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# Prevalence of multi-drug resistant tuberculosis among adult patients at Ndola Central Hospital, Ndola, Zambia

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***Abstract***

*Study aimed at determining prevalence of Multi Drug Resistance Tuberculosis at Ndola Central Hospital among Adults, Ndola, Zambia.*

*A retrospective cohort study review was conducted among adult MDR-TB patients at Ndola Central Hospital from 15th August to 22nd August 2014. All records for MDR TB patients from MDR TB ward were reviewed (January 2010 up to June 2014). Sample size was 114, Convenient sampling was done using MDR- TB treatment register and laboratory results. Data was analyzed using Epi Data version 3, and Pearson Chi square. The findings revealed that 48.2% of the patients with MDR TB had sputum positive results for culture, compared to 6.6% whose sputum was negative. The study also found that, of all (114) MDR TB patients who were admitted in MDR TB ward at Ndola Central Hospital, only 44% had Multi drug resistance , 33% had Mono resistance, while 22.6% had Poly resistance. The findings revealed that 29.8% were new cases, 23.7% treatment failure, and 4.9% relapse. Discussion of findings shows that; almost 50% of the respondents had MDR TB which was confirmed by sputum culture results and others had poly resistance and mono resistance. The respondents were either new cases, treatment failure or relapse cases, which showed that there could be other factors associated with drug resistance.*

***Conclusion:*** *prevalence rate of MDR TB was 44% and is major threat for TB control measures and proper treatment options.*

***Keywords:*** *Prevalence, MDR-TB Resistance, Ndola, Zambia.*

## Chapter one

### 1.0 “Introduction”

MDR TB is a major health hazard in many countries worldwide and is considered a major threat to TB control and eradication. Globally, 3.5% of new and 20.5% of previously treated TB cases was estimated to have had MDR-TB in 2013. This translates into an estimated 480 000 people having developed MDR-TB in 2013 (1). In Zambia TB is a major public health problem which causes increased morbidity and mortality. The advent of MDR-TB impinges of the successful treatment of this preventable and curable infectious disease.

Analyses of MDR TB Epidemiological changes in Zambia were done in order establish the magnitude of the problem, so that prioritization of interventions on disease prevention and control are implemented for policy and practice. MDR TB is defined as Tuberculosis that is resistant to at least Isoniazid (INH) and Rifampcin (RMP) (2), with or without resistance to other drugs. MDR TB can either be due to acquired resistance or primary resistance. In Zambia we have the National TB Control Programme (NTP) which works in close collaboration with the National TB reference laboratory network to ensure early diagnosis and treatment. Therefore, appropriate management of MDR- TB cases would allow the NTP to achieve good cure rates and reduce the risk of transmission of resistant strains. The prevalence of MDR TB in Zambia is low as there have been scarce studies done to establish the disease burden at national level and district level.

Ndola Central Hospital has been reporting increased incidence and prevalence of MDR TB cases since 2009. It is a referral center for Copperbelt, Northwestern, Northern, Muchinga and Luapula Province covering the northern part of the country. Therefore, the investigator would like to establish the disease burden of MDR- TB.

## 1.2 Literature review:

This chapter reviewed the literature related to MDR- TB. The literature review provided the reader with an overview of major academic works done by other scholars. An electronic search on key words published only in peer reviewed articles in data bases where university of Zambia subscribes were performed to compile the main body of literature that have been reviewed. Journal articles were also reviewed and made consultation to people involved in TB research for current facts on MDR-TB.

### 1.2.1 Disease burden

WHO, estimated that, there were about 0.5 million new MDR-TB cases in the world in 2011, and 60% of these cases occurred in Brazil, China, India, the Russian federation and South Africa alone (7). However, WHO 2014 report revealed that there are five high MDR-TB burden countries (Ethiopia, Kazakhstan, Myanmar, Pakistan and Viet Nam) achieved treatment success rates of ≥70%. However, overall only 48% of patients with MDR-TB were successfully treated, largely as a result of high mortality and loss to follow-up (1). The study revealed that proportion of TB cases with drug resistance was about 3.7% of new tuberculosis patients in the world have MDR strain (2). However, recent studies done by NRITLD 2013 revealed that, there about 425000 new MDR TB cases occur in the world and constituted about 5% of overall TB burden (4). Its prevalence worldwide was approximately 2 to 3 times this number (5).

