AN EPIDEMIOLOGICAL ANALYSIS OF HIV-RELATED TUBERCULOSIS

IN GHANZI DISTRICT

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AN EPIDEMIOLOGICAL ANALYSIS OF HIV-RELATED TUBERCULOSIS IN GHANZI DISTRICT

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Dr KN Ntumba, MBChB, MPH
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<tr>
<td>AIDS</td>
<td>Acquired Immunodeficiency Syndrome</td>
</tr>
<tr>
<td>AFB</td>
<td>Acid-Fast Bacilli</td>
</tr>
<tr>
<td>ART</td>
<td>Anti-Retroviral Therapy</td>
</tr>
<tr>
<td>BAIS III</td>
<td>Botswana AIDS Impact Survey III</td>
</tr>
<tr>
<td>BCG</td>
<td>Bacilli Calmette Guerin Vaccine</td>
</tr>
<tr>
<td>BNTP</td>
<td>Botswana National Tuberculosis Programme</td>
</tr>
<tr>
<td>CSO</td>
<td>Central Statistics Office</td>
</tr>
<tr>
<td>DOTS</td>
<td>Direct Observed Treatment Support</td>
</tr>
<tr>
<td>ETR</td>
<td>Electronic Tuberculosis Register</td>
</tr>
<tr>
<td>HIV</td>
<td>Human Immunodeficiency Virus</td>
</tr>
<tr>
<td>HRDC</td>
<td>Health Research &amp; Documentation Commission</td>
</tr>
<tr>
<td>INH</td>
<td>Isoniazid</td>
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<tr>
<td>IPT</td>
<td>Isoniazid Prevention Therapy</td>
</tr>
<tr>
<td>IRB</td>
<td>Institutional Review Board</td>
</tr>
<tr>
<td>MLG</td>
<td>Ministry of Local Government</td>
</tr>
<tr>
<td>MDR-TB</td>
<td>Multi Drug Resistant Tuberculosis</td>
</tr>
<tr>
<td>MTB</td>
<td>Mycobacterium Tuberculosis</td>
</tr>
<tr>
<td>PLWH</td>
<td>People Living With HIV</td>
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<td>SCC</td>
<td>Short-course Chemotherapy</td>
</tr>
<tr>
<td>TB</td>
<td>Tuberculosis</td>
</tr>
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<td>WHO</td>
<td>World Health Organization</td>
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Chapter 1: Introduction

1.1 Background

Botswana is among the world’s hardest hit countries in the Human Immuno-deficient Virus (HIV) epidemic resulting in high prevalence of Tuberculosis (TB) essentially among HIV infected individuals.

The country has a strong national program for TB prevention, care and treatment that enjoy high-level of governmental support including funding and training of staff. Tuberculosis services are free and available to all citizens and non-citizens of Botswana.

The Botswana National Tuberculosis (BNTP) program was launched in 1975 with technical assistance from World Health Organization (WHO). The BNTP seek to improve the health and survival of citizens infected and affected by Tuberculosis and to eliminate new TB cases across the country. The BNTP introduced short course chemotherapy for treatment of TB in 1986 and adopted the Direct Observation Treatment Support (DOTS) strategy in 1993. The success of BNTP can be highlighted by the fact that there was a significant decline in TB notification cases from 506/100,000 in 1975 to 199/100,000 in 1989 (MOH 2007).

The era of HIV/AIDS has dramatically changed the profile and the natural history of TB in Botswana. HIV/AIDS combined with the TB epidemic continues to be the major cause of death, affecting every family, community and the nation at large. According to MOH (2007) TB cases began to rise during the early 1990s; In 2005, the national estimated TB notification rate reached 10228/100,000. There was indication that the proportion of TB patients who are co-infected with HIV in Botswana range from 60-86% (MOH 2007). Similarly, tuberculosis in Botswana is actually responsible for 13% of all adults’ deaths and 40% of deaths among people living with HIV/AIDS (MOH 2007).

Realising the potential negative impact of the TB epidemic in HIV infected individuals; the Government of Botswana introduced the national free Isoniazid Prevention Therapy (IPT) programme in public health facilities in 2001. Isoniazid (INH) is administered for six months to eligible HIV infected individuals to prevent the development of active Tuberculosis.
In terms of coordination, both the BNTP and the IPT programmes fall under the Department of Public Health and have the same implementing partners at the national and district level. Though both programs are extremely successful in some areas of the country, nevertheless there are areas such as Ghanzi that remain a challenge.

