Mwancha-Kwasa C; MBCHB, MPH**,** County government of Kiambu-Health Department. Karumbi J,BPharm, MSc**,** Department of Curative and Rehabilitative Services, Ministry of Health Kenya. Kilonzo M; MBCHB, MMed**,** Department of Obstetrics and Gynaecology, University of Nairobi. Gwako G; MBCHB, Mmed, Department of Obstetrics and Gynaecology, University of Nairobi. Ondieki D; MBCHB, MMed**,** Department of Obstetrics and Gynaecology, University of Nairobi. Tanui L; RCO, BSC HSM**,** Ministry of Health Kwale County. Juma F M; RCO, HND Anesthesia, County government of Kiambu-Health Department. Nderitu M; MBCHB, MSC**,** County government of Kiambu-Health Department. Mwangi J; MBCHB, M.Med, County government of Kiambu-Health Department. Kamenye K; MBCHB, Dip Epidem, MPH**,** National Tuberculosis Leprosy and Lung Disease Program, Kenya. Omesa E; MBCHB, MPH**,** National Tuberculosis Leprosy and Lung Disease Program, Kenya. Enos Masini, MBChB, National Tuberculosis Leprosy and Lung Disease Program, Kenya. Kimani E; MBCHB, MPH**,** County government of Kiambu-Health Department. Kihara A; MBChB, Mmed Department of Obstetrics and Gynaecology, University of Nairobi.

VARIATIONS IN METHODS OF DIAGNOSIS OF PULMONARY TUBERCULOSIS AT INITIATION OF TREATMENT IN KIAMBU COUNTY BETWEEN 2012 AND 2016

MWANCHA-KWASA C, ,KARUMBI J; KILONZO M, GWAKO G, ONDIEKI D, TANUI L; JUMA F M, NDERITU M, MWANGI J, KAMENYE K, ENOS MASINI, KIMANI E, KIHARAN. A

ABSTRACT

Background: The World Health Organization's end TB strategy recommends that over 90% of TB patients should be diagnosed based on testing. The modalities available for TB testing in Kiambu County are the X-ray, Sputum Smear Microscopy, Cultures and GeneXpert MTB/RIF. There is minimal knowledge on the uptake of these diagnostics in actual practice in the county.

Objective: To assess the variations in methods of diagnosis amongst patients at initiation of TB treatment seen in Kiambu county between 2012 and 2016

Design: A cross-sectional study

Setting: Kiambu County, Kenya

Population: 11,841 patients notified into TIBU within Kiambu County

Results: In the study period, there was a gradual increase in the uptake of bacteriological confirmation from 43.6% in 2014 to 58.2% in 2016. Chest X-rays were mostly used in children (62.9%) while Sputum Smear Microscopy was used mostly in adults (69.1%). Uptake of culture was very poor with use in only 1% of adults, and no use (0%) in children in the whole study period. Use of GeneXpert MTB/RIF was also low, though there was a drastic improvement in 2016 with a 500% increase in the absolute number of tests done in comparison with 2015.

Conclusion: Our study showed that there is low uptake of TB diagnostic modalities, especially amongst children, in Kiambu County. However, there was a gradual increase in their use since 2014. Further efforts are needed to increase clinician awareness and use of diagnostics.

INTRODUCTION

Tuberculosis (TB) is one of the major communicable diseases responsible for global mortality and its diagnosis is the cornerstone for detection, case notification and initiation of management.

The End TB strategy by WHO "focuses on early detection, treatment and prevention for all TB patients with the 1st key component being the "early diagnosis of TB, including drug susceptibility testing (1). TB is either clinically diagnosed or bacteriologically confirmed(2).The gold standard for the diagnosis of pulmonary TB (PTB) is Sputum Smear Microscopy (SSM) while for extra-pulmonary TB (EPTB) is culture. GeneXpert MTB/RIF (GeneXpert) test is the gold standard of diagnosis in children. Globally, the diagnosis of TB is made using various modalities including radiological, like the Chest X-ray (CXR)(3), microscopy based, like SSM(4) and Microscopic Observation Drug Susceptibility (MODS)(5), as well as Mycobacterial culture(6). Others are DNA based like TB-loop-mediated isothermal amplification.