According to WHO 2014, reported that in 2013, there were 480 000 new cases of MDR-TB worldwide, and approximately 210 000 deaths from MDR-TB. Among patients with pulmonary TB who were notified in 2013, an estimated 300 000 had MDR-TB. More than half of these patients were in India, China and the Russian Federation (1). The study done in South Africa revealed that provincial differences confirmed case yield of 32% (range 24%- 45%), smear positive 79% (range (72%- 84%), S - / C+ proportion 21% (range 16% - 28%). The treatment success was 89%, while treatment failure was 10.4% and treatment effectiveness accounted success of 49.2% as an outcome of all patients started on treatment (9). A study done in Ethiopia reported a high prevalence rate of MDR-TB which ranged from 3.3%-46.3% (15).

In Zambia TB is one of the major Health problems with National prevalence of 568/100 000 (14). A retrospective review of national surveillance of MDR- TB data was done in Zambia from 2001 to 2011, the finding revealed that total number of DST performed during 11 year period was 2,038 which accounted for 2.6% (2,038/78,639) of all the retreatment cases notified (12).

Ndola Central hospital has been receiving patients with MDR – TB as a referral center. Review of data shows that there has been an increase in the disease burden as shown below for the year 2013.

## 2013 first quarter MDR TB new admissions

**Table 1:** NCH/MDR- Tb ward/ Hmis 2013 (12) showing that there were 26 cases of MDR- TB admissions, among these one died in second quarter.

| | January | February | March | Total |
|---|---|---|---|---|
| Male | 10 | 3 | 2 | 15 |
| Female | 15 | 3 | 3 | 21 |
| Death | 0 | 1 | 0 | 1 |

### 1.3 Statement of the problem

Review of data highlights an increase in the prevalence of MDR-TB globally. The global MDR – TB in 2010 was estimated to be 650 000 cases of which majority were reported from Eastern Europe and Asia, with sub-Saharan Africa for a very small undefined proportion (14). According to WHO report there were 480 000 new cases of MDR-TB worldwide, and approximately 210 000 deaths from MDR-TB (1). In Africa data on MDR-TB is scarce, however, between 2007 and 2012, a total of 65,422 MDR-TB cases were reported by 15 countries (15). WHO reported that South Africa comprises of 87.9% of the African burden of MDR-TB with estimated MDR-TB prevalence among all cases in South Africa of 15,419 cases (16). In Zambia 446 cases were reported in 2011 through the National surveillance review (11). However, there has been a steady increase in the number of MDR – TB cases as shown by the statistics from Ndola Central Hospital MDR- TB ward. In 2009 when the Centre was opened there were 4 cases of MDR- TB which were notified as new cases and analysis of 2012 records revealed an increase in the disease burden of 30 cases recorded at NCH/MDR- TB ward. Currently, there are 11 patients admitted with MDR –TB, of these 5 are males and 6 females in 2014 up to June (10). In view of the above, the investigator would like to establish the disease burden in order to explore and recommend interventions which can help curb the scurge and for policy prescription. What could be escalating the prevalence of MDR –TB in Ndola, Zambia? How many patients were admitted at NCH with MDR- TB from 2010 to 2014?

### 1.4 Justification

The investigator aimed at establishing the magnitude of MDR- TB at NCH among adults as it is a major threat to the health of the nation. The investigation from the public health perspective will help in understanding the disease burden in order to come up with good policy prescriptions in the prevention and control of MDR- TB. The study also generated first hand data based on local experience and strengthens planning and implementation of interventions.

### 1.5 Case finding

According to the Zambian MDR- TB guideline, MDR- TB should be suspected when a patient has persistent positive acid fast bacilli smear or culture (beyond five months of treatment with category I) or clinical progression of TB while on standard chemotherapy (12).

## Chapter two: Objectives

### 2.0 General Objective

To determine the prevalence of MDR TB: Ndola Central Hospital, Ndola, Zambia

### 2.1 Specific Objective

1. To establish the proportion of MDR- TB cases at Ndola Central Hospital.
2. To identify factors escalating MDR –TB.

### 2.2 Research Question

"How many patients were admitted at NCH with MDR- TB from 2010 to 2014?"

### 2.3 Definitions

#### 2.3.1 General definitions of resistance (10)

The category IV diagnostic criteria is defined as "chronic cases" i.e. still smear positive after supervised retreatment; proven or suspected MDR- TB.

A patient is determined to have drug resistant TB only through laboratory confirmation (culture and drug susceptibility testing) of resistance of one or more first line anti-tuberculosis treatment.

Multi-drug resistant (MDR-TB) tuberculosis that is resistant to at least Isoniazid and Rifampcin.

Drug resistance refers to patient pulmonary tuberculosis coughing out bacilli resistant to one or more anti-tuberculosis drugs.