1.2 Study Area
Situated in the western part of Botswana, Ghanzi is one of the countries sixteen districts. Covering an area of 117 000 square kilometres (sq.km). It shares border with Namibia in the west, Ngamiland district in the north, Boteti and Central district, Kweneng west and Kgalagadi district. There are numerous smaller settlements and farms scattered over Ghanzi district. (See Appendix A).

Ghanzi district is sparsely populated. According to the 2001 population and housing census, a total of 32 481 people reside in Ghanzi district, and thus accounts for 2% of the country’s population. The major centre of abode is Ghanzi Township with a population of 9,934 followed by Charles hill with 2,051 (CSO 2001). Within the district, there are numerous smaller Settlements located in remote areas with relatively small populations (as few as 300 in the smallest settlement).

Throughout the district, there are 23 health facilities including: One primary hospital, 4 clinics with maternity, 1 clinic without maternity services and 17 health posts.

1.3 Literature Review
Tuberculosis (TB) remains a public health concern worldwide. The prevalence of tuberculosis is not static across borders. From time to time, new cases are diagnosed. WHO in reporting the study of (Dye C et al., 2000) indicated that nearly one third of the global population is infected with mycobacterium tuberculosis. From the same source, more than eight million people are developing active tuberculosis every year and around two million die yearly from this disease (WHO 2003). The global burden of tuberculosis remains enormous, mainly because of poor control in Southeast Asia, sub-Saharan Africa, and Eastern Europe, and
because of high rates of M. tuberculosis and HIV co-infection in some African countries (Christopher et al. 1999).

It was acknowledged that multiple factors contribute to the recent increases in the number of TB cases. The source of TB transmission is mainly individuals infected with active pulmonary TB, particularly cases with positive acid-fast bacilli (AFB) sputum smears. Tuberculosis is spread through contact with tiny airborne particles expelled by infected person during coughing or sneezing. The progression of the TB disease is facilitated by continuous spatial proximity to a patient infected with tuberculosis as well as the history of co-morbidities, such as smoking, alcohol consumption, Diabetes, silicosis, homelessness and malnutrition in exposed person.

Similarly, studies have shown that HIV epidemic has had a dramatic impact on rates of tuberculosis (TB) and on TB control in populations where both infections are prevalent (Cantwell and Binkin 1996). HIV does not only increase the risk of reactivating latent Mycobacterium tuberculosis (MTB) infection (Bucher et al 1999), it also increases the risk of rapid TB progression soon after infection or re-infection with MTB (Daley et al. 1992 and Shafer et al. 1995). In addition to increasing individual susceptibility to TB following MTB infection, the increased burden of HIV-associated TB cases also increases MTB transmission rates at the community level, threatening the health and survival of HIV-negative individuals as well (Odhiambo et al 1999).

Tuberculosis infection can be active or latent. Adults who have active TB disease usually have many of the following symptoms: cough for more than two weeks, shortness of breath, chest pain, haemoptysis, loss of appetite, weight loss of ten or more pounds over a short period of time, fever, chills and night sweats.

The disease may be pulmonary and/or extra-pulmonary. The body areas in which TB is most likely to develop include the apices of the lungs, lymph nodes, Kidneys, brain and bone. Apart from symptoms described above, patients affected with extra-pulmonary tuberculosis can experience swelling of glands and joints, severe headache, severe bones pain, abdominal pain and distension and diarrhea.
The diagnosis of active TB in HIV-infected and non-infected patients is based on an assessment of the likelihood of infection by epidemiologic history and tuberculin testing, a high index of suspicion and recognition of atypical presentations of TB in the presence of HIV, and appropriate use of clinical, radiological and laboratory examinations.