(LAMP) for diagnosis (7) and Line Probe Assays (LPAs) for drug resistance testing (8) and others are Nucleic Acid Amplification Tests (NAATs) such as

MATERIALS AND METHODS

Study design: A cross-sectional study, using routinely collected TB program data.

Setting: Kiambu County is one of the 47 counties in Kenya. It borders Nairobi county, one of the top three TB burden counties in Kenya (11), to the South. (12) Kiambu County is classified as a moderate TB burden county with a case notification of 240/100,000 in 2014. It has 131 TB treatment sites, 76 of which are also diagnostic sites. Currently there are two laboratories that serve the entire nation for TB culture, the Tuberculosis Central Reference Laboratory and the Kenya Medical Research Institute laboratory both located in the Capital Nairobi. Kiambu culture samples are referred to these laboratories. Due to the proximity to Nairobi, some clients seek diagnostic services there directly without referral.

Specific setting. Kiambu, part of the Nairobi metropolitan region and hosts a large part of the

GeneXpert (9). These different modalities have various sensitivities, specificities and unique characteristics. In Kenya, diagnostic devices available for the diagnosis of TB include chest radiography and are used together with the clinical algorithm of current cough, fever, weight loss or night sweats(2,10) to give the classification of clinically diagnosed TB. SSM, culture and GeneXpert give the diagnostic classification of bacteriologically confirmed TB.

The WHO End TB strategy recommends the use of bacteriological confirmation over clinical diagnosis for the diagnosis and treatment of TB as much as is practically possible With the global and local improvement in the availability of devices available for diagnosis of TB, we sought to analyze the variations in methods of diagnosis amongst patients at initiation of PTB treatment in Kiambu County between 2012 and 2016.

metropolitan population. This Nairobi metropolitan region also has the highest case notification of tuberculosis in the country (13). Daily, these workers commute to Nairobi for work in the mornings and evenings using the public transport system, the matatus. There are approximately 20,000 matatus serving Nairobi and its environs. In view of this, the "Fungua Dirisha" (open the window) initiative was rolled out where stickers were placed in matatus to encourage commuters to open their windows during the commute and decrease the chances of TB infection.(14)

Context: In Kenya, as in other low and middle income countries, the 125 year old (15) sputum smear microscopy (SSM) has been the backbone of TB diagnosis at the point of care as it is robust, inexpensive and easy to perform.

It has a low sensitivity of 70% (4), which can drop to as low as 35% if there is TB/HIV co-infection, or rise to as high as 95-98% if there is high quality microscopy of two consecutive specimens(16), which is dependent on the skill and competence of the laboratory technician. After the introduction of GeneXpert in 2011, awareness of its utility among clinicians was noted to be inadequate. (17) In July 2016, the government through the ministry of health issued a circular clarifying eligible patient groups and the benefits of the test. GeneXpert was introduced in Kiambu County at Thika Level 5 hospital in May 2014, AIC (Africa Inland Church) Kijabe hospital in May 2015, Kiambu level 4 hospital in June 2015, and at Tigoni level 4 hospital in November 2015.

Study population: The study included 11,841 patients notified into Tuberculosis Information from Basic Units Platform (TIBU)(2) within Kiambu County between January 2012 and December 2016.

Data collection: The TB Program utilizes TIBU data management as central database of the National Tuberculosis and Lung Diseases Program (NTLD-P) which is a web based solution integrated with mobile/tablet technology developed and introduced in Kenya in the year 2012 with inter-sector support. Patients with TB upon diagnosis, are notified, treated and followed up with primary record capture obtained from patient records and Multi-Drug Resistant TB MDR log book entered into registers as a summary of the data entered in the registers. This data is subsequently uploaded at Sub – County level into TIBU by sub-county TB coordinators electronically via mobile computer tablets. Information on diagnostic modality is entered during primary record capture.

Data Validation: TIBU has internal consistency checks to ensure that data entry errors are minimized. The TB program has quarterly data quality audits at the county level and biannually at the national level.

