International Journal of Innovative Research and Advanced Studies (IJIRAS)
Volume 10 Issue 9, September 2023

ISSN: 2394-4404

Prevalence Of Multi-Drug Resistant–Tuberculosis (TB) Amongst TB Patients In Turkana Central Sub County, Kenya

Ilikwel Joyce Erupe

MPH candidate at Mount Kenya University, Kenya

Dr. Peter Edome Akwee

School of Science and Technology, Turkana University College

Dr. Gichunge Catherine

School of Nursing and Public Health, Chuka University, Kenya

Abstract: ***Multidrug-Resistant Tuberculosis (MDR-TB) is an increasing public health concern worldwide. The great burden is in India, Russia, China and the African Countries. The extent and burden of TB varies significantly from country to country but is more prevalent in poor countries. Kenya ranks among 22 countries with the highest burden of TB. The purpose of the study was to establish the association between health-related characteristics of TB patients and MDR-TB in Turkana Central Sub County, Kenya. The study adopted a cross sectional mixed method design, combining qualitative and quantitative data. TB patients attending clinic at the Lodwar County Referral Hospital were targeted. 164 respondents were selected using systematic random sampling technique to participate in quantitative survey while eight health care workers were selected using purposive sampling technique to serve as key informants. Quantitative data was collected using questionnaires while qualitative data was collected using an in-depth interview. Descriptive statistics were used to analyze quantitative data with the aid of statistical package of social science (SPSS) version 20. Qualitative data was analyzed thematically by identifying key themes. Data was presented in form of frequency tables. Majority of the participants were males (57.9 %, N=69), Christians (84.8%, N=139), married (53.4%, N=87) and had attained primary education level (68.3%, n=112). MDR-TB was positively correlated with being under TB medication (r=0.387, p=0.000), being aware of MDR-TB (r=0.430, p=0.000), attending TB clinic (r=0.508, p=0.000) as well as the frequency of clinic attendance (r=0.197, p=0.019). There was a significant relationship between HIV/AIDS and MDR-TB co-infection (r= 0.176, p=0.034) and access to a health care worker (r=0.240, p=0.004). The study recommends strengthening of access to management of ordinary TB cases across all population groups through strengthening of DOTs, expanding MDR-TB surveillance to cover all patients with history of previous treatment for tuberculosis and all HIV positive TB patients, strengthening the MDR-TB tracing, screening and documentation within the sub-county and beyond as well as scaling up of health promotion efforts to enhance awareness about the socioeconomic factors contributing to the development of MDR-TB. The study findings are expected to contribute positively towards effective management of TB and MDR-TB.***

Keywords: Multidrug-Resistant Tuberculosis (MDR-TB), HIV/AIDS, Tuberculosis (TB) Rifampicin Resistant

I. INTRODUCTION

Tuberculosis (TB) is a chronic disease caused by Mycobacterium tuberculosis bacterium and is transmitted from person to person, through inhalation of droplet nuclei aerosolized by coughing of an infected person. The disease affects lungs and other parts of the body such as brain, kidneys, skin and bones. The disease is curable but can kill if not treated properly. MDR-TB is resistant to Isoniazid and Rifampicin. MDR and XDR-TB is resistant to rifampicin, isoniazid, fluoroquinolone and injectables like amikacin and kanamycin. XDR is almost resistant to all the drugs leaving patients with few treatment options. (CDC,2016). Multi-drug resistant (MDR-TB) also refers to resistance in vitro to at least

Isoniazid (INH) and rifampicin (RIF) [World Health Organization (WHO, 2015)]. Resistance to at least two drugs other than the combination of INH and RIF is known as poly-resistant tuberculosis and non-resistance is the resistance due to only one anti-tuberculosis medication (Skrahina, 2014).

Multi-drug resistant tuberculosis is an increasing global problem. Most of the cases arise from healthcare workers' errors and non-compliance on the side of the patients in the course of treatment for tuberculosis. Globally according to Centers for Disease Control and Prevention (CDC, (2015] and World Health Organization (WHO, 2015) TB is a leading cause of morbidity and mortality and ranks among the ten most common causes of death worldwide. The emergence of drug-resistant strains of *M. tuberculosis* and HIV/AIDS is substantially challenging the goal of elimination of TB in the 21st century. According to the WHO (2017), the median prevalence of primary and acquired MDR-TB globally was 2.9% and 15.3 %t, respectively. In India, the available information from the several drug resistance studies suggests that the rate of MDR-TB is relatively low in India (Shah, Shah, & Dave, 2018). The prevalence of MDR-TB is 1–3 % in new cases and around 12 % in re-treatment cases in India, while in Gujarat, the prevalence of MDR-TB was found 2.4 % in new cases and around 17.4 % in previously treated cases (Shah, Shah, & Dave, 2018).

