)		Number with no Tuberculosis n=1217 (%)		p- value
Lymphadenopathy					
None	87	(86.1)	1185	(97.4)	
Matted	9	(8.90)	11	(0.9)	<0.0001
Discrete	5	(19.2)	21	(1.7)	
Lymph node site					
Cervical	13	(12.9)	18	(1.5)	
Axillary	0	(0)	2	(0.2)	<0.0001
Inguinal	1	(0.9)	5	(0.4)	
Presence of BCG scar	50	(49.5)	763	(62.4)	0.01
Hair changes	34	(33.7)	58	(4.8)	0.0001
Pallor	32	(31.7)	38	(3.1)	<0.0001
Kaposis sarcoma	5	(4.9)	18	(1.4)	0.0001
Pruitic Papular Eruption	15	(14.9)	55	(4.5)	<0.0001
Candidiasis	24	(23.8)	60	(4.9)	<0.0001
Crackles	40	(39.6)	16	(1.3)	0.0001
Consolidation	19	(18.8)	7	(0.6)	0.0001
Pleural effusion	7	(6.9)	1	(0.1)	<0.0001
Ascites	3	(3.0)	2	(0.2)	0.01
Hepatomegally	3	(3.0)	5	(0.4)	0.01
Spleenomegally	6	(5.9)	10	(0.8)	0.0001
Abdominal masses	2	(2.0)	2	(0.2)	0.001

Clinical and Socio-demographic features of HIV patients with respect to TB status

By univariate analysis a number of features could differentiate TB from other clinical conditions among subjects with HIV infection. These included low level of education, evening fevers, night sweats, weight loss, cough, difficulty in breathing, lymph node swelling and a history of previous TB. Signs included cervical lymphadenopathy, hair changes, pallor, oral candidiasis, crackles and consolidation. These are shown in

Table 7.

Table 7: Features distinguishing Tuberculosis from non-Tuberculosis among HIV infected subjects by univariate analysis

CHARACTERISTIC	Subjects with tuberculosis n=70	(%)	Subjects with no tuberculosis n=277	(%)	p-value
Sex:					
Male	34	(25.4)	100	(74.6)	
Female	36	(16.9)	177	(83.1)	0.055
Education					
None	5	(23.8)	16	(76.2)	
Primary	56	(27.3)	149	(72.7)	0.0006
Secondary	9	(7.8)	107	(92.2)	
University	0	(0.00)	5	(100)	
Symptoms					
Fever	43	(43.6)	58	(57.4)	0.0001
Night sweats	41	(56.9)	31	(43.1)	0.0001
Weight loss	46	(39.0)	72	(61.0)	0.0001
Dry cough	10	(40.0)	15	(60.0)	0.01
Productive cough	41	(56.2)	32	(43.8)	0.0001
Haemoptysis	3	(60.0)	2	(40.0)	0.06
Difficulty in breathing	5	(714)	2	(28.6)	0.005
Abdominal distension	1	(100)	0	(0.00)	0.20
Odynophagia	8	(42.1)	11	(57.9)	0.014
Lymph node swelling	8	(61.5)	5	(38.5)	0.001
Previous TB	25	(33.8)	49	(66.2)	0.001
Signs					
Lymphadenopathy					
None	56	(18.1)	253	(81.9)	
Matted	9	(64.3)	5	(35.7)	0.001
Discrete	5	(23.8)	19	(79.2)	
Hair changes	34	(39.0)	53	(61.1)	0.001
Pallor	28	(45.9)	33	(54.1)	0.001
Oral candidiasis	24	(28.6)	60	(71.4)	0.027
Crackles	28	(71.0)	11	(28.2)	0.000
Consolidation	15	(75.0)	5	(25.0)	0.000
Pleural effusion	2	(66.7)	1	(33.3)	0.043

However, following a multivariate analysis, the symptoms that were independently associated with active tuberculosis in HIV infected patients were lymph node swelling, cough, night sweats and previous history of tuberculosis. Furthermore, the important signs were pleural effusion, crackles, consolidation, matted lymph nodes, and hair changes. This is shown in table 8.