There are several differences between HIV-infection and uninfected patients with TB that have practical diagnostic implications. First, a false-negative tuberculin skin test is more likely in an HIV-infected patient and is increasingly likely with increasing immune-suppression (Markowitz et al. 1993). Second, the radiographic appearance of TB, which usually provides diagnostic information, is nonspecific in HIV-infected patients. Furthermore, unrecognized pulmonary TB poses a serious risk of transmission. Therefore, for any HIV-infected patient with unexplained pulmonary disease, strong consideration should be given to testing respiratory secretions for M. tuberculosis and applying respiratory isolation measures until infectious TB is excluded. Third, some studies have found that sputum smear examination is less sensitive in HIV-infected patients (Elliott et al. 1993); however, this observation has not been confirmed (Long et al. 1991). When the sputum smear is positive for acid-fast bacilli, the patient should usually be treated for presumptive M. tuberculosis disease until the species has been identified (FitzGerald et al. 1996). Polymerase chain reaction techniques can help in making this distinction rapidly. Positive blood culture results for M. tuberculosis, uncommon in HIV-negative patients with TB, may be diagnostic for disseminated TB in patients with advanced HIV infection (Bouza et al. 1993). The typical granulomatous histologic features of TB may also be altered, particularly in profoundly immune-suppressed patients. Granulomata may be poorly formed or absent, and there may be greater numbers of organisms.

Strategies to control tuberculosis comprise of: case treatment, preventive treatment, and vaccination with BCG, with the expectation that improved socio-economic conditions will lead to a decline in disease incidence (Narain et al. 1992 and Kochi 1991). In Botswana, the current recommendation for initial treatment of an active tuberculosis case consists of the administration of standardized short-course chemotherapy regimens with first-line drugs including isoniazid, rifampicin, pyrazinamide, and streptomycin or ethambutol or both in the intensive treatment phase. Since 1993 the World Health Organization has recommended that
this treatment be given as part of a comprehensive policy known as DOTS (Directly Observed Treatment, short course).

Preventive treatment aims to eradicate latent infection with MTB before active disease. In Botswana, TB prevention is based on the administration of INH among eligible HIV infected individuals. This intervention was recommended by WHO in 1998 in view of the fact that HIV infected individuals are at particular risk of tuberculosis. Mosimaneotsile et al. (2009) indicated that six months of Isoniazid Prevention Therapy (IPT) is relatively safe and well-tolerated by people living with HIV (PLWH) in Botswana. Adherence to IPT is significantly better among those receiving antiretroviral therapy (ART). (Mosimaneotsile et al. 2009).

The prognosis of TB disease depends mainly on the adherence to treatment and co-morbidities associated or related to tuberculosis. Similarly, outcomes are poor when patients who are infected with Mycobacterium tuberculosis resistant to isoniazid and rifampicin (multidrug resistant tuberculosis) are treated with this standard regimen. Reserve or second line anti-tuberculosis drugs have therefore become components of treatment regimens. This approach is known as DOTS-plus.

In summary, Tuberculosis is one of the most common causes of morbidity and death in HIV-positive adults living in less-developed countries (Thongcharoenet al. 1992 & Rana et al. 2000), yet it is a preventable and treatable disease. TB and HIV infection interact in fundamentally important ways, patho-physiologically, clinically and epidemiologically. Physicians caring for patients with HIV must have a high index of suspicion for TB, and those treating patients with TB should consider the possibility of HIV.

Ongoing surveillance of high-risk populations, as well as liberal use of prophylaxis, is required. In those who develop active TB, careful management and an awareness of the greater risk of side effects and drug interactions mandate careful follow-up and expert advice.
1.4 Problem Statement

A major consequence of the HIV epidemic in developing countries is the increasing incidence of TB (Cantwell and Binkin 1997 & Corbett et al. 2003). Human Immunodeficiency Virus infection seems to be a potent risk factor for TB genesis. Bucher et al. (1999) and Daley et al. (1995) indicated that HIV does not only increase the risk of reactivating latent Mycobacterium tuberculosis (MTB) infection but also increases the risk of rapid TB progression soon after infection or re-infection with MTB. Therefore, Tuberculosis is the most common HIV related disease.

In Botswana, it is acknowledged that the burden of HIV-related tuberculosis is increasing rapidly. According to MOH (2007) Tuberculosis cases began to rise during the early 1990s. The proportion of TB cases co-infected with HIV in Botswana range between 60 and 86%.

With regards to Ghanzi district, data from the MOH (annual report 2006) indicated that The TB notification at Ghanzi district (1170/100,000) was twice higher in comparison to the rest of the country. Meanwhile, the district has an estimated HIV prevalence (13.5%) lower as compared to the rest of the country (BIAS III 2008). From above data, it was expected a TB notification lower at Ghanzi district as compared to the national data. Any increase in TB notification cases could be related to improvement in health care availability and access in Ghanzi district as a whole. Other possible factors for this increase could be the high mobility of Ghanzi population combined with factors such as HIV and poverty.