WHO has recommended direct observed treatment (DOTs). Treatment is expensive and based on drug susceptibility. The extent and burden of tuberculosis varies from country to country as well as from region to region. The greatest burden of MDR-TB is from high burden resource poor countries. The diagnosis of TB is a challenge in poor countries. Resource rich countries are able to carry diagnosis of MDR effectively. There should be a strong suspicion in treatment failure or with history of previous treatment. MDR drugs like delamanid, bedaquiline and linezolid which have life –threatening side-effects discourage patients from completing their drug regimen leading to the development of MDR/XDR-TB. The spread of MDR-TB is due to weak medical systems, incorrect treatment, transmission in communities and health facilities (Yi Wen,2018).

The latest anti-TB drug resistance surveillance data by WHO (2017) indicate that 4.1% of new and 19% of previously treated cases of TB in the world were estimated to have rifampicin- or multidrug-resistant tuberculosis (MDR/RR-TB). In 2016, an estimated 600, 000 new cases of MDR/RR-TB emerged globally (WHO, 2017). MDR/RR-TB caused 240. 000 deaths in 2016. Most cases and deaths occurred in Asia. About 6.2% of TB cases have additional drug-resistance, extensively drug-resistant TB (XDR-TB). In 2016, 41 % of laboratory confirmed TB patients notified globally were tested for MDR/RR-TB, up from 11 percent in 2012 (WHO, 2017). In many countries a steady increase has occurred in recent years, driven by the continued expansion in the use of rapid molecular tests. In spite of increased testing, the number of MDR/RR-TB cases detected in 2016 only reached 153 000, a slight increase from the 132 000 cases reported in 2015. In 2016, 8000 cases of XDR-TB were reported worldwide. To date, 121 countries have reported at least one XDR-TB case (WHO, 2017). In Africa, which is a home to over 1 billion people, a great portion of its population is affected by tuberculosis.10.4 million cases of tuberculosis are from Africa. MDR cases are largely missed in Africa with 93,000 cases estimated in 2016while 828 were diagnosed (WHO Global data, 2016).

In sub-Saharan Africa, the greatest region with high incidence was South Africa (3.1% to 4.2%) of tuberculosis were drug resistant. Central (2.1%), Western (1.9%)and Eastern (1.7%) (Musa et al 2014). The burden of MDR is found in Naigeria (20,000) cases, South Africa (19,000) i.e 42% of estimated burden. Democratic Republic of Congo (7600) Mozambique (7500) and Ethiopia (5800) are the second with Multi-drug resistant tuberculosis. A survey done in South Africa showed (1.8% to 3.4%)rate of resistance due to missed diagnostic opportunities.70% of cases in Africa are missed.1092 XDR-TB cases were notified out of which 967were in South Africa. Missing cases are greater than notified. There are limited National laboratories in the African Region. Most patients are lost to follow up or have died in the community (Musa et al, 2018).

In Kenya, TB Prevalence Survey 2015-2016 where over 63,000 people across 45 counties were screened, it was revealed that there are more TB cases in Kenya than previously estimated, with a prevalence of about 558 per 100,000 [National Tuberculosis, Leprosy and Lung Disease Program (NTLDP, 2017]. Consequently, TB has been identified as the fourth leading cause of mortality in Kenya. MDR-TB is of major public health concern in Kenya. According to the NTLDP (2017), Kenya is among the 22 countries with the highest burden of TB, and in 2014, there were an estimated 110,000 TB cases (NTLDP, 2017). Extensively drug-resistant TB (XDR-TB) is a less common form of multidrug-resistant TB in which bacteria develop resistance to INH and RIF, as well as to second line drugs used for the management of multidrug resistant TB (any fluoroquinolone and at least one of three injectable second-line drugs) (WHO, 2015; CDC, 2015). Multidrug-resistant TB has become a major public health problem and presents new barriers to the control of TB. The extent and burden of TB varies significantly from country to country. The estimated global number of multidrug-resistant (MDR) and extensively drug-resistant (XDR)-TB cases among newly diagnosed patients with pulmonary TB in the year 2012 was 450 000 (range 300 000–600 000) (WHO, 2015).

In Turkana county in Kenya, the first multi- drug resistant tuberculosis was diagnosed in 2011.Unfortunately, the patient succumbed to the killer disease in 2012. The first XDR-TB patient was identified in in Turkana in 2017 and was referred to Kenyatta National hospital for treatment. He recovered and alive and well. This study seeks to address this gap by establishing the prevalence of MDR-TB in Turkana Central Sub-county. There is no empirical evidence on the factors associated with MDR-TB as well as the association between MDR-TB and HIV/AIDS.

The prevalence of multidrug-resistant TB has increased in Kenya over the last few years, from 0.04% in 2005 to 0.16% in 2011-a four-fold increase in six years, partly because of poor adherence (NTLDP, 2017). Evidence suggests that the major factor responsible for the high MDR-TB prevalence is the concurrent HIV/AIDS pandemic (NTLDP, 2017). Other factors associated with the MDR-TB morbidity include

ISSN: 2394-4404

poverty and social deprivations (Hirpa, Medhin, Girma, Melese, & Mekonen, 2013). A study conducted between 2011 and 2012 showed that the level of MDR-TB in Nairobi's Kibera slums was typically between 0.5% and 1% among new TB cases and 8.5% among recurrent TB cases (Kidenya, 2014).