Table 8: Features Distinguishing Tuberculosis from those without Tuberculosis among HIV Clients- Multivariate Analysis

CHARACTERISTIC	REGRESSION COEFFICIENT	ODDS RATIO	p-value
Symptoms			
Night sweats	1.4106	4.0984	0.0002
Productive cough	1.7393	5.6932	0.0000
Lymph node swelling	2.0689	7.9160	0.0028
Previous TB	0.8448	2.3275	0.0188
Signs			
Crackles	2.9227	18.5922	0.0000
Consolidation signs	2.6250	13.8047	0.0000
Pleural effusion	3.0147	20.3833	0.0174
Lymphadenopathy			
Matted	2.3094	10.0685	0.0004
Discrete	0.1910	1.2104	0.7672
Hair changes	0.9330	2.5422	0.0097

As depicted in table 9, it was further found that on discriminant analysis only 12 features were predictive of tuberculosis in an HIV infected patient. These were a low level of education, presence of a history of night sweats, lymph node swelling, previous tuberculosis, cough, odynophagia, and evening fevers. The features on physical examination were presence of pallor, crackles, signs of consolidation and pleural effusion.

Table 9: Variables Discriminating TB Among HIV Patients by Discriminant Analysis

VARIABLE	WILKS' LAMBDA*	p-value
Education	0.58537	0.0000
Symptoms		
Night sweats	0.78016	0.0000
Fever	0.58887	0.0000
Productive cough	0.61268	0.0000
Dry cough	0.59756	0.0000
Lymph node swelling	0.64388	0.0000
Previous TB	0.62970	0.0000
Odynophagia	0.60431	0.0000
Signs		
Pallor	0.59226	0.0000
Pleural effusion	0.62142	0.0000
consolidation	0.66450	0.0000
crackles	0.69388	0.0000

nb: * Wilks' Lambda is the ratio of within group sum of squares to the total sum of squares. A lambda of 1 occurs when all group means are equal. Values close to 0 occur when within group variability is small compared to the total variability, that is most of the variability is attributable to differences between the means of the groups.

It was also found that the discriminant analysis could classify correctly 74.3% of the proven tuberculosis patients among the HIV infected individuals as well as the 88.8% of the HIV infected patients without tuberculosis as shown in table 10. In this analysis, eighteen patients (25.7%) would have been falsely missed, while 31 (11.2%) would have been falsely diagnosed to have tuberculosis.

Table 10. Classification by Discriminant Analysis of HIV infected Patients into either Tuberculosis or no Tuberculosis based upon the presence of the features described in table 9.

Actual group	Number of HIV cases	Number with Tuberculosis (%)	Number with No tuberculosis (%)
Tuberculosis	70	52 (74.3)	18 (25.7)
No tuberculosis	277	31 (11.2)	246 (88.8)

Following the discriminant analysis, an estimated coefficient specific for each of the discriminating feature was calculated, and these are shown in the key below:

Table 11.Key below showing the Estimated Coefficients (B) for the variables following discriminant analysis

VARIABLE	Estimated coefficient (B's)
Night sweats	0.6372469
Crackles	1.726441
Consolidation	1.185610
Lymph node swelling	1.815104
Previous TB	0.3932095
Pleural effusion	2.056238
Productive cough	0.9675238
Odynophagia	0.9291572
Dry cough	0.7734658
Pallor	0.4860261
Fever	-0.3875577
Education	0.2029303

By employing a linear discriminant equation (shown below), a scoring system could then be adopted that utilizes the specific estimated coefficients being substituted into the equation.

Linear discriminant equation $D= B_0 + B_1X1 + B_2X_2 +..... BpXp$

Where D is the discriminating score

B_0 is a constant = -20.58460

B's are the estimated coefficient for the different variables (features) see table 9 and their specific constants are shown in the key above table 11.

X's are the values of the variables/features where 1 is substituted if the variable is present and 2 if absent.

If D is less or equal to -0.5 then this patient is classified as having tuberculosis

If D is greater than 1 then the patient is classified as not having tuberculosis

If the patients score lies between -0.5 to 1.0 then this patient is misclassified (grey area)

As shown in table 10, with such a scoring system, individuals will therefore fall in three categories: Patients who have tuberculosis of which 74.3% were correctly classified as having tuberculosis. Patients who do not have tuberculosis; among which 88.8% were found not to have tuberculosis. Lastly those who are in between, either they don't have tuberculosis but classified as having tuberculosis and thus will undergo unnecessary treatment or do have tuberculosis and are classified as not having tuberculosis, and therefore denied treatment. Thirty one (11.2%) of the patients were falsely diagnosed to have tuberculosis and eighteen (25.7%) who had tuberculosis were missed by this screening.