Data analysis: data was downloaded from TIBU data set into an Excel data base and then transferred to STATA Version 13 (StataCorp. 2013. *Stata Statistical Software: Release 13*. College Station, TX: StataCorp LP) for cleaning using pre-developed cleaning do-files. Descriptive analysis was then done where continuous data were summarized by means (±SD) and Medians as appropriate. The study was purely descriptive and used the whole population (Kiambu TIBU database) and as such, no inferential statistics were done. Categorical data was summarized using percentages. All this data was then presented using tables and graphs.

Ethics Approval: This study was approved by the Moi University College of Health Sciences (MU/CHS) and Moi Teaching & Referral Hospital (MT&RH) Institutional Review Board (IREC).

RESULTS

In Kiambu County, 20,132 patients were notified in TIBU from 2012 to 2016. The highest number were notified in 2012
(4,177), and the lowest in 2015 (3,734), as shown in Figure 1.

Figure I

Annual trend of TB patient notification into TIBU in Kiambu County between 2012 and 2016
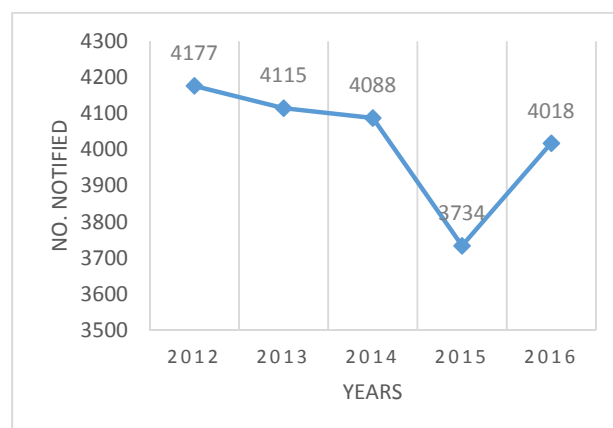
Of the patients notified, 12,734(63.3%) were male. 14,957(74.3%) were diagnosed in public health facilities. PTB cases made up 16,813(83.5%) of those notified. The HIV status of 19,260(95.7%) of the patients was established and documented. TB cases were highest in the age group 25-34 years at 6,091(30.3%). Amongst children (<15yr), those aged 0-4yr at 833/1492 (55.8%). At the time of diagnosis, 7,649/16916(45.2%) had a normal BMI of 18.5 to 24.4. (Table 1)

Table 1
Demographic and Clinical characteristics of patients notified into TIBU in Kiambu County, 2012-2016

Demographic Characteristics		
Sex (n=20132)		%
Female	7398	36.7
Male	12734	63.3
Age (n=20105)		
0-4yr	833	4.1
5-9yr	366	1.8
10-14yr	293	1.5
15-24yr	2988	14.9
25-34yr	6091	30.3
35-44yr	5177	25.7
45-54yr	2599	12.9
55 & above	1758	8.7
Sector (n=20132)		
Prisons	178	0.9
Private	4997	24.8
Public	14957	74.3
Clinical Characteristics		
Type of TB (n=20132)		
Extra Pulmonary	3319	16.5
Pulmonary	16813	83.5
BMI (n=16916)		
<16.5	2418	14.3
16.5-18.4	5299	31.3
18.5-24.4	7649	45.2
24.5-30.4	1261	7.5
>30.5	289	1.7
HIV Status (n=20132)		
Not Done	872	4.3
Done	19260	95.7