### 2.3 Bacteriology and sputum conversion

Bacteriological examinations in patients with drug resistant TB should include sputum smear microscopy and culture. All patients suspected of having MDR- TB must have two sputum samples collected at the health facility. Direct smear can be analyzed at the nearest diagnostic facility, however on sample must be sent for culture and DST (10).

## Chapter Three: Methodology

### 3.1 Research Design

A Retrospective Cohort study using the existing data and laboratory results in patient files and MDR TB register was reviewed at Ndola Central Hospital for all MDR TB patients who had their culture and drug susceptibility test done at Ndola Central Hospital. Period under review involved patients who were admitted between 2010 and June 2014. Data on the patient's characteristics were obtained from the MDR- TB treatment file and MDR-TB register.

### 3.2 Research Setting

The study was carried out at Ndola Central Hospital MDR TB ward as it is the second referral centre for MDR-TB in Zambia. The site had been purposely selected as it is a referral centre covering Copperbelt Province, North Western, Luapula, Northern and Muchinga Province.

### 3.3 Study Population:

A cohort of all 114 MDR- TB patients who were admitted at Ndola Central Hospital for MDR TB between January 2010 and 2014 June in MDR TB ward.

### 3.4 Sample Selection

Convenient sampling method was used as it involved the use of all research subjects at the research site.

**Inclusion criteria:** All MDR- TB patients category IV cohort, who were confirmed with smear positive or negative, Notified, on treatment and/ or completed treatment at Ndola Central Hospital from 2010 to 2014 June.

**Exclusion criteria:** All MDR- TB patients category IV cohort, who were confirmed with smear positive or negative, Notified, on treatment and/ or completed treatment outside Ndola central hospital from 2010 to June 2014.

### 3.5 Data collection tool

Structured checklist modified from the Zambia National Tuberculosis and Leprosy Control program for category IV treatment MDR- TB guideline was used during review of records (see appendix II).

### 3.6 Data collection technique

This study used a structured checklist through observation to enhance proper data collection on the existing data base in the patient's file and MDR- TB patient register. Data was collected from 18th to 23rd August 2014.

### 3.7 Sample size:

The sample size was 114 patients who were notified since January 2010 to June 2014, this was a population study.

### 3.8 Ethical consideration:

Consent was obtained from Ndola Central Hospital to review the register and patients' files. There was no risk and immediate benefits to those patients whose - files were reviewed. Consent was not obtained from patients whose records were reviewed as permission was sort from Ndola central hospital. Patients were in a natural setting and hence were not exposed to emotional or physical harm since there was no contact with the investigator. Confidentiality and anonymity was maintained to all patients records as their names did not appear on the checklist, instead the serial number were used. Privacy was maintained as all patients records were reviewed in a in a private room and filled in checklists were kept under lock and key after each review.

## Chapter Four: Data presentation and analysis

### 4.0 Introduction

The study aimed at determining the prevalence of MDR TB among adult patients who were admitted at NCH in MDR TB ward. A Total of 114records were reviewed for MDR TB patients who were admitted in the MDR TB ward at NCH from January 2010 to 2014 June. Category IV treatment cohort consisted of a subset of patients recorded in category IV register who started category treatment during the specified time period (2010 to 2014 June).The findings of the study were based on analysis of data collected from the patients' records and MDR TB register. The data was sorted out for completeness, categorized and coded. Data was analyzed using Epi Data version 3, and 95% confidence interval was set together with estimates using Pearson Chi square.

Cut off point for significance was set at 5%. Statistical significance achieved if P value is 0.05 or less, thereby rejecting the null hypothesis. The data was analyzed by univariate analysis to make frequency tables, then bivariate analysis to make cross tabulations. The data was presented using tables and graph for easy communication.

### 4.1 Demographic Data

**Table 2:** Sex (n=114)

| Sex | | Frequency | Percent |
|---|---|---|---|
| | 1(Males) | 77 | 68.1 |
| | 2 (Females) | 37 | 31.9 |
| Total | | 114 | 100.0 |

Table above shows that majority 68.1% of the MDR TB patients were males, while 31.9% were females.

**Table 3:** Frequency of MDR TB patients according to years (n = 114)

| Years | Frequency | Percent |
|---|---|---|
| 2010 | 28 | 24.6 |
| 2011 | 21 | 18.4 |
| 2012 | 30 | 26.3 |
| 2013 | 17 | 14.9 |
| 2014 | 18 | 15.8 |
| **Total** | **114** | **100.0** |

Table 3 revealed that there were more cases 26.3% of MDR TB patients who were admitted in 2012 than 14.9% in 2013.