On the other hand, by employing this scoring system, HIV infected patients excluded to have TB could be considered for isoniazid prophylaxis.

Primary anti TB drug resistance

Among the 127 sputum samples and 13 lymph node samples, 35 sputum and 5 lymph node samples grew significant *M. tuberculosis* organisms that were subsequently sub-cultured in media containing the specific anti-TB drugs. It was found that the isolated *M. tuberculosis* was sensitive to the tested anti tuberculosis drugs in all the sub cultures, signifying absence of primary drug resistance with these isolates.

DISCUSSION

The study population consisted of individuals seeking HIV testing at Muhimbili health information centre and Mnazi Mmoja voluntary counselling and testing centre both located within Ilala district in Dar-es-salaam. Despite the location of the study sites being in Ilala, the attendees were from all the three districts within Dar-es-salaam.

A significantly higher proportion of women, 52.8%, sought HIV testing as compared to men. This finding is in-keeping with what was seen in Sansai (Thailand) where 53% of the clients who sought HIV testing voluntarily were females, as well as the findings from the 9 states in America and Puerto Rico. [124,125]

A preponderance of females in VCT centres could be due to the fact that higher proportions of women are HIV infected in the community as compared to men. It has been shown from a study in South Africa that the prevalence of HIV infection in Africa is substantially higher among young women than it is among young men, [126] and studies in Tanzania have also shown the same as was reported for the year 2002 the prevalence of HIV infection among females was 12.3% as compared to males which was 9.1%[6]

There were various reasons cited for seeking HIV screening. As seen in this study, the majority of subjects who sought HIV screening were self referred (63.4%) and most of them, tested because of fear of being infected with HIV as they had various risk factors including unprotected sex, multiple sexual partners, promiscuous spouse while the others suspected that they might be HIV infected because the spouse tested

positive for HIV or due to death of a spouse which was suspected to be due to HIV or recurrent illness or chronic illness of a child. As it was seen in Thailand [124]most of the VCT attendees were also self referral (52.5%) with similar reasons as found in this study. Report from a similar study in Haiti found that 66% of the VCT attendees were self referred .[127]

Another group of self referred subjects (34.4%) included those who were curious of their health status. This group wanted to know their status but did not volunteer to give a specific reason for testing other than "just to find out if I am infected or not". Thirty six percent (36.6%) of all study participants who came to test involved referred clients who were referred by Priests, Embassy's, Doctors or Schools because their HIV status was needed for applications for study, employment, travel or prerequisite for getting married.

Prevalence of Tuberculosis

In this study, it has been found that tuberculosis is a significant problem among clients visiting the VCT centres. The overall prevalence of TB in the centres was 7.7%. These results are in keeping with findings from studies conducted in other countries. A study in Haiti that involved one HIV testing centre showed that at least 6% of the attendees who presented with symptoms of cough had active tuberculosis. [128] Similar results were found in a voluntary counselling and testing site in Uganda, where the TB prevalence was 6%. [129] In Santo Domingo, another tropical and developing country just like Tanzania, the prevalence was found to be 9.7%.[130]

However, there are also reports of lower TB prevalence than that found in this study. A study in Soleil Haiti revealed a prevalence of 2.3%. It should be noted though that in this study the lower prevalence could be due to the fact that tuberculosis was screened at VCT centres as well as in the general community among individuals who agreed to be tested for HIV. The latter could thus have diluted the TB prevalence since they had stayed at home, indicating that they were not sick and hence seen no reason for attending a VCT.[131]

On the other hand, hospital studies in Tanzania do portray a much higher TB prevalence among the HIV infected, as exemplified in a study done by Atzori in Iringa rural (Tanzania) where the prevalence of tuberculosis was found to be 38.5 %,[49] This is to be expected though since his study was a hospital based, consisting of a selected population of HIV infected patients who presented with respiratory symptoms, thus increasing the likelihood for the diagnosis of tuberculosis, as opposed to this study that involved attendees of VCT centres only.