The efforts to mitigate the increasing threat of MDR-TB in Kenya have been hampered by various factors. The influx of refugees has become a burden in our health facilities because quantification of medicines is based on the Kenyan population and not on the refugee figures. According to the recent data from the National Tuberculosis, and Leprosy Control Program, Kenya has a total of 437 cases of MDR-TB while the burden has been on the rise over the last few years, from 0.04 % in 2005 to 0.16 % in 2011.

Despite being a major public health concern in Turkana County, no previous study has attempted to identify the exact prevalence of MDR-TB in the County yet adequate information is required for control and effective treatment of MDR-TB. The exact prevalence of MDR-TB in Turkana County remains unclear due to poor reporting and referral of cases from the lower level facilities yet Turkana is amongst the four counties that account for 32 % of Kenya's burden of MDR-TB. This study seeks to determine the prevalence of MDR-TB among Tuberculosis (TB) patients in Turkana Central Sub County, Kenya.

II. METHODOLOGY

This study was conducted in Turkana Central Sub-County, Turkana County, which is one of the six sub counties in the county. The major health facility in the study area is Lodwar County Referral Hospital (LCRH). According to the 2009 Kenya National Bureau of Statistics Population Census, Turkana central Sub County has a population of 134, 674, consisting of 23, 681 households. The study adopted a cross sectional mixed method design, combining qualitative and quantitative data. TB patients attending clinic at the Lodwar County Referral Hospital were targeted. 164 respondents were selected using systematic random sampling technique to participate in quantitative survey while eight health care workers were selected using purposive sampling technique to serve as key informants. Quantitative data was collected using questionnaires while qualitative data was collected using an in-depth interview. Descriptive statistics were used to analyze quantitative data with the aid of statistical package of social science (SPSS) version 20. Qualitative data was analyzed thematically by identifying key themes. Data was presented in form of frequency tables.

III. RESULTS AND DISCUSSIONS

A. GENERAL CHARACTERISTICS

The findings indicate that majority (57.9 %) (95) of the participants were males while 42.1 % (69) were females. The results indicate that majority of the study participants (45.1%) were below 30 years, 39.6% were aged 31-40 years, 10.9% were aged 41-50 years while 4.8% were above 50 years. Majority (52.7%) (87) were in a marriage union, 37.4% were single, 4.3% were widowed whereas 4.9% were either divorced or separated. Majority (68.3 %) (112) had primary level education, 22.0% (36) had attained secondary education level while only 1.2% (2) had attained university or college education level. 84.8 % (139) were Christians, 14.6% (24) were Muslims while only 0.6% belonged to other religious groups. A cross tabulation of the diagnosis status of MDR-TB and the demographic variables is also provided in Table 1.

Demographic Variable	Frequency (N)	(%)
Gender		
Male	95	57.9%
Female	69	42.1%
Age Group (Yrs)		
<30 years	74	45.1%
31 – 40	65	39.6%
41-50	18	10.9%
>50	8	4.8%
Marital status		
Single	61	37.4%
Married	87	53.4%
widowed	7	4.3%
Divorced/separated	8	4.9%
Educational level		
Not attended school/illiterate	14	8.5%
Primary	112	68.3%
Secondary	36	22.0%
College/university	1	1.2%
Religion		
Christian	139	84.8%
Muslim	24	14.6%
Others	1	0.6%

Table 1: Showing General Demographic Characteristics

A cross tabulation of all the demographic variables against the occurrence of MDR-TB is also provided in Table 2. In terms of gender, there was a relatively higher proportion of females (55%) diagnosed with MDR-TB compared to males (45%). In terms of age, a higher percentage of MDR-TB was found among those 41-50 years (56%). Those who were divorced or separated had the highest proportion of MDR-TB (75%) compared to single (44%), married (44%) and widowed (29%). A higher proportion of MDR-TB was found among Christians (38%) compared to Muslims (21%) and other religions (0%).

Demographic Variable	(N)	(%)	MDR-TB	
			Yes (N) (%)	No (N) (%)
Gender				
Male	95	57.9%	43 (45%)	52 (55%)
Female	69	42.1%	38	31 (45%)

ISSN: 2394-4404

			(55%)	
Age Group (Yrs)				
<30 years	74	45.1%	36 (49%)	38 (51%)
31 – 40	65	39.6%	33 (51%)	32 (49%)
41-50	18	10.9%	10 (56%)	8 (44%)
>50	8	4.8%	3 (38%)	5 (62%)
Marital status				
Single	61	37.4%	27 (44%)	34 (56%)
Married	87	53.4%	38 (44%)	39 (56%)
Widowed	7	4.3%	2 (29%)	5 (71%)
Divorced/separated	8	4.9%	6 (75%)	2 (25%)
Educational level				
Not attended school/illiterate	14	8.5%	5 (36%)	9 (64%)
Primary	112	68.3%	55 (49%)	57 (51%)
Secondary	36	22.0%	15 (42%)	21(58%)
College/university	1	1.2%	1 (100%)	0 (0%)
Religion				
Christian	139	84.8%	53 (38%)	86 (62%)
Muslim	24	14.6%	5 (21%)	19 (79%)
Others	1	0.6%	0 (0%)	1 (100%)