Therefore, the main scope of this preliminary epidemiological study is to determine the impact of the HIV epidemic on tuberculosis caseload in Ghanzi district and, to determine potential difference in terms of disease classification, patient’s category and treatment outcome between HIV infected and uninfected patients.

1.5 Study Justification

An enquiry to the Health Research and Documentation Commission(HRDC) and an online search using Medline, Biomedicalcentral and the ‘freebooks4doctors’ internet search engine were used in order to find researches done on HIV related tuberculosis in Ghanzi district. As
results, there was no research conducted in Ghanzi district on this specific topic from 1990 up to date.

Therefore, this study was prompted by the absence of publications concerning HIV related and/or associated Tuberculosis at Ghanzi district, Botswana and the knowledge that determination of the above outlined scope of the study is necessary for preventing TB dissemination at the district level.

1.6 Research questions

i. What are the most common demographic factors associated to TB at Ghanzi district?

ii. Is Tuberculosis linked to human immunodeficiency virus (HIV) infection at Ghanzi district?

iii. Does diseases classification and treatment outcomes differ between HIV infected and uninfected patients?

A null hypothesis that was tested was that there is no association between TB and HIV infection in this population.

1.7 Objectives of the Study

The overall objective of the study was to understand the epidemiological context around MDR-TB and HIV related and/or associated TB rates in Ghanzi district.

The specific objectives are:

1. To examine the demographic distribution of TB and MDR-TB at Ghanzi district.

2. To describe patient category, disease classification and treatment outcomes between HIV infected and uninfected patients.

3. To determine the prevalence and TB fatality rates in Ghanzi district.

4. To determine the relationship between TB and HIV at Ghanzi district.
Chapter 2: Methodology

2.1 Study design and population
This study was conducted in Ghanzi district, Botswana. Data was originated from district Electronic TB Register (ETR). A retrospective cross-sectional study design was used to study demographics and clinical characteristics of individuals infected by Tuberculosis as described below. The sampling scheme used was a full census of TB notification cases from 1st January 2006 to 31st December 2009 and, from 1st January 2006 to 31st December 2010 for MDR-TB patients.

Figure 2.1: The analytic diagram of the study Design

2.1.1 Inclusion Criteria
- All patients diagnosed as having TB illness and with available HIV Sero-status results from any Ghanzi district health facilities.
- Availability of Patient age and gender, patient category, Disease classification and treatment outcome data.
- All patients diagnosed as having MDR-TB illness regardless of HIV status results.
2.2 Data collection procedure
Secondary data from ETR and MDR-TB registers were used as data record set. Data from the ETR and manual registers was captured on a quarterly basis from the TB registers in health facilities by the TB Coordinator. The ETR deals automatically with issues of completeness, double counting of patients and other obvious errors and inconsistencies.

Data that exists in the ETR was extracted using a data sheet as per appendix B. After verification of completeness and consistency of data extracted, Data was entered in the Excel spreadsheet.

2.3 Data Analysis procedure
EpiInfo software was used for data analysis. The Excel spreadsheet containing data was linked to EpiInfo software for descriptive and analytic analysis purpose.

2.3.1 Descriptive analysis
The variables of interest under this study included:
- Demographic variables: age, gender, settlement of origin,
- Clinical variables: Disease classification, patient category, HIV status, History of IPT, History of HIV treatment, and outcome of the disease,

Descriptive analysis was used for examining the overall percentage and frequency distributions of variables under the rationale of this study. Data was summarised and displayed with tables, cross-tabulations, graphs and figures.

2.3.2 Measures of association and Hypothesis Testing
a) Measures of Association
To determine whether an association exists between HIV infection and/or Tuberculosis and other variables of interest, such as outcome of treatment, gender and age:
- We identified a population of TB-persons for study and determined the group by presence or absence of HIV infection and outcome of interest for each variable. Then, we constructed the two-by-two table.
- We calculated the prevalence of outcome of interest in patients with HIV infection and compared this with the prevalence of outcome of interest in patients with non-HIV infection.
- We calculated the odds ratio (OR) by dividing the odds of having an outcome of interest in HIV-positive by the odds of having an outcome of interest in non-HIV infected individuals.
- The exact 95% Confidence Interval (CI) around these estimates and the p-value were computed.

In addition, the related test of statistical significance such as Pearson uncorrected $\chi^2$, Yates corrected $\chi^2$, and Mantel-Haenzel $\chi^2$ were computed. The Fisher exact test was used when any cell of the two-by-two table was less than 5.