It is important also to note that the findings of this study could be an overestimate of the real situation in the general population and hence need to be cautiously interpreted. As the prevalence of active TB found in individuals seen at the HIV testing sites will not be a representative of the prevalence in the community from which those people came. Because the reasons for seeking HIV testing for some of the individuals were ill health and symptoms, which were caused by TB. Thus it is not surprising that the prevalence of active TB recorded here is much higher than

would be expected from the case notification rates of TB in Tanzania and Dar-es-Salaam for the year 2002 which was 186/100,000 and 653/100,000 [27]

It was found in this study; having excluded subjects who came with a diagnosis of TB, that 4.9% of the remaining had TB. A significant proportion of them 82.5%, (52/63) had pulmonary TB and EPTB, was diagnosed in 16%. It is generally known though, that among HIV infected patients, EPTB is more common. This discrepancy could be due to the fact that patients with extra-pulmonary tuberculosis are more likely to go to a hospital for treatment than a VCT centre because they are clinically ill and would require additional types of clinical treatment which they can only receive from a hospital. However there are also reports suggesting that extra-pulmonary tuberculosis is much less common than pulmonary tuberculosis [132]. Indeed, although extra-pulmonary tuberculosis occurs more frequently among persons who are infected with HIV, pulmonary TB remains the most common type of TB in this group world wide.[131]

More males were found to have tuberculosis as compared to females. This finding is in-keeping with what has been reported in the general population report of the National TB & Leprosy Control Programme of Tanzania for the year 2002 which found that more males 15,056 were affected compared to females 9,080 giving a male to female ratio of 1.7:1.For Dar-es Salaam the ratio was 1.8:1 respectively. [27] This male predominance was also been reported by Egwaga in 2000 where the ratio was 1:0.7 [26]. Connolly also reported an increase in prevalence of tuberculosis in

males after adolescence, as was shown from data collected worldwide by the tuberculosis research and surveillance unit of WHO. [133]

Subjects with lower levels of education were noted to have a higher prevalence of TB compared to those with higher levels. This aspect has been reviewed by Harries where he associated an increase of tuberculosis with social, cultural and economic issues such as poverty and illiteracy. He argues that these factors do affect access to care, diagnosis and delivery of care, all of which have an important bearing on illness and death.[122]

It was striking that 40% of patients diagnosed with pulmonary tuberculosis at the VCT centres had positive sputum smears on microscopy. It follows that such individuals do pose a risk of transmitting *M tuberculosis* to their household contacts, staff at the VCT's, as well as their fellow clients attending the VCT's. It is imperative therefore that such individuals are identified s early as possible and prompt therapy is instituted.

Prevalence of HIV

The overall prevalence of HIV in this study was found to be 26.3%. Indeed this is higher than the 10% national average HIV prevalence, among individuals aged 15 years and above. [5] This is an expected finding and it suggests that most study participants who visited the sites were at a higher risk for HIV. Similar findings have been reported from Zambia where the prevalence of HIV in the VCT's was 30% [134] as well as in Sansai, Thailand (Asia) a semi urban district, where the

prevalence of HIV among clients who sought HIV testing for the year 1999 was 29 %[124] In Haiti, a similarly high HIV prevalence of 36% was noted among adults aged 18 and above who sought HIV testing in the year 1997.[128]

It was noted that females had a higher HIV prevalence compared to males 30.6% versus 21.5% respectively, and that the age group commonly affected was 36-55 years, in keeping with the surveillance report for Tanzania mainland for the year 2002 which found that the age at which most cases of HIV were found was 20-49 years.[6]

There was a pattern among those who tested positive for HIV whereby those with the least education presented with the highest prevalence while those who had at least a secondary level of education had the least prevalence. These findings are similar to what was found in Sansai Thailand and in Haiti in which one of the risk factors noted for HIV infection was no formal education having an odds ratio of 1.3 [124,127]

It was also found that a higher proportion of widows were HIV infected compared to the other marital status categories. This could be due to the fact that either their spouse died of HIV or after the death of their spouse they had multiple sexual partners. This finding is similar to what Niles found in his study conducted in a rural district in Zimbabwe among women of fertile age where he found that women who are divorced or widowed had twice as high risk of being HIV positive as compared to single women, with an odds ratio of 2.03. [(135)] However this finding differs from what was seen in the surveillance report of Tanzania for the year 2002, where 56% of

the HIV infected were married while widows accounted for only 1% of the HIV cases. [6]This finding could be explained by the fact that individuals who report to VCT centres including widows are at an increased risk if being HIV infected compared to other widows in the general population

Prevalence of TB/HIV co-infection

In this study, HIV infected subjects had a higher (20.3%) prevalence of TB compared to the prevalence of 3.2% among attendees with no HIV infection. This is similar with the findings from a Dominican study[95] which found prevalence rates of 15 % and 5% respectively. This study was also conducted in a VCT setting and in a third world country just as Tanzania. On the other hand, a study done in Uganda revealed that only 2.6% of HIV positive clients had tuberculosis [129]while a study done in Kenya found that 19% of HIV positive household contacts of tuberculosis patients in Nairobi had this co-infection.[79]

The TB prevalence of 3.2% among HIV uninfected attendees suggests that TB symptoms may be on of the reasons for seeking HIV screening at the VCT's.