Table 2: Demographic Variables Against Mdr-Tb

HIV/AIDS CONTRIBUTION TO MDR-TB

The level of awareness about HIV/AIDS among the participants was 98.8% (163) with only 0.6% (1) indicating lack of awareness. 39.0% (64) of the participants had been diagnosed with HIV/AIDS while 61.0% (100) had not been diagnosed with HIV/AIDS. The findings are presented in Table 3.

				Yes (N, %)	**No (N, %)**
Awareness of HIV/AIDS	Yes	163	98.8%	73 (45%)	90 (55%)
	No	1	0.6%	0 (0%)	1 (100%)
Diagnosed with HIV/AIDS	Yes	64	39.0 %	37 (58%)	27 (42%)
	No	100	61.0 %	36 (36%)	64 (64%)

Table 3: Hiv/Aids Contribution To Mdr-Tb

An in-depth interview was conducted with eight health workers to supplement the quantitative data findings. The respondents were drawn from TB isolation ward 'Manyatta' and TB Clinic. They included two clinicians and nurses working in TB clinic at LCRH. Five respondents were males while three were female. All the respondents had worked at the facility for more than five years; hence they were adequately knowledgeable to respond to the interview questions. The following were the major issues which emerged from the interview.

The respondents indicated that new MDR-TB cases are encountered at the facility. *"We get about five to ten MDR-TB patients every year, roughly more than four in every three months"* (Key Informant 1). The responses indicated that a number of socioeconomic factors could lead to MDR-TB. Key among these includes poverty, poor housing conditions, overcrowding, illiteracy, refugee influx and negative cultural beliefs. As one responded said, "*Poverty can lead to MDR-TB since a poor person is likely to lack food and education. Lack of food can lower the person's immunity hence his/her body cannot fight infections including TB"* (Key Informant 2). As one Clinician put forward, "illiteracy can contribute to MDR-TB due to lack of understanding of the TB causes and ways of avoiding the contagious disease".

Cultural beliefs were linked to MDR-TB as some people with TB believe in seeking treatment from herbalists. Besides, such beliefs lead to delays in diagnosis and treatment as one respondent said "some of the TB patients believe that they have been bewitched or cursed and this leads to delay in going for treatment. They only come to hospital when it is too late". The influx of refugees to the country was also cited as a contributing factor to MDR-TB. Another factor cited was the migratory way of life in the community. "*Moving from one place to another in search of grass and water for livestock makes it difficult for TB patients to adhere to treatment as well as to trace and refer the TB cases from the community, which may contribute to development of MDR-TB"*(Key Informant 3).

The respondents revealed that HIV/AIDS contributed to the development of resistance to TB medication. The health workers reported that HIV/AIDS has a direct effect on TB patients as it reduces immunity, making the patient vulnerable to develop MDR-TB. One respondent added on the association between HIV/AIDS and MDR-TB, "*TB is also a chronic disease which reduces the patient's immunity, which can adversely affect the outcomes of treatment in the long run"* (Key Informant 4).

These findings have been corroborated by other studies which have reported an increased TB morbidity and mortality among the youths, mostly between 15 – 44 years of age (WHO, 2015; Kipkoech, Kandie, Korir, and Mutai, 2015). However, there was no significant relationship between participants' age and MDR-TB in the bivariate analysis.

The bivariate analysis indicated that there was no significant correlation between gender, education level, and religion and MDR-TB. Slightly more than half (57.9 %) of the participants were males while 42.1 % (69) were females. However, the findings are in agreement with WHO (2015) report which indicated that a higher number of females were affected by TB in the study population considering Kenya's MOH report of 2005 which indicated that males are 1.4 times more likely to have TB than females (WHO, 2015). As reported by Kipkoech *et al.* (2015), high levels of education were expected to positively impact on slowing the occurrence of MDR-TB because high literacy has been positively associated with good health perception and positive health seeking behaviour.

The study findings indicate a relatively high level of awareness about MDR-TB (73.8 %) among the participants. The correlation analysis indicated a strong positive correlation between MDR-TB and awareness of MDR-TB, being under TB-medication, attending TB clinic and frequency of attending TB clinic. Findings from other studies indicate that though effective anti-TB drugs have been available for over five decades, TB is still a leading cause of morbidity and mortality in many parts of the world (WHO, 215; CDC, 2015). Kenya has a large and increasing burden of TB and is ranked among the twenty-two countries that cumulatively account for about 80 % of the world's TB cases (WHO, 2015; Kidenya, 2014).