B) Hypothesis Testing
In order to test the null hypothesis (Ho) of no relationship between HIV infection and TB the followings were valid:
- We assumed that the data was from a normally distributed population, and, that it meets the requirement for the application of the chi-square test ($\chi^2$).
- The $\chi^2$ values were computed from the two-by-two or two by N tables.
- The level of significance ($\alpha$) used during hypothesis testing was 5% and the critical value of $\chi^2$ considered was 3.84.

2.4 Ethical Consideration
In this study, ethical standards were adhered to as stated below

2.4.1 Access to data
The TB Coordinator was the custodian of the ETR and therefore was ensuring that clients whose data was examined remains anonymous to research team throughout the study as well as making sure that the data is kept in a secure location.
2.4.2 Permission to Conduct the Study
Permission to carry out this research was sought from Ministry of Health in the HRDC and MLG/IRB and from District Council Secretary in order to access the ETR for research purposes only.

2.4.3 The Principle of Anonymity and Confidentiality
We used anonymous data from clinic registers protecting the identity of patients as their names were not needed for the study. Data collection officers had access to data from the ETR after names and identification numbers of clients were removed by the TB Coordinator.

2.4.4 Protection of Data
All information extracted from the ETR was password protected and only made available to research team by the TB Coordinator.
Chapter 3: Study Results

3.1 Demographic profile of study subjects

3.1.1 Demographic profile of TB patients.
A total of 1043 (40.7%) TB patients and 29 MDR-TB (100%) medical records made up the study population. The distribution of TB cases by age group and HIV sero-status is presented in Figure 3.1.1

![Figure 3.1.1: Distribution of TB caseload by Age-group and HIV Sero-status](image)

From Figure 3.1.1 above, it can be seen that the age range was relatively and evenly spread. Nearly 65% of study population was between 15 and 44 years of age. The mean age of TB patients was 33.4 years and the standard deviation was 16.8 years. The minimum age was <1 year, maximum was 88 years and the mode was 34 years.

The study TB population was predominantly made up of HIV negative (59.6%) subjects. The overall ratio between HIV Negative and HIV positive TB cases was 1.4:1 and, the mean age
difference between HIV positive and HIV negative (2 years) was not statistically significant (P > 0.05).

The following Figures 3.1.2 and 3.1.3 provides a demographic information in understanding difference in occurrence of HIV related tuberculosis in Ghanzi district.

![TB Caseload by Agegroup and Sex](image)

**Figure 3.1.2: TB Caseload by Age group and Sex**

From the above figure (3.1.2) it can be seen that, Tuberculosis is predominant among female subjects in under 35 years meanwhile, predominant in male above 35 years. The analysis of data did not show any statistical significance between sex and HIV sero-status in TB genesis (OR = 0.6 and 95% CI = 0.5 to 0.8).

From figure 3.1.3, it can be seen that out of 20 locations, more than 60% of TB cases were centered between Ghanzi township (37.9%), D'Kar (8.2%), Charleshill (7.6%), Grootlaagte (5.7%), Kuke (5.2%) and Kalfontein (5%).

Tuberculosis was predominant in HIV infected subjects only in location such as Charleshill (64.6%), Nojane (59.4%) and Kole (52.2%), also it was predominant in HIV negative in the 17 remaining locations (p < 0.005).
Figure 3.1.3: Distribution of TB Cases by location

3.1.2 Demographic profile of MDR-TB patients

- Female 15 (51.7%); Male 14 (48.3%)
- Mean age = 36.1          SD = 14.5
- Minimum age = 20
- Maximum age = 82 ;     Mode = 25

Figure 3.1.4: Distribution of MBR-TB Cases by age group and gender

From the figure 3.1.4 it can be seen that, of 29 MDR-TB patients, the disease was predominant between 15 to 54 years. The mean age of MDR-TB patients was 36.1 years
with a standard deviation of 14.5 years. The minimum age was 20 years while; the maximum age was 82 years. MDR-TB disease was equally distributed by gender. Of the 20 locations assessed; MDR-TB cases were predominantly in Ghanzi Township, D’kar and Kacgae followed by Karakubis, Qabo, Ncojane, Kalfontein and Charleshill.

