

Geo-Spatial Distribution of Frequencies of MTB/RIF Detected Specimens based on Requesting Health Facilities in Manicaland Zimbabwe for 2017 and 2018

K Zvinoera¹, J Mutsvangwa², E Chikaka¹, T D Coutinho³, V Kampira⁴, S Mharakurwa¹

¹ Department of Health Sciences, College of Health Agriculture and Natural Sciences Africa University, Zimbabwe

² Biomedical Research and Training Institute, Harare Zimbabwe

³ Department of Geography and Environmental Science University of Zimbabwe

⁴ Mutare Provincial Hospital, Ministry of Health Zimbabwe

ABSTRACT

Objectives: The aim of this study was to produce Geo Spatial Distribution of Frequencies of MTB/RIF Detected Specimens based on Requesting Health Facilities in Manicaland Zimbabwe for 2017 and 2018, so as to give insight to TB program managers. Focusing elimination interventions on hot pockets of Tuberculosis (TB) strengthens rationale use of resources in resource limited countries like Zimbabwe. Early detection and early treatment is backbone of breaking TB transmission. Drug resistant tuberculosis (DRTB) control interventions like Programmatic Management of Drug Resistant TB or mentoring on Short, all Oral Regimen for Rifampicin resistant Tuberculosis (ShORRT) will be driven by science.

Materials and Methods: The retrospective study was carried out in Manicaland, Zimbabwe. Manicaland one of the 10 provinces in Zimbabwe, has 7 districts with 308 health facilities. During this retrospective cross sectional study 2221 MTB detected results of 2017 and 2018, downloaded from 14 of the 15 Genexpert sites in Manicaland were employed to generate hotspot maps. Fifteenth Genexpert site lost its electronic records when

Genexpert CPU crashed. Geographical Positioning System (GPS) of the health facilities were recorded. The study used MTB detected frequencies at a facility in relation to surrounding facilities in Manicaland, then ran optimised hotspot analysis function in Arc Map 10.5 to implement the Gi* statistic.

Results: Overall provincial MTB detected positivity was 2221/36055 (6.2%). Overall provincial Rifampicin Resistant (RR) positivity was .111.2221(5.0%). Geo-spatial map of Manicaland showed 10 facilities that are RR hotspots with 7/10 (70%) of the facilities in Buhera district. Chipinge district had facilities that were MTB detected high hotspots. For the whole of Manicaland, Buhera district had 100% MTB detected low hotspots facilities. Ninety percent hotspots were clustered around 2 of the 15 Genexpert Sites in Manicaland, namely Murambinda Mission Hospital and Chipinge District Hospital.

Conclusion: Study identified health facilities with high frequencies of RR areas. For the identified health facilities with high frequencies of RR specimens, NTP may focus DRTB control interventions like PMDT, or mentoring on ShORRT. For the health facilities with high frequencies of MTB detected NTP can focus trainings in TB Case

Corresponding author:

Zvinoera Katherine
Cell phone +263777398293
Email- zvinoerak@africau.edu

Key Words: Genexpert MTB/Rif, Geographical Positioning System, Geo Spatial Mapping

Management. Instead of uniformly spreading the limited resources to all 325 facilities, efforts streamlined to manageable number of 20 facilities in commensurate with identified gap(e.g. objective selection of cadres for training, data driven supportive supervision & targeted awareness campaigns).

INTRODUCTION

Utilization of geo-spatial mapping enables assessing of geographical distribution of infectious diseases. Tuberculosis (TB) like other infectious diseases, have epidemiological patterns that differ across geographical regions.^{1,2,3} Early TB detection and early treatment is the backbone to breaking transmission. In attempts to manage TB, the World Health Organization (W.H.O.)'s End TB Strategy, has a goal to end the TB epidemic by reduction to <10 cases per 100 000 population by 2035.⁴ Zimbabwe is among the 14 countries with a triple burden of TB, Human Immunodeficiency Virus positive people co-infected with TB (TB/HIV) and multi-drug resistant TB (MDR-TB). Incidence of TB in Zimbabwe in 2018 was estimated to be 210 per 100,000 population. Further estimates were that 62% of patients diagnosed TB, were HIV co-infected. Lastly among multi drug resistant TB (MDR-TB) patients HIV prevalence was 80%.⁵