On the other hand, it was found in this study that 70% of patients diagnosed with tuberculosis were HIV infected. These findings are in-keeping with what was found in Malawi where by 77% of the TB patients who accepted HIV testing were HIV positive in the year 1999 and 2000, for a cross-sectional and cohort study respectively.[53, 126,137]However the estimated HIV prevalence among TB patients for the year 1992 for Tanzania was 50%.[137] While in Cote d'Ivoire, prevalence of HIV among 17,946 TB patients who consented for HIV testing was 43.2% [138]

In this study most patients with HIV/TB co-infection had a pulmonary type of tuberculosis. These findings are different from hospital based studies, where extra-pulmonary form of tuberculosis is much common among HIV infected individuals. Chaisson found in his study that patients with tuberculosis and AIDS had significantly more extra-pulmonary involvement than did patients with tuberculosis without AIDS. In his study 60% of the patients with extra-pulmonary tuberculosis had AIDS.[55]The findings could be due to the fact that, most of the patients with extra-pulmonary form of tuberculosis present with severe illness, and would prefer to go to a hospital for treatment of their disease, where they can subsequently be requested to test for HIV while in the hospital, therefore having no reason to attend a VCT.

However, it has been found in this study that a number of patients diagnosed with extra-pulmonary tuberculosis had a less severe form of the disease, and these included TB lymphadenitis which comprised of 50% of all the extra-pulmonary cases. This finding can be explained by the fact that people in the general population associate enlargement of lymph nodes with HIV/AIDS. Therefore, individuals presenting with such symptoms are likely to seek HIV testing earlier than the rest of the population.

All patients who were diagnosed to have TB adenitis were HIV positive. These results are similar to previous studies that have indicated an association between extra-pulmonary TB and HIV. Perenboom found in her study that 76% of the patients with TB adenitis in MMC were HIV positive. [139]It was also the finding of

Chaisson that the most common site for extra-pulmonary tuberculosis involvement in AIDS patients was the lymphatic site (31%). [55]

CLINICAL CHARACTERISTICS

As seen in this study patients with tuberculosis presented with a number of symptoms and signs which differed significantly from those without tuberculosis. These included fevers, night sweats weight loss, productive and dry cough pleuritc pain and difficulty in breathing. Signs found among study subjects with tuberculosis which significantly differed from those without tuberculosis were presence of matted cervical lymph nodes, hair changes, pallor, oral candidiasis, crackles and signs of consolidation, pleural effusion on chest examination and spleenomegally on abdominal examination. These signs and symptoms don't differ from TB patients diagnosed in hospitals.[31, 32]

It was further found that 11 simple features, namely night sweats, evening fevers, cough, level of education, lymph node swelling, previous tuberculosis, odynophagia, pallor, crackles, signs of consolidation, and pleural effusion could discriminate TB from non-TB in HIV infected patients. The discriminant analysis could correctly classify 74.3% of the proven tuberculosis patients among HIV infected individuals, and 88.8% of the patients without tuberculosis. However eighteen (25.7%) would have falsely been missed, while 31 (11.2%) would have been falsely diagnosed to have tuberculosis. Similarly a study conducted in Brazil revealed that fever and weight loss were the most frequently encountered symptoms among patients co-infected with TB and HIV[140] Based on the findings of this study, a scoring system is

being proposed that once validated can be used in a VCT setting to identify HIV infected subjects with TB. By employing this system, such patients could easily be identified even in the absence of sophisticated investigational tools like CXR, or microscopy. Prompt diagnosis and consequent early therapy of such subjects is important in view of the well established influences of HIV on TB progression, as well as the influence of HIV on TB progression. On the other hand, exclusion of active TB will result into initiation of appropriate chemoprophylaxis.