3.2 Epidemiological and Clinical considerations
3.2.1 Patients category
Patients who have never had treatment for TB, or who have taken anti-TB treatment for less than one month (new TB case) were the most predominant and accounted for 825 (79.1)% of all TB cases. Meanwhile, the overall district TB re-treatment (default, relapse and failure) rate was 218 (20.9%). Re-treatment due to relapse was the most predominant and accounted for 72.5% followed by defaulters and failures at 20.2% and 7.3% respectively. The distribution of TB patient’s category by HIV sero-status is shown in Figure 3.2.1

![Figure 3.2.1: Distribution of TB patients by Category and HIV Status](image)

The analysis of Data indicated that TB patient’s category was strongly associated to the age, location, disease classification and treatment outcome (p < 0.005). Meanwhile, there was no statistical relationship between sex, HIV sero-status and patient’s category (p > 0.05).

Of 218 (20.9%) district re-treatment (relapse, default and failure) TB cases, Ghanzi township accounted for 107 (49.7%) followed by Charleshill 17 (7.8%), Grootlagte 16 (7.3%), Ncojane 12 (5.5%) and Kacgae 10 (4.6%). The other locations have a re-treatment rate of < 4%.
When stratifying TB re-treatment cases by age group as shown in Figure 3.2.2, there was a gradual increase of TB re-treatment cases among under 25 years followed by gradual decrease among those who were above 45 years of age. The re-treatment rate was lower in subjects under 25 and above 44 years of age. Patients with pulmonary and both (pulmonary and extra-pulmonary) tuberculosis were more likely to re-treatment TB as compared to those who had only extra-pulmonary tuberculosis. With regards to MDR-TB caseload, the following figure 3.2.3 gives an overview of MDR-TB patients by history of tuberculosis and year.

**Figure 3.2.2:** Distribution of TB Re-treatment case by Age group

**Figure 3.2.3:** Distribution of MDR-TB cases by Year and TB History
From figure 3.2.3 above, it can be seen that MDR-TB cases were predominant among patients who fail the previous TB regimen followed by new MDR-TB cases. Of 29 MDR-TB cases, 21 (72.4%) were MDR confirmed, 5 (17.2%) had poly-resistant MDR-TB and 3 (10.3%) were MDR suspect cases.

### 3.2.4 Disease Classification

In this section, we present an overview of TB classification in patients seen during the study period. Pulmonary tuberculosis (84.5%) remains the most common disease among Ghanzi population. Meanwhile, the commonest Extra-pulmonary tuberculosis among study subjects include: TB lymph-nodes and Pleural tuberculosis. The overall TB classification among study subjects is presented in figure 3.2.4.

Data have revealed that, the disease classification was significantly related to the HIV sero-status, age, patient category and treatment outcome ($p < 0.05$). With regards to HIV sero-status; the analysis of Data have shown that HIV positive subjects were more likely to develop extra-pulmonary TB than HIV negative subjects ($p = 0.004$).
3.2.5 Treatment Outcome.

The treatment outcome of TB caseload was strongly related to age, HIV sero-status, patient category and disease classification (p < 0.005).

There was no history of failing regimen in under 15 years (n = 123) as compared to other age groups. Similarly, the fatality rate was as well lower in the same age-group as compared to the above 15 years.

Re-treatment patients were 8 times more likely to fail the regimen and 2 times more likely to be discharge dead as compared to new TB cases.

HIV positive patients were more likely to be discharged dead as compare to those counterpart HIV negative. Similarly, there was indication that HIV negative subjects are more likely to default and fail treatment than their counterpart HIV positive (p < 0.005).

The overall treatment outcome of TB patients is presented in Table 3.2.1.

**Table 3.2.1: Treatment outcome by HIV sero-status.**

<table>
<thead>
<tr>
<th>Treatment Outcome</th>
<th>HIV Negative</th>
<th>HIV Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Freq</td>
<td>%</td>
</tr>
<tr>
<td>Cured</td>
<td>187</td>
<td>30.1</td>
</tr>
<tr>
<td>Completed</td>
<td>315</td>
<td>50.6</td>
</tr>
<tr>
<td>Defaulted</td>
<td>58</td>
<td>9.3</td>
</tr>
<tr>
<td>Died</td>
<td>41</td>
<td>6.6</td>
</tr>
<tr>
<td>Failed</td>
<td>21</td>
<td>3.4</td>
</tr>
<tr>
<td>Total</td>
<td>622</td>
<td>100</td>
</tr>
</tbody>
</table>

With regards to MDR-TB caseload, of 15 MDR-TB patients who completed treatment, 11(73.3%) were discharged cured and 4(26.7) were discharged dead. Similarly, it is
important to underline that 4 MDR-TB cases were dead before starting treatment and 10 were still on treatment.