The findings in this study indicate that majority of the participants had a low monthly income. The bivariate analysis indicated a strong correlation between family income and MDR-TB. Studies have shown that poverty compels people to live in overcrowded environment with poorly ventilated rooms, conditions known to favour increased TB prevalence (Kipkoech *et al.*, 2015). The Kenya Demographic and Health Survey of 2015 ranked Turkana County as among the poorest in the country (KDHS, 2015). This suggested that poor participants' experiences contributed to increased prevalence of MDR-TB, which is attributed to low disposable income due to low income. This could be attributed to increased likelihood for such households' failure to adopt appropriate and effective TB treatment.

There was a significant correlation between access to health care worker/services and MDR-TB. This was consistent with what was reported in the qualitative data. These findings are consistent with a study by Mburu et al., (2016) which suggested that poor socio-economic status leads to low access to health services which have been identified as contributing factors to high MDR-TB burden. Poor socio-economic status also contributes to poor adherence to TB treatment, thereby resulting to the emergence of MDR-TB (Saira, Tyaba, and Khawaja, 2010).

The study findings indicated a significant association between diagnosis with HIV/AIDS and having MDR-TB. The burden of MDR-TB in Kenya has been mainly attributed to the high prevalence of HIV, estimated at 7.1 % according to Sentinel surveillance of 2014 (WHO, 2015). The prevalence of HIV/AIDS worldwide has been reported to be high among the youth within the above age bracket while the HIV/AIDS prevalence in Kenya is estimated at 7.1% of the general population (WHO, 2015). According to the WHO Global Tuberculosis Report of 2010, 41% of TB patients in Kenya had HIV co-infection, which is 9 % below the findings recorded in this study.

Tuberculosis is the most frequent opportunistic infection detected among HIV patients and the interaction between the TB and the HIV epidemics is particularly fatal because TB adds to the illness burden of HIV-infected persons and shortens their life expectancy, while the HIV epidemic stimulates TB spread (Lange *et al*, 2014). The high mortality rate of HIV patients with TB co-infection is also linked to community's loss of confidence in the curability of HIV, which further increases the level of non-adherence to treatment (Seddon *at al*, 2014). HIV/AIDS infection also predisposes TB patients to development of drug resistant TB and the study outcome indicated a significant relationship between HIV/AIDS and MDR-TB co-infection. This suggested that high prevalence of HIV/AIDS co-infection was not only predisposing patients to TB, but also raises the chances of developing MDR-TB. Besides, TB is strongly associated with HIV/AIDS by the community since many symptoms of TB, such as weight loss, fever, and chronic cough, are associated with AIDS, which in turn leads to patients' discrimination and stigmatization (Kipkoech et al, 2015).

IV. CONCLUSIONS

The study findings have confirmed that there was a relatively high level of awareness about MDR-TB amongst participants hence contributing to high prevalence of having MDR-TB burden. There is a strong positive correlation between MDR-TB and awareness of MDR-TB.

V. RECOMMENDATIONS

The study recommends escalating the MDR-TB surveillance to cover all patients with history of previous treatment for tuberculosis, all patients with tuberculosis and all HIV positive TB patients. Screening patients with cough of any duration. Screening all TB patients for Multi-drug resistant tuberculosis. Screening all MDR patients for Xtra-drug resistant tuberculosis because resistant strains are being transmitted from one person to the other especially in overcrowded places. Early detection will lead to high success in treatment outcomes.

REFERENCES

[1] Abubakar, I., Zignol, M., Falzon, D., Raviglione, M., Ditiu, L., Masham, S. (2017). Multidrug resistant tuberculosis in Ethiopian settings and its association with previous history of anti-tuberculosis treatment: a systematic review and meta-analysis. BMC Infectious Diseases, 17, 219.

[2] Adler-Shohet, F.C. Low, J., Carson, M., Girma, H., Singh, J. (2014). Management of latent tuberculosis infection in child contacts of multidrug-resistant tuberculosis. Pediatr Infect Dis J. 33(6), 664-666.

[3] Ahuja, S.D., Ashkin, D., Avendano, M., Banerjee, R., & Bauer, M. (2012). Multidrug resistant pulmonary tuberculosis treatment regimens and patient outcomes: an individual patient data meta-analysis of 9,153 patients. PLoS Med. 9 (8):e1001300.

[4] Aia, P., Kal, M., Lavu, E., John, L.N., Johnson, K., & Coulter, C. (2016). The Burden of drug-resistant tuberculosis in Papua New Guinea: results of a large population-based survey. PLoS ONE 11(3): e0149806. Retrieved April 4, 2017 from doi: 10.1371/journal.pone.0149806.