To end TB successfully, disease elimination campaigns need to be characterized by locally tailored responses that are informed by evidence based medicine(e.g. objective selection of cadres for training, data driven supportive supervision & targeted awareness campaigns). For such a response to tuberculosis, a three-step process is vital, which includes, using existing programmatic data to guide decisions, collection of additional data (e.g. geographic information, drug resistance, and risk factors) to aid creation of tailored responses. Geo-Spatial distribution maps improve understanding of TB transmission dynamics. Focus on eliminating hot spots of TB is one strategy to meet the WHO end TB target of zero death due to TB by 2035⁶. Decisions made from spatial mapping include

rationale repositioning of resources, a must in resource limited countries like Zimbabwe. Resources like TB case management training, Programmatic Multi Drug Resistant Tuberculosis training, Mentoring through on site supportive visits, community awareness campaigns in targeted communities⁷. **Geo Spatial Distribution of Frequencies of MTB/RIF Detected Specimens based on Requesting Health Facilities** in Manicaland had not been created, judging by the lack of literature. There was need to generate geo-spatial distribution mapping of Genexpert MTB/Rif's semi quantitative results in Manicaland. Question on hand was what the **Geo Spatial Distribution of Frequencies of MTB is/RIF Detected Specimens based on Requesting Health Facilities in Manicaland Zimbabwe for 2017 and 2018**? The aim of this study was to generate geo-spatial distribution maps of Genexpert MTB/Rif results in Manicaland, Zimbabwe so as to give insight to TB program managers. In the study a spatial map was generated showing the **Geo Spatial Distribution of Frequencies of MTB/RIF Detected Specimens based on Requesting Health Facilities in Manicaland Zimbabwe for 2017 and 2018**. Focusing elimination interventions on hot pockets of Tuberculosis (TB) strengthens rationale use of resources in resource limited countries like Zimbabwe. Early detection and early treatment is backbone of breaking TB transmission. Drug resistant tuberculosis (DRTB) control interventions like Programmatic Management of Drug Resistant TB or mentoring on Short, all Oral Regimen for Rifampicin resistant Tuberculosis (ShORRT) will be driven by science.

MATERIALS AND METHODS

The study design employed was retrospective cross sectional design. The study was carried out in Manicaland Province (figure1). Figure 1 has Zimbabwe map on top left corner, with Manicaland located on the Eastern part of Zimbabwe. Figure 1 has enlarged map of Manicaland, which covers a total area of 36,459 square kilometres. It is the

second most populous province after Harare with a population total of 1.75million (Census, 2012). It is the third most densely populated province after Harare and Bulawayo. According to Zimbabwe District Health Information System (DHIS2) the province has 308 health facilities in 7 districts served by 15 Genexpert sites. The study population was MTB/Rif results analysed in Manicaland for the period 2017 and 2018. Complete enumeration was used. Study data sources were Laboratory TB registers, Genexpert machines and GPS coordinates captured for the 308 requesting health facility. Unit used for recording coordinates was requesting facility.

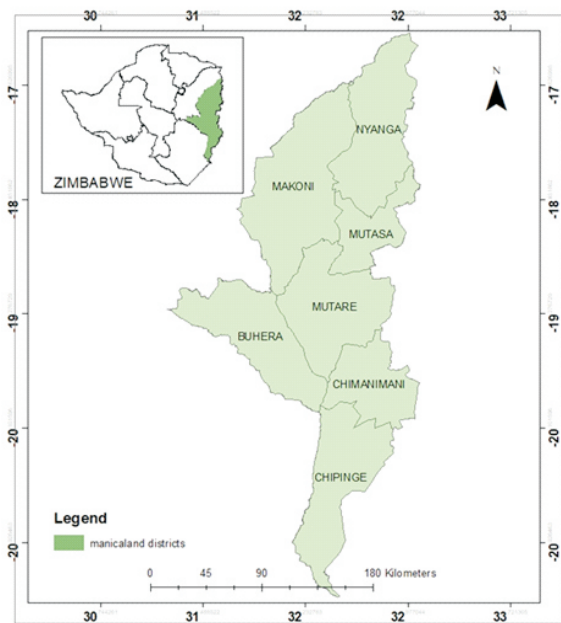


Figure1: Districts of Manicaland Province.

Genexpert MTB/Rif Excel sheet data was downloaded directly from the Genexpert machines to electronic format. Data from paper based TB registers was merged into the electronic format, the excel sheet and de-identified. Data was entered as line item capturing independent variables and outcome or depended variables. MTB/Rif data produced a categorical variable of; MTB detected high, MTB detected medium, MTB detected low and

MTB detected very low, MTB detected trace. Each followed by rifampicin resistant result (RR); RR not detected RR detected or RR indeterminate.