3.2.4 TB Fatality rate.
This study revealed that the overall TB fatality rate in Ghanzi district is 10.3%. Female subjects died more younger (25 – 34 years) as compared to male (35 to 44 years).

When stratifying fatality by HIV sero-status, this yielded an overall case fatality rate of 15.7% in HIV positive patients and 6.6% in HIV negative. The mean age at death in HIV negative and positive subjects was 49.9 years and 35.3 years respectively. The mean age difference between HIV negative and HIV positive at death (14.6 years) was statistically significant (p < 0.005).

3.2.5 Prevalence of HIV related Tuberculosis.
This study revealed the prevalence of HIV-related tuberculosis in Ghanzi district is 40.4%.

3.2.6 Relationship between HIV and Tuberculosis.
As described above, the study population was predominantly made up of HIV negative (59.6%) subjects. The overall ratio between HIV Negative and HIV positive TB cases was 1.4:1. The mean age difference between HIV positive and HIV negative (2 years) was not statistically significant (P =0.16). Therefore, this study failed to establish any statistical relationship between HIV and tuberculosis.

When stratifying by age-group (25 – 44 years, n = 514), HIV positive subjects account for 269 (52.3%) of this age-group. The prevalence ratio between HIV positive and HIV negative TB cases was 1.1:1 (p = 0.1). Therefore, there is a weak association between HIV and TB in this particular age-group.

3.3 Limitations of the study
The limitations encountered during the course of this study included:

i. Secondary data: Data was extracted from ETR and District TB and MDR-TB registers. Therefore, we did not crosscheck Data with health facilities TB and MDR-TB registers

ii. Time frame: We conducted this study in three calendar months.
Chapter 4: Discussion

Kenyon et al (1999) indicated that, during the HIV and TB co-epidemics in sub-Saharan Africa, DOTS may help to control drug-resistant TB. However, the TB case rate can be expected to continue to rise in spite of the implementation of the DOTS strategy. In Ghanzi district, more TB cases occurred than in any part of Botswana. Data from Botswana National TB program (BNTP) indicated that TB notification rate in Ghanzi was two fold higher as compared to the national. Because our primary intent was to investigate the relationship between HIV and TB genesis in Ghanzi district, we used a cross-sectional study design, and our inferences statistics refer to the Ghanzi district individuals rather than to the nation as whole.

Whereas Cantwell and Binkin (1996) and Shafer et al. (1995) have shown a strong association between HIV and TB, this study failed to establish any statistical relationship between TB and HIV. The overall ratio between HIV Negative and HIV positive TB cases was 1.4:1 and, the mean age difference between HIV positive and HIV negative was not statistically significant. Findings of our study likely differ from observations at the national level for two main reasons. Firstly the lowest HIV prevalence among Ghanzi district residents as compare to other districts. Secondly, TB notification rates had various underlying causes. Out of HIV infection, historic trends in TB disease have shown a relation between paediatric TB and poverty in Chicago, Ill (Reinhard et al. 1997), and between adult TB and indices of social deprivation in Liverpool, United Kingdom (Spence et al. 1993 and Tocque et al. 1999). Excess cases of TB have been noted to occur in only the poorest areas in England and Wales (Bhatti et al. 1995), and changes in unemployment were associated with a change in TB rates in London, England, from 1982 to 1991 (Mangtani et al. 1995). Similarly, Reinhard et al (1997) and Drucker et al. (1994) indicated that residential crowding was associated with TB genesis.

MDR-TB in Ghanzi district seems also to be associated with the high TB notification rate, failure to manage TB patients according to national guidelines and social deprivation among population under this study. Findings of this study revealed that the ratio between HIV negative and HIV positive subjects affected with MDR-TB was 1.6:1. Similarly, with regards
to previous TB history, findings of this study revealed that 61.5% of MDR-TB patients are due to failure of previous TB regimen meanwhile, MDR-TB due to TB relapse and new MDR-TB accounted for 15.4% of all MDR-TB cases respectively.