Sample sizes differ due to missing data for different variables

From 2012-2016 the zone of Thika sub-county had the highest number of notified cases of tuberculosis in all 4 years (figure 2).
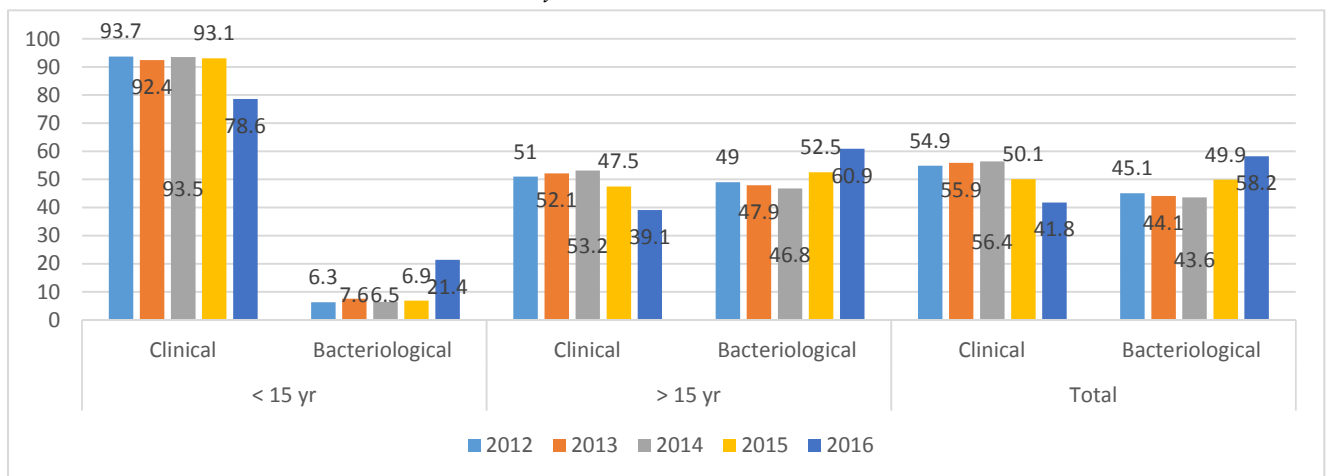
Figure II

Annual trend of notification of Kiambu county TB patients from 2012 to 2016 per zone
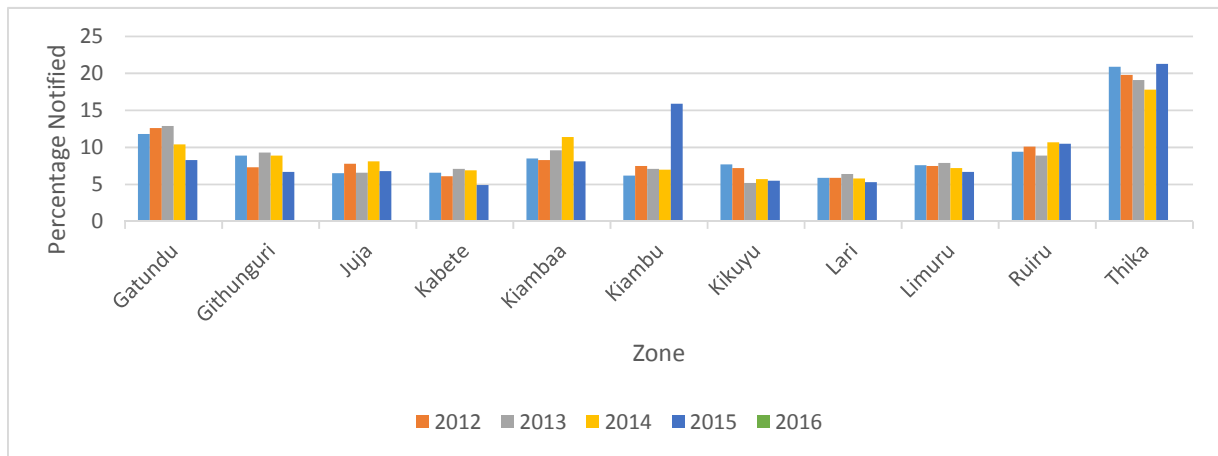
A total of 9,681(48.1%) patients were started on TB treatment based on bacteriological confirmation. In children (<15yrs), notification rate based on bacteriological confirmation was at 9.4% while in adults (>15yrs) it was 51.4%. Initiation of therapy based on clinical diagnosis ranged between 41.8% in 2016 and 56.4% in 2014. (Figure 3