The geographic locations of health facilities were collected using Google earth pro. The geographic coordinates for Manicaland health facilities were then entered in a spread sheet and converted into a comma-separated values (csv) file for use in a GIS environment. The points were mapped using arcGis version 10.5 for visual analysis of MTB cases. The study used MTB detected frequencies at a facility in relation to surrounding facilities to run optimised hotspot analysis function in Arc Map 10.5 to implement the G_i^* statistic. The Getis-Ord (G_i^*) statistic assesses the extent to which events such as MTB data exhibit identifiable spatial patterns in space as hotspots and cold spots. Hotspots occur when areas with high values are surrounded by high MTB values while cold spots are locations with typically low values surrounded by similarly low values, from a given location i at spatially varying distances. The optimised hotspot analysis function in Arc Map 10.5 was used to implement the G_i^* statistic. The selection of the optimised hotspot analysis was based on its ability to correct for multiple testing as well as spatial dependence. The Z-scores and p-values measure statistical significance, influencing the decision whether to reject or fail to reject the null hypothesis. A high z-score and small p-value for a feature indicates a spatial clustering of high values. A low negative z-score and small p-value indicates a spatial clustering of low values. The higher the z-score, the more intense the clustering. A z score near zero indicates no apparent spatial clustering⁸. The study was approved by Manicaland Provincial Directorate, Africa University Research Ethics Committee (AUREC) and Medical Research Council of Zimbabwe (MRCZ).

RESULTS

Figure 2 shows how we downloaded 48260 Genexpert MTB/Rif results and ended up with 2221

results for this study. The findings in this study were overall provincial MTB detected positivity was 2221/36055 (6.2%). Overall provincial Rifampicin Resistant (RR) positivity was 111/2221(5.0%).

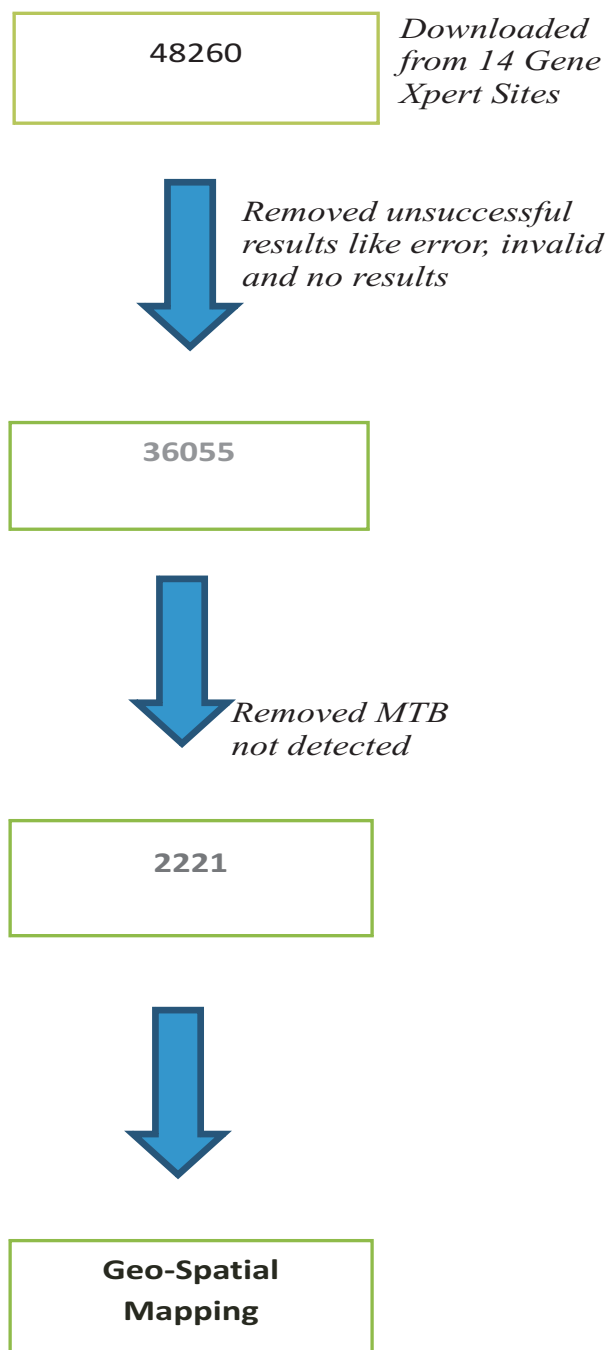


Figure 2: Flow Chart of Study Samples

Health Facilities that Submitted High frequencies of Rifampicin Resistant (RR) Specimens in Manicaland for 2017 and 2018