In summary, poverty and social deprivation in Ghanzi district may be linked to TB and MDR-TB through a variety of identifiable risk factors over time and, as such, can be thought of as a "fundamental social cause" of above diseases. It may not be possible to correct the burden of HIV disease linked to TB and expect the socio-economic gradient to resolve. The introduction of widespread antiretroviral therapy in homeless shelters, prisons, and hospitals in Ghanzi will reduce the total burden of HIV disease. However, it is unlikely that the association of TB and poverty will disappear. Therefore, priority should be given to uplifting socio-economic status of this impoverished neighbourhood.
Chapter 5: Conclusion and Recommendations

5.1 Conclusion

Tuberculosis is the most common public health problem in Ghanzi district. With the advent of HIV/AIDS, it was necessary to study the epidemiology of tuberculosis in order to understand the extent to which HIV/AIDS may change the epidemiology and natural history of tuberculosis in Ghanzi district.

The findings of this study suggested that subjects economically productive (15 – 44 years) at the district level are the most affected with TB and MDR-TB disease. For all age combined tuberculosis affect predominantly male subjects meanwhile, female are affected during reproductive ages.

Ghanzi Township remains the area with huge number of TB and MDR-TB cases. With regard to HIV sero-status, findings of this study indicated that the prevalence of HIV-related tuberculosis in Ghanzi district is 40.4%. The overall ratio between HIV Negative and HIV positive subjects affected by tuberculosis and MDR-TB was 1.4:1; 1.6:1 respectively.

Subjects aged between 25 to 44 years were the most infected and affected by both TB and HIV illnesses and, the analysis of data indicated a weak association between HIV and tuberculosis in the above mentioned age-group. Meanwhile, for all ages combined, this study fails to establish any statistical relationship between HIV and Tuberculosis. HIV related and / or associated tuberculosis was common in areas such as Charleshill, Ncojane and Kule villages.

Primary tuberculosis (new cases) is the most common in the district and, accounted for 79.1% of all TB cases. There is indication that re-treatment TB cases essentially relapse are predominant in selected locations such as Ghanzi Township, Charleshill, Grootlagte, Ncojane and Kacgae. Similarly, findings of this study highlighted that re-treated TB patients were at very high risk of failing regimen and dying from tuberculosis.
With regard to disease classification, pulmonary tuberculosis was the commonest especially in HIV negative subject. Meanwhile, extra-pulmonary tuberculosis essentially TB pleural and lymph-nodes TB were common among HIV positive individuals. Patients infected with pulmonary tuberculosis or both (pulmonary and extra-pulmonary) were more likely to retreatment as compare those with only extra-pulmonary tuberculosis.

The treatment outcome was strongly associated to the age of the patient, HIV sero-status, patient category and disease classification. As for age, children have shown a very good response to TB treatment. Deaths due to tuberculosis and subjects failing regimen were not common among under 15 years of age. Finally, findings of this study indicated that, while fatality was higher among HIV positive subjects, failing regimen and defaulting treatment was predominant among HIV negative individuals.

5.2 Recommendations
Ghanzi district has a very high incidence of TB in Botswana. As a result, TB should be approached as an emergency in Ghanzi. Apart from HIV prevention and care, the district TB control programmes need to emphasize risk factors such as socio-economic inequality, ethnic differences, adult crowding, family structure, gender, and poor housing conditions. In order to reverse the spread of TB and MDR-TB in the district and ensure effective and efficient infection control measures, district leaders should consider the following:

i. Upgrade some health post into clinics.
ii. Construct or renovate an appropriate TB isolation ward.
iii. Accelerate the implementation of Community TB Care.
v. Revitalize the farm health aider’s programme.
v. Consider to improve living condition of the population

Similarly, different Stakeholders and community members need to be involved and play a pivotal role in addressing issues related to their organization within the TB programme, i.e. moral support, treatment, advocacy for resources, financial support and emotional support.
References


De Cock KM, Soro B, Coulibaly IM, Lucas SB. Tuberculosis and HIV infection in sub-Saharan Africa. JAMA 1992; 268: 1581-1587


- Ministry of Health (MOH); National Tuberculosis Programme Manual.MOH, 2007


- WHO, Treatment of Tuberculosis; Guidelines for National Programmes, 2003
Appendix A: Map of Botswana showing the study area
## Appendix B: AN EPIDEMIOLOGICAL ANALYSIS OF HIV-RELATED TUBERCULOSIS IN GHANZI DISTRICT

### DATA COLLECTION SHEET

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Where: 1 = Facility Number; 2 = Year initiated on treatment; 3 = Patients registration number at the facility; 8 = Localization of Extra pulmonary TB