**Table 4:** Sputum Culture Results (n= 74)

| Sputum results(culture) | Frequency | Percent |
|---|---|---|
| 1 (positive) | 65 | 87.8 |
| 2 (negative) | 9 | 12.2 |
| Total | 74 | 100 |

Table 4 shows that majority 87.8% sputum results were positive, while 12.2% were negative.

**Table 5:** Sputum Microscopy (n = 114)

| Sputum result | Frequency | Percentage |
|---|---|---|
| Positive | 106 | 92.7% |
| Negative | 8 | 7.0% |
| **Total** | **114** | **100%** |

Table 5 shows that, 92.7% of sputum results for microscopy were positive, while 7% were negative.

**Table 6:** Drug Sensitivity Test (DST) Result (n=114)

| DST results | Frequency | Percent |
|---|---|---|
| 1(Mono) | 28 | 33.3 |
| 2 (MDR) | 37 | 44.0 |
| 3 (Poly) | 19 | 22.6 |
| **Total** | **84** | **100** |

The above table shows that only 44% of admitted patients had MDR TB, 33% had Mono resistance, while 22.6% had Poly resistance to TB drugs. However, 26.3% had incomplete or missing records.

**Table 7:** Reason for Category IV Treatment Card

| Reason for CAT IV | Frequency | Percent |
|---|---|---|
| After default | 7 | 6.1 |
| After failure of first treatment | 27 | 23.7 |
| New | 34 | 29.8 |
| Relapse | 17 | 14.9 |
| After failure of re treatment | 1 | .9 |
| transfer in | 1 | .9 |
| **Total** | **114** | **100.0** |

The table above shows varied reasons for MDR TB, findings revealed that 29.8% were new cases, 23.7% were due to failure of first line treatment, 14.9% were due to relapse, 0.9% due to failure of re treatment, while 6.1% were due to default.

**Table 8:** Drug Sensitivity Test Result (DST) and Reason for CAT IV Treatment

| Reasons for cat iv | DST results | | | Total |
|---|---|---|---|---|
| | 1Mono | 2 MDR | 3 Poly | |
| 1 Default | 2 (40%) | 1 (20%) | 2 (40%) | *5(100%) |
| 2 Failure of first line treatment | 5 (23.8%) | 13 (61.9%) | 3 (14.2%) | *21 (100%) |
| 3 New | 15 (53.5) | 6 (21.4%) | 7 (25%) | *28 (100%) |
| 4 Relapse | 0 (0%) | 10 (83.3%) | 2 (16.6%) | *12(100%) |
| 5 After failure of re treatment | 1 (4.3%) | 0 (0%) | 0 (0%) | *1(100%) |
| **Total** | **23 (34.3%)** | **30 (44.7%)** | **14 (20.8%)** | **67 (100%)** |

*Note: Interpretation should be done with caution because denominator is less than 30.

Table 8 shows that most of the patients with failure to first line treatment were due to MDR 61.9%, while Mono resistance was 23.8% and Poly was 14.2%. Pearson Chi square 20.872a, df = 8, P value 0.007 (significant at $p < 0.05$)

**Table 9:** DST Result and Sex (n = 114)

| | | DST result | | | Total |
|---|---|---|---|---|---|
| | | 1 Mono | 2 MDR | 3 Poly | |
| SEX | 1(Males) | 17 (30.9%) | 26 (47.2%) | 12 (21.8%) | 55 (100%) |
| | 2 (Females) | 11 (37.9%) | 11(37.9%) | 7 (24.1%) | 29 (100%) |
| **Total** | | **28 (33.3%)** | **37 (44%)** | **19 (22.6%)** | **84 (100%)** |

Table 9 shows that there were 47.2% males with confirmed MDR TB compared to 37.9% females. However, these proportions were not significantly different (Pearson Chi square 0.702, df = 2, P value = 0.704).

**Table 10:** Sputum Culture and Drug Resistance

| Sputum result | Drug resistance | | | Total |
|---|---|---|---|---|
| | 1 Mono | 2 MDR | 3 Poly | |
| 1 (positive) | 20 (34.4%) | 28 (48.2%) | 10 (17.2%) | 58 (100%) |
| 2 (negative) | 1 (25%) | 2 (50%) | 1(25%) | 4 (100%) |
| **Total** | **21 (33.8%)** | **30 (48.3%)** | **11 (17.4%)** | **62 (100%)** |

Table 10 shows that almost half 48.2% (28) of the patients with MDR TB had sputum positive results for culture, compared to 6.6% (2) whose sputum was negative. Pearson Chi square 0.229a, df = 2, P value 0.892. (Not significant at $P< 0.05$)

## Chapter five: Discussion of Findings

### 5.0 "Introduction"

The main objective of the study was to determine the prevalence of MDR TB among adult patients who were admitted at Ndola Central Hospital in MDR TB ward from 2010 to 2014 June. The Cohort study involved review of 126 patients' records and MDR TB register which were obtained from MDR TB ward at NCH and only 114 records met the criteria for selection into the study. Review of records was done from 18/08/14 to 22/08/14 using a structured checklist. In this

study the themes used to discuss the findings are: Demographic Characteristics and Drug resistance results.