The red exes are the areas of concern in Figure 3. Our findings suggest that 7 facilities in Buhera district, 2 in Chipinge and 1 in Makoni district; Munyanyi clinic, Rambanepasi clinic, Mombeyarara Rural Health Centre, Gombe clinic, Murambinda Mission Hospital, Nyashanu Mission Clinic, Chiwese clinic, Matotwe Rural Health Centre, Kopera Rural Health Centre, Gaza clinic. There was intra-provincial epidemiological difference according to geographical setting. Intra-provincial epidemiological difference of RR allows focusing of MOHCC interventions to problem areas. NTP needs to further interrogate these findings to rule out practices leading to manmade drug resistance in the facilities that are RR hot spots. Other covariates have to be investigated such as facility ownership and specimen transport network at facilities.

Health Facilities that Submitted High frequencies of MTB Detected High Specimens in Manicaland for 2017 and 2018

Semi quantitative MTB results gave further insight; the GPS mapping data showed which requesting health facilities were surrounded by higher or lower concentrations of TB. One of the indicators of how good the TB program is at a health facility is reflected by diagnosis of TB at the earliest stages of the disease when the semi quantitative result is still trace or low, instead of high or moderate. A health facility which diagnoses mostly MTB detected high or MTB detected medium is an indication of poor performance of the TB program at the health facility. Facilities identified as TB hot spots require interventions to break chain of transmission to be applied or invested to decrease chances of community exposure to TB. May be sign of low index of TB suspicion at facility or may be poor health seeking behaviour of population near MTB detected high hot spots.

Our findings in figure 4, suggest that Chipinge district has 9 of the 14(64.3%) health facilities identified as MTB detected high hot spots in Manicaland. These results are not comparable to any in Zimbabwe, due to lack of literature on similar studies. Chirenda et al 2020 also carried out spatial mapping, but of TB patients archived in the Harare City registry. Their findings were that the home addresses of the TB patients formed hotspots in the peri urban area where there were no amenities. The lowest unit for our study was requesting health facility. The findings show that the hotspots are facilities that form a cluster around the Chipinge district hospital Genexpert site. The plausible reason could be that patients move (patient referral followed by specimen referral to Genexpert site) to clinics served by reliable integrated specimen transport system (IST). That means patients could be transient and not permanent residence of requesting facilities. High bacillary density facilities could be due to low index of suspicion. Or could be low health seeking behavior of the population around the facility. Further research has to be carried out to get more insight, however these findings have allowed stream lining of elimination intervention efforts. The intervention efforts could be training clinicians manning the hotspots to TB Case Management, mentoring via telemedicine or supportive visits. Hosting awareness campaigns such as the World TB day in hotspots would be another intervention strategy. These initial results help NTP to narrow down on a few health facilities, which can be further investigated. Consolidated MTB results hot spots further investigation should establish if specimens were submitted from local population, or could be people flocking from outside the district or the province. Rule out movement of people from within the district for temporary residence at convenient health facilities served by integrated specimen transport. NTB has fuel coupons to supplement motorized EHTs. The identified hot spot facilities could have population at risk such as prison or miners or people dwelling in overcrowded conditions.

Health Facilities that Submitted High frequencies of MTB Detected Low Specimens in Manicaland for 2017 and 2018

Our findings in figure 5, suggest that Buhera has hotspots of MTB detected low at Chapwanya clinic, Garamwera clinic, Murambinda Mission Hospital, Gombe clinic, Nyashanu Mission Clinic, Mombeyarara Rural Health Centre and Munyanyi clinic. These findings may be sign of good TB program at health facility with high index of suspicion. Another plausible reason may be early health seeking behaviour of catchment population. MTB detected low incident showed that TB disease was diagnosed before the patient had a chance to infect others in the community.

Health Facilities that Submitted High frequencies of MTB Detected Very Low Specimens in Manicaland for 2017 and 2018

Our findings in figure 6, suggest that Districts represented as follows; 3 requesting facilities from Chipinge district, 7 requesting facilities from Buhera district, 2 requesting facilities from Mutasa district.

MTB detected low incident shows TB disease diagnosed before the patient transmits TB in community. The results of MTB detected very low are not conforming to the expectations set by the other hotspot maps in this study. The plausible reason for these unexpected results, could be supporting the fact that it's not catchment population, but transient patient who temporarily move to near Genexpert sites to seek Genexpert MTB/Rif testing services.