[5] Al-Dabbagh M, Lapphra K, McGloin R, et al. Drug-resistant tuberculosis: pediatric guidelines. [Review] Pediatr Infect Dis J. 2011;30(6):501-505.
[6] Amanullah, F., Ashfaq, M., Khowaja, S., et al. (2014). High tuberculosis prevalence in children exposed at home to drug-resistant tuberculosis. Int J Tuberc Lung Dis. 18(5), 520-527.
[7] American Academy of Pediatrics. (2012). Red Book: 2012 Report of the Committee on Infectious Diseases. Pickering LK, ed. 29th ed. Elk Grove Village, IL: American Academy of Pediatrics.
[8] Bacci ,C., Galli, L., de Martino, M., Chiappini, E. (2015). Fluoroquinolones in children: update of the literature. Journal Chemotherapy, 27(5), 257-265.
[9] Becerra, M. C., Sasha, C. A., Molly, F., & Katiuska, C. (2011). Tuberculosis burden in households of patients with multidrug-resistant and extensively drug-resistant tuberculosis: a retrospective cohort study. Lancet 377, 147–152.
[10] Becerra, M.C., Franke, M.F., Appleton, S.C., et al. (2013). Tuberculosis in children exposed at home to multidrug-resistant tuberculosis. Pediatr Infect Dis J. 32(2), 115-119.
[11] Biadglegne, F., Tessema, B., Rodloff, A.C., Sack, U. (2013). Magnitude of gene mutations conferring drug resistance in mycobacterium tuberculosis isolates from lymph node aspirates in Ethiopia. International Journal of Medical Sciences, 10 (11), 1589-1594.
[12] Bradley, J.S., Kauffman, R.E., Balis, D.A., et al. (2014). Assessment of musculoskeletal toxicity 5 years after therapy with levofloxacin. Pediatrics, 134 (1), e146-153.
[13] Cain, K. P., Marano, N., Kamene, M., Sitienei, J., Mukherjee, S., & Galev, A. (2015). The movement of multidrug-resistant tuberculosis across borders in East Africa needs a regional and global solution. PLoS Med 12(2).
[14] Centers for Disease Control and Prevention CDC (2015). Drug Resistant TB. Retrieved April 7, 2017 from http://www.cdc.gov/tb/topic/drtb/Accessed 26/01/2016.
[15] Centers for Disease Control and Prevention. (2013). Managing Drug Interactions in the Treatment of HIV-Related Tuberculosis.
[16] Cox, H., Ford, N. (2012). Linezolid for the treatment of complicated drug-resistant tuberculosis: a systematic review and meta-analysis. Int J Tuberc Lung Dis. 16(4), 447-454.
[17] Dalton, T., Cegielski, P., Akksilp, S., Asencios, L., Campos, C. J, & Cho, S. N. (2012). Prevalence of and risk factors for resistance to second-line drugs in people with multidrug-resistant tuberculosis in eight countries: a prospective cohort study. Lancet 380, 1406–1417.
[18] Dara, M., Petrova-Benedict, R., Centis, R., Zellweger, J., Sandgren, A., & Heldal, E. (2012). Minimum package for cross-border TB control and care in the WHO European region: a Wolfheze consensus statement. European Respiratory Journal 40(5), 1081–1090.
[19] Das, M., Parker, G., & Hyett, M. (2014). HIV, multidrug-resistant TB and depressive symptoms: when three conditions collide. Global Health Action 7 (24912), 1–5.
[20] de Kock, L., Sy, S.K., Rosenkranz ,B. et al. (2014). Pharmacokinetics of para-aminosalicylic acid in HIV-uninfected and HIV-coinfected tuberculosis patients receiving antiretroviral therapy, managed for multidrug-resistant and extensively drug-resistant tuberculosis. Journal of Antimicrobial Agents Chemotherapy, 58(10), 6242-6250.
[21] Ettehad, D., Schaaf, H.S., Seddon, J.A., Cooke, G.S., Ford, N. (2012). Treatment outcomes for children with multidrug-resistant tuberculosis: a systematic review and meta-analysis. [Review] Lancet Infect Dis. 12(6), 449-456.
[22] Fantahun, B. & Arne, C. (2014). Multidrug-resistant tuberculosis in Ethiopia: efforts to expand diagnostic services, treatment and care. Antimicrobial Resistance and Infection Control, 3, 31.
[23] Furin,J.J., Brigden, G., Lessem, E., Becerra, M.C. (2013). Novel pediatric delivery systems for second-line anti-tuberculosis medications: a case study. Int J Tuberc Lung Dis. 9, 1239-1241.
[24] Garcia-Prats, A.J., Rose, P.C., Hesseling, A.C., Schaaf, H.S. (2014). Linezolid for the treatment of drug-resistant tuberculosis in children: a review and recommendations. Tuberculosis 94(2),93-104.
[25] Gegia, M., Magee, M.J., Kempker, R.R., Kalandadze, I., Chakhaia, T., Golub, J.E., et al. (2015). Tobacco smoking and tuberculosis treatment outcomes: A prospective cohort study in Georgia. Bull World Health Organ, 93, 390-9.
[26] Gumbo, T., Louie, A, Deziel, M.R, Liu, W., Parsons, L.M., et al. (2007). Concentration-dependent Mycobacterium tuberculosis killing and prevention of resistance by Rifampicin. Antimicrobial Agent Chemotherapy, 51, 3781-3788.
[27] Gupta, R., Gao, M., Cirule, A., Xiao, H., Geiter, L. (2015). Delamanid for extensively drug-resistant tuberculosis. [correspondence] N Engl J Med. 373, 291-292.
[28] Gupta,.., Mathuria, J.P., Singh, S.K., Gulati, A.K, Anupurba, S. (2011). Antitubercular drug resistance in four healthcare facilities in North India. J Health Popul Nutr 29,583-92.
[29] Hirpa, S., Medhin, G., Girma, B., Melese, M., Mekonen, A. (2013). Determinants of multidrug-resistant tuberculosis in patients who underwent first-line treatment in Addis Ababa: a case control study. BMC Public Health, 13: 782.
[30] Jenkins, H.E., Tolman, A.W., Yuen, C.M., et al. (2014). Incidence of multidrug-resistant tuberculosis disease in children: systematic review and global estimates. [Review] Lancet, 383(9928), 1572-1579.
[31] Kidenya, B.R. (2014). Epidemiology and genetic diversity of multidrug-resistant tuberculosis in East Africa. Tuberculosis, 94 (1), 1-7.
[32] Kipkoech, L. K., Kandie, S. C., Korir, R. K. & Mutai, C. (2015). Factors contributing to drug resistant tuberculosis: a case study of tuberculosis patients attending Rift Valley Provincial General Hospital Nakuru, Kenya. Science Research. 3 (3), 45-52.