In this study majority 68.1% of the MDR TB patients were males, while females accounted 31.9%. However sex was not associated with MDR TB (P value 0.704). This could be attributed to poor health seeking behavior by most males as they seem to be busy and attach little attention even to their own health, however, females have a caring role for all family members and seek medical attention early.

The study findings revealed that, there were 114 cases of MDR TB among adults who were admitted at NCH during the period under review, of these, 26.3% (30) of MDR TB patients were admitted in 2012 while 14.9% (17) in 2013.

Findings revealed that most 87.8% of sputum results for culture were positive, while 12.2% were negative; however, 35.1% had no results. This could be attributed to poor record keeping, poor screening practices or inconsistent laboratory operations due to insufficient reagents. The findings further revealed that, most 92.7% of the sputum results for microscopy were positive, while 7% were negative. This is almost similar with the findings done in South Africa by Weyner who stated that smear positivity was 79%, while S-/C+ proportion was 21% (9). The study findings revealed that there is no association between sputum for culture result and MDR TB (P value 0.892).

The study showed that almost half 48.2% (28) of the patients with MDR TB had sputum positive results for culture, compared to 6.6% (2) whose sputum was negative. This shows that there could be an association between positive sputum result and MDR TB. The study further revealed that, of all (114) MDR TB patients who were admitted in MDR TB ward at NCH, only 44% (37) of these patients had Multi drug resistance , 33% had Mono resistance, while 22.6% had Poly resistance to TB drugs. There was no XDR-TB case found. However, 26.3% had incomplete or missing records. This finding supports the findings of Kapata N (2013) done in Zambia on National Surveillance of MDR TB data reported that the total MDR TB cases were 446, poly resistance was 18.9% and Mono resistance was 8.8% and no case of XDR-TB reported (11).

The findings also showed varied reasons for MDR TB prevalence, findings revealed that 29.8% were new cases, 23.7% were due to failure of first line treatment,14.9% were due to relapse, 0.9% were due to failure of re treatment, while 6.1% were due to default. The findings revealed that there was a significant relationship between reasons for failure and MDR TB (P value 0.007). This compliments the study findings done by NRITLD (2013) whose findings reported that MDR TB was approximately 5% among new TB and 48.2% among re treatments in Iran (5). Study done by Weyner in South Africa revealed that MDR TB in New cases was 1.6%, while in retreatment was 6.7% (9). However, there are variations in these findings as the percentage of new cases in Ndola is higher than theirs and vise versa. This could be attributed to other factors.

## 5.1 Limitation and strengths of the study

Lack of adequate resources such, as funds and the time frame, in which the research project was completed. Delay in ethical approval was a major challenge. Ndola has been selected for convenience purposes. Notable strength of the study it is the first known research step towards addressing the various implementation problems that constrain service delivery.

## 5.2 Conclusion

MDR TB is Major threat to successful management of patients due resistance to first line treatment which is cheaper. The study revealed that there was inconsistence in the performance of sputum for culture and drug sensitivity test as a gold standard in determining MDR TB as there were gaps, as some patients were treated based on assumptions.

The other problem was that of incomplete recording system and poor filing of patients' records, and poor follow up to ascertain patient's outcome. Gaps were seen in infection prevention as visitors and patients moved freely without infection prevention measure being observed. Therefore, there is need to ensure that management of patients is done by skilled health staff based on analysis of epidemiological disease pattern and understanding treatment modalities. Significant strengthening of human and technical resources, accompanied by sufficient financial resources to create a conducive environment for the admitted patients as it is in deplorable state. There is need to develop and/or reorganize existing logistical operations to improve service delivery. Therefore, there is need to ensure prompt case management and early diagnosis, and Contact tracing is important in managing exposed contacts.

### 5.3 Recommendations

- Also community sensitization on importance early seeking behavior must be emphasized and MDR TB must be treated as a priority because of its severity and contagiousness.
- Need to strengthen infection prevention practices in MDR TB ward at NCH
- NCH to lobby for funds from MOH to rehabilitate and equip the ward as it is in deplorable state.
- There is need to invest in research of Drug resistance tuberculosis so as to establish the magnitude of the problem.
- NCH to lobby for more staffing for MDR TB ward as there is critical shortage to improve Service delivery.

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