It has to be emphasized though that the scoring system will also identify patients who will fall in the "grey" area that is those who do not have TB but classified as TB, and those having no TB but classifies as having TB. It is these patients who lie within this grey area, who would then be investigated further so as to reach an accurate diagnosis in order to be managed accordingly.

PRIMARY RESISTANCE

In this study primary anti TB drug resistance has not been demonstrated, however this may not reflect what is in the general population taking into account of the small sample size. Similar findings have been reported by Atzori in 1993 in rural Iringa who found that all confirmed culture positive samples (13.2%) were sensitive to the tested antituberculosis medications.[49]

Low levels of primary anti-TB drug resistance have been reported in Tanzania where it was found that about 90% of all newly diagnosed sputum smear positive cases are sensitive to streptomycin, isoniazid and thiacetazone. Only in 8% were the bacilli

resistant to isoniazid, in about 1-2% to streptomycin and in further 1-2% to isoniazid and streptomycin while the resistance to rifampicin in Tanzania is so far very low reported to be less than 1 %.[141]

WHO/IUATLD reported that levels of primary resistance worldwide for the years 1985-1994 ranged from 0-16.9% with a median of 4.1%. [112] In Kenya 638 patients were screened and 90.8% were fully sensitive while 9.2% had a strain resistant to one or more drugs [142]

While in Malawi a study that involved 1121 patients revealed that 9.6% of the patients were resistant to any of the first line drugs while 7.2% were resistant to isoniazid and the prevalence of multi-drug resistance was 0.5%[143]

In Ethiopia, a study that involved nation wide health facilities, 167 isolates were tested and primary resistance to two or more drugs was 7.2% while the overall primary drug resistance was found to be 15.6%[144]

It was noted in a global survey, that in most African countries, despite the high incidence of HIV related tuberculosis there was a low prevalence of drug resistant tuberculosis. This low prevalence was explained by the fact that rifampin has recently been introduced in African countries with the use of rifampin free regimens in the continuation phase of therapy and the growing use of direct observation of treatment. Multi-drug resistant tuberculosis continues to be a serious problem, particularly among some countries in Eastern Europe. This survey also identified

China and Iran to be areas with high prevalence of multi-drug resistant tuberculosis with prevalence's of 10.8% and 5% respectively[113]

CONCLUSION AND RECOMMENDATIONS

This study has revealed that the prevalence of tuberculosis among clients attending voluntary counselling and testing centres to be high, occurring in 7.7%, and so is the number of open TB cases 39.68%. These patients are a potential source of transmission of M. tuberculosis to other individuals in the community. These patients miss the opportunity of being offered early treatment. They consequently have an increase in the risk of complications.

It is therefore recommended that tuberculosis be aggressively screened in VCT centres so as to identify patients with tuberculosis, and to this effect the simple scoring system developed in this study can be employed. This scoring approach will make a clinical diagnosis without unnecessarily subjecting the patients to superfluous investigations therefore saving time cost and resources. This will result into early treatment and consequent reduction of spread of the disease to other members in the community. For those who are HIV infected, the early recognition and treatment of tuberculosis will reduce the progression of both HIV and TB.

Although in this study primary resistance to anti-tuberculosis drugs was not detected, it is further advised that more vigilance be employed in following up the problem. It is therefore strongly recommended that VCT centres be aggressively engaged in the screening for tuberculosis.

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APPENDIX A

QUESTIONAIRE

A. Demographic characteristics

1. ID number
2. Age
3. Sex
4. Address
5. Education

   0-none 1.primary 2.secondary 3.others

   Specify
6. Occupation
7. Marital status

   1.single 2.monogamous 3.polygamous 4.cohabiting 5.divorced 6.widowed
8. Smoking Y N Number per day duration.
9. Drinking Y N Quantity duration.
10. Reason for attending a VCT
    1. Referred due to recurrent illness
    2. Part of medical examination –travel, employment
    3. Curious about health status
    4. Others specify

Clinical characteristics.