[33] Lange R. A., Levine, G.N., Maddox, T. M., Naidu, S., Ohman, E. M., & Smith, P. K. (2014). Management of patients with multidrug-resistant/extensively drug-resistant tuberculosis in Europe: a TBNET consensus statement. European Respiratory Journal 23-63; DOI: 10.1183/09031936.00188313.
[34] LCRH Manyatta. (2017). Q4, Q1, Q2 Data.
[35] Li,J., Rayner, C.R., Nation, R.L., Oven, R.J., Spelman, D., et al. (2006). Heteroresistance to colistin in multidrug resistant Acinitobacter Journal of Antimicrobial Agents Chemotherapy, 50, 2946-2950.
[36] Lukoye, D. & Meehan, C. J. (2015). Variation and risk factors of drug resistant tuberculosis in Sub-Saharan Africa: a systematic review and meta-analysis. BMC Public Health, 15(1), 1–13.
[37] Manjelievskaia, J., Erck, D., Piracha, S., & Schrager, L. (2016). Drug-resistant TB: deadly, costly and in need of a vaccine. Trans R Soc Trop Med Hyg, 110 (3), 186-191.
[38] Marks, S.M., Flood, J., Seaworth, B. (2014). Treatment practices, outcomes, and costs of multidrug-resistant and extensively drug-resistant tuberculosis, United States, 2005–2007. Emerging Infectious Diseases 20, 812-820.
[39] Mase, S., Jerab,J., Gonzales, D., et al. (2015). Pharmacokinetics and dosing of levofloxacin in children treated for active or latent multidrug-resistant tuberculosis, Federated States of Micronesia and Republic of the Marshall Islands. Pediatr Infect Dis J.
[40] Mburu, G., Kipruto, H., Mung'atu, J., Ogila, K., Adem, A., Mwalili, S. & Masini, E. (2016). Detention of people lost to follow-up on TB treatment in Kenya: the need for human rights-based alternatives. Health and Human Rights Journal, 8(1), 43-54.
[41] Migliori, G. B., Besozzi, G., & Girardi, E. (2012). Multidrug-resistant tuberculosis in Eastern Europe: still on the increase? European Respiratory Journal 39(6), 1290–1291.
[42] Minion, J., Gallant, V., Wolfe, J., Jamieson, F., & Long, R. (2013). Multidrug and extensively drug-resistant tuberculosis in Canada 1997–2008: demographic and disease characteristics. PLoS One 8.
[43] Nagaraja, C., Shashibhushan, B.L., Asif, M., Manjunath, P.H., Sagar, C. (2012). Pattern of drug-resistance and treatment outcome in multidrug-resistant pulmonary tuberculosis. Indian J Chest Dis Allied Sci, 54, 23-6.
[44] National Tuberculosis, Leprosy and Lung Disease Program (NTLDP). (2017). Tuberculosis and Leprosy situation. Ministry of Health. Retrieved April 7, 2017 from http://nltp.co.ke/tuberculosis-leprosy-situation/
[45] Nicol, M.P., Zar, H.J. (2011). New specimens and laboratory diagnostics for childhood pulmonary TB: progress and prospects. [Review] Paediatr Respir Rev. 12(1), 16-2.
[46] Nkhoma, W. A. (2012). Multidrug-resistant and extensively drug-resistant tuberculosis in the African region. African health monitor, 2, 2425. Retrieved November 17, 2016 from http://www.aho.afro.who.int/sites/default/files/ahm/reports/421/ahm1505.pdf.
[47] Okorie, O. J., Kanu1, E. Vivienne E., & Nnamani, U. J. (2016). The Prevalence of drug-resistant tuberculosis among people living with HIV (PLHIV) in Abia State. Advances in Infectious Diseases, 6, 63-69. Retrieved April 4, 2017 from http://dx.doi.org/10.4236/aid.2016.62009.
[48] Prasad,R., Gupta, N. (2015). Clinical Tuberculosis-Diagnosis and Treatment. 1st ed. New Delhi: Jaypee brothers.
[49] Royce, S., Falzon, D., van Weezenbeek, C., Dara, M., & Hyder, K. (2015). Multidrug resistance in new tuberculosis patients: burden and implications. International Journal of Tuberculosis and Lung Diseases, 17, 511–513.
[50] Saira Z., Tyaba H., Khawaja T.M. (2010). Socioeconomic factors contributing to multidrug-resistant tuberculosis (MDR-TB). Journal of Biomedical Science and Research, 2 (4), 279-283.
[51] Seddon, J. A. (2013). Risk factors for infection and disease in child contacts of multidrug-resistant tuberculosis: a cross-sectional study. BMC Infectious Diseases, 13, 392.
[52] Seddon, J.A., Furin, J.J., Gale, M., et al. (2012). Caring for children with drug-resistant tuberculosis: practice-based recommendations. [Review] Am J Respir Crit Care, 186(10), 953-964.
[53] Seddon, J.A., Hesseling, A.C., Willemse, M., Donald, P.R., Schaaf, H.S. (2012). Culture-confirmed multidrug-resistant tuberculosis in children: clinical features, treatment, and outcome. Clin Infect Dis. 54(2), 157-166.
[54] Shah, A.M., Shah, R.B., Dave, P.N. (2018). Factors contributing to development of multidrug-resistant tuberculosis. Natl J Physiol Pharm Pharmacol 8(10), 1463-1469.
[55] Sharma, S. K. (2011). Prevalence of Multidrug-Resistant Tuberculosis among Newly Diagnosed Cases of Sputum-Positive Pulmonary Tuberculosis. Indian Journal of Medical Research, 133(3): 308–311.
[56] Skrahina, A. (2013). Multidrug-resistant tuberculosis in Belarus: the size of the problem and associated risk factors. Bull World Health Organ, 91, 36–45.
[57] Starke, J.R. (2014), Committee on Infectious Diseases. Interferon-gamma release assays for diagnosis of tuberculosis infection and disease in children. Pediatrics, 134 (6), e1763-1773.
[58] Sterling, T.R., Villarino, E., Borisov, A.S., et.al. (2011). Three months of rifapentine and isoniazid for latent tuberculosis infection. New Eng J Med. 365(23), 2155-2166.
[59] Sulis, G., Roggi, A., Matteelli, A., & Raviglione, M. C. (2014). Tuberculosis: epidemiology and control. Mediterranean Journal of Hematology and Infectious Diseases, 6(1).
[60] Svensson, E.M., Dooley, K.E., Karlsson, M.O. (2014). Impact of lopinavir-ritonavir or nevirapine on bedaquiline exposures and potential implications for patients with tuberculosis-HIV coinfection. Journal of Antimicrobial Agents Chemotherapy, 58(11),6406-6412.
[61] Tanrikulu, A.C., Abakay, A., Abakay, O. (2010). Risk factors for multidrug-resistant tuberculosis in Diyarbakir, Turkey. Med Sci Monit , 16:PH57-62.