CONCLUSION

Our findings demonstrate that there is variation in epidemiological pattern of TB in Manicaland. NTP may mobilise resources to enable focused TB elimination interventions in the identified facilities that are hot spots. NTP be guided by science to enable rational use of its limited resources. The

package of intervention may be more streamlined or specific type of elimination intervention strategy incommensurate with identified gap i.e. hotspot for RR or MTB detected high or MTB detected low.

RECOMMENDATIONS

Based on these findings M.O.H.C.C. to make use of the evidence generated to distribute the scarce TB elimination intervention resources to the identified hot spots (e.g. objective selection of cadres for training, data driven supportive supervision & targeted awareness campaigns). NTP be guided by science to enable rational use of its limited resources. The package of intervention may be more streamlined or specific type of elimination intervention strategy in commensurate with identified gap i.e. hotspot for RR or MTB detected high or MTB detected low. For the identified health facilities with high frequencies of RR specimens, NTP may focus DRTB control interventions like PMDT, or mentoring on ShORRT. For the health facilities with high frequencies of MTB detected NTP can focus trainings in TB Case Management.

Future Research

Suggestion for future research is to carry out a research focusing on hotspots to enable covariate analysis.

Acknowledgements

Biomedical Research and Training Institute (BRTI) for facilitating the research

This study was funded by Trials of Excellence in Southern Africa II (TESAII).

REFERENCES

1. Global tuberculosis report 2018. World Health Organization 2018. Available from: <https://apps.who.int/iris/handle/10665/274453>
2. Robsky KO, Kitonsa PJ, Mukiiibi J, Nakasolya O, Isooba D, Nalutaaya A, Salvatore PP, Kendall EA, Katamba A, Dowdy D. Spatial

- distribution of people diagnosed with tuberculosis through routine and active case finding: a community-based study in Kampala, Uganda. *Infect Dis Poverty*. 2020 Jun 22; 9(1):73. doi: 10.1186/s40249-020-00687-2. PMID: 32571435; PMCID: PMC7310105.
3. Maciel EL, Pan W, Dietze R, Peres RL, Vinhas SA, Ribeiro FK, Palaci M, Rodrigues RR, Zandonade E, Golub JE. Spatial patterns of pulmonary tuberculosis incidence and their relationship to socio-economic status in Vitoria, Brazil. *Int J Tuberc Lung Dis*. 2010 Nov; 14(11):1395-402. PMID: 20937178; PMCID: PMC3713790.
4. Zimbabwe Tuberculosis National Strategic Plan (2017 to 2020) Ministry of Health and Child Care
5. Timire C, Sandy C, Kumar AMV, Ngwenya M, Murwira B, Takarinda KC, Harries AD. Access to second-line drug susceptibility testing results among patients with Rifampicin resistant tuberculosis after introduction of the Hain® Line Probe Assay in Southern provinces, Zimbabwe. *Int J Infect Dis*. 2019 Apr; 81:236-243. doi: 10.1016/j.ijid.2019.02.007. Epub 2019 Feb 15. PMID: 30776546.
6. Theron G, Jenkins HE, Cobelens F, Abubakar I, Khan AJ, Cohen T, Dowdy DW. Data for action: collection and use of local data to end tuberculosis. *Lancet*. 2015 Dec 5; 386(10010):2324-33. doi: 10.1016/S0140-6736(15)00321-9. Epub 2015 Oct 26. PMID: 26515676; PMCID: PMC4708262.
7. Chirenda J, Gwitira I, Warren RM, Sampson SL, Murwira A, Masimirembwa C, Mateveke KM, Duri C, Chonzi P, Rusakaniko S, et al. Spatial distribution of Mycobacterium Tuberculosis in metropolitan Harare, Zimbabwe. *PLoS One*. 2020 Apr 21; 15(4):e0231637. doi: 10.1371/journal.pone.0231637. PMID: 32315335; PMCID: PMC7173793.

8. Getis, A. & Ord, J.K. (1992). The analysis of spatial association by use of distance statistics, *Geographical Analysis*, 24, 189-206. <http://dx.doi.org/10.1111/j.1538-4632.1992.tb00261.x>
9. Chamie G, Wandera B, Marquez C, Kato-Maeda M, Kanya MR, Havlir DV, Charlebois ED. Identifying locations of recent TB transmission in rural Uganda: a multidisciplinary approach. *Trop Med Int Health*. 2015 Apr; 20(4):537-45. doi: 10.1111/tmi.12459. Epub 2015 Feb 4. PMID: 25583212; PMCID: PMC4355181.