11. When were you last well weeks.

Symptoms and duration.(weeks)

12.	Fever	Y	N	duration
13.	Night sweats	Y	N	duration.
14.	Weight loss	Y	N	duration
15.	Cough (dry)	Y	N	duration.
16.	Productive cough	Y	N	duration.
17.	Haemoptysis	Y	N	duration.
18.	Pleuritic pain	Y	N	duration
19.	Non Pleuritic pain	Y	N	duration.
20.	Difficulty in breathing	Y	N	duration.
21.	Abdominal distension	Y	N	duration.
22.	Diarrhoea	Y	N	duration
23.	Dysphagia	Y	N	duration
24.	Odynophagia	Y	N	duration
25.	Numbness	Y	N	duration
26.	Lower limb Weakness	Y	N	duration
27.	Athralgia/arthritis	Y	N	duration
28.	Back pain	Y	N	duration
29.	Swelling at the back	Y	N	duration.
30.	Skin itch	Y	N	duration
31.	Any skin disease	Y	N	duration.

32. Swelling of the LNs Y N duration.

Past medical history

33. Previous blood transfusion Y N year

34. Previous TB Y N year

35. Any other illness specify

Physical examination

Lymph node enlargement

1. None 3. Discrete
2. Matted

Site 1.cervical 2.axillary 3.inguinal.

Skin and mucous membranes

1. Hair changes Y N
2. Pallor Y N
3. Jaudice Y N
4. Oedema Y N
5. Kaposis sarcoma Y N
6. Seborrheic dermatitis Y N
7. Herpes zooster Y N
8. Herpes simplex Y N
9. Scabies Y N
10. Taenia Y N
11. PPE Y N

12.	Oral candidiasis	Y N
13	Others	specify

Lungs

1.	Crackles	Y N
2.	Rhonchi	Y N
3.	Pleural rub	Y N
4.	Consolidation	Y N
5	Pleural effusion	Y N
6.	Others	specify

Abdomen

1.	Ascites	Y N
2.	Hepatomegally	Y N
3.	Spleenomegally	Y N
4.	Palpable masses	Y N
5.	Others	specify

Spine

1.	Swelling	Y N
2.	Tenderness	Y N

Heart

1. Pericardial Effusion Y N

2. Others specify

Working diagnosis

HIV test positive Negative

Laboratory test ordered

Sputum smear

Sputum culture

Pleural aspirate (AFB)

Pleural aspirate (culture)

Pleural biopsy (AFB) smear

Pleural histology

Peritoneal biopsy (AFB) smear

Peritoneal biopsy histology

Lymph node biopsy (AFB) smear

Lymph node for Histology

Aspirate for biochemistry (exudates/transudate)

Chest x-ray

X-ray spine

Mantoux test

ESR

Result for the investigations

Treatment offered

Resistance to Anti TB YES NO

Rifampicin

Isoniazid

Ethambutol

Streptomycin

APPENDIX B

INFORMATION SHEET ENGLISH VERSION.

TITLE OF THE STUDY.TUBERCULOSIS AMONG CLIENTS ATTENDING VOLUNTARY COUNSELING AND TESTING CENTRES.

PURPOSE: The purpose of the study is to determine the magnitude of tuberculosis among clients attending voluntary counselling and testing centres as well as to describe the primary drug resistance patterns to anti tuberculosis drugs in this study anti-tuberculosis drugs will be offered as recommended by the national guidelines to all those who will be found to be having tuberculosis after being investigated. I intend to enrol 1300 clients. You have been invited to participate in this study because you fit the enrolment criteria. If you agree to participate in this study you will be asked some questions about your health and will be investigated for tuberculosis as well.

PROCEDURES

In this study the researcher will collect specimen samples of sputum, pleural, peritoneal fluid and biopsy from clients who will be having a clinical suspicion of pulmonary or non-pulmonary tuberculosis only, radiological investigations, which will include chest and spinal x-rays, will also be done.

RISK AND DISCOMFORT

There is no risk for you to participate in this study. You may experience mild pain at the site of biopsy if you will undergo a biopsy but this will recover relatively within a short while.

BENEFITS

Participation in this study will help in identifying tuberculosis patients and getting them treated promptly so as to reduce the risk of transmission .The individual will benefit in that he/she will receive treatment, which will account for his/her well being.

CONFIDENTIALITY.

Your study records will be kept confidential and will not be disclosed to anyone who is not involved in the study unless you agree to have the records given out. Neither your name nor your study number will be used for publication or publicity purposes.

PARTICIPATION.

Your participation in this study is voluntary, if you choose not to participate in this study, still your decision will be respected.

SIGNATURE.

If you agree to participate in this study, I request you or your guardian to sign or press your fingerprint below.

Signature of the subject Date

Signature of the investigator Date