ISSN: 2394-4404

[62] Thomas, B. E. (2016). Psycho-socio-economic issues challenging multidrug resistant tuberculosis patients: a systematic review. PLoS ONE 11(1): e0147397.
[63] Thuridur, A. (2009). Tuberculosis and Public Health-Policy and Principles in Tuberculosis control. Paris: IUATLD.
[64] Tripathi, K.D. (2013). Essentials of Medical Pharmacology. 7th ed. New Delhi: Jaypee Brothers.
[65] Veziris, N., Truffot, C., Mainardi J-L., Jarlier, V. (2011). Activity of carbapenems combined with clavulanate against murine tuberculosis. Antimicrob Agents Chemother. 55(6), 2597-2600.
[66] Wells, C., Gupta, R., Hittel, N., et al. (2015). Long-term mortality assessment of multidrug resistant tuberculosis patients treated with delamanid. Eur Respir J. 45, 1-3.
[67] WHO (2015). Multidrug-Resistant Tuberculosis (MDR-TB) 2015 Update. Retrieved April 7, 2017 from http://www.who.int/tb/challenges/mdr/mdr_tb_factsheet.pdf.
[68] World Health Organization, (2017). Global tuberculosis report (Geneva: WHO)
[69] Yen, Y.F., Yen, M.Y., Lin, Y.S., Lin, Y.P., Shih, H.C., Li, L.H., et al. (2014). Smoking increases risk of recurrence after successful anti-tuberculosis treatment: A population-based study. Int J Tuberc Lung Dis 2014; 18:492-8.
[70] Zaira, Z. (2010). Socioeconomic factors contributing to multidrug-resistant tuberculosis (MDR-TB). Journal of Biomed Sciences and Research, 2 (4), 279-283.