Figure III

Trends of clinically diagnosed and bacteriologically confirmed TB in children (<15yr) and adults (>15yr) in Kiambu county from 2012 to 2016.
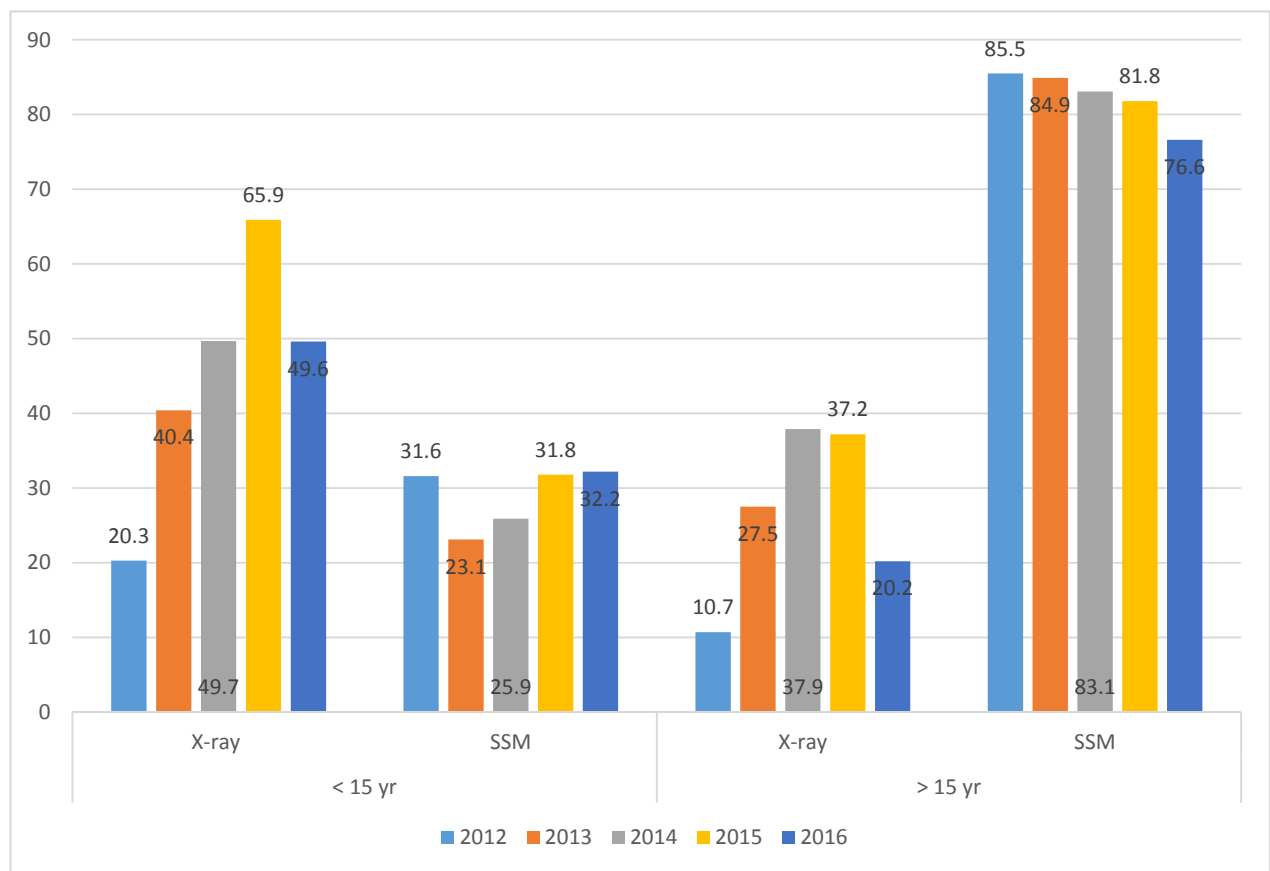
Between 2012 and 2016 cumulatively, 1,440 diagnostic tests were carried out in children aged less than 15yr. Of these, 906(62.9%) were X-rays. In adults, of the 22,108 tests done, 15,287(69.1%) were SSM. (Figure 4)

Figure IV

Trends of uptake of X-ray and Sputum Smear Microscopy by children and adults in Kiambu County between 2012 and 2016.

Of the patients notified into TIBU in this period, 18,613(92.6%) were adults and 1,492(7.4%) were children. Mycobacterial culture was done for 209(1.1%) adults, and none (0%) for children. For geneXpert 4,690(9.1%) were done in adults, and 368(5.6%) tests in children.

Figure V
Trends of uptake of Mycobacterial culture and GeneXpert by children and adults in Kiambu County between 2012 and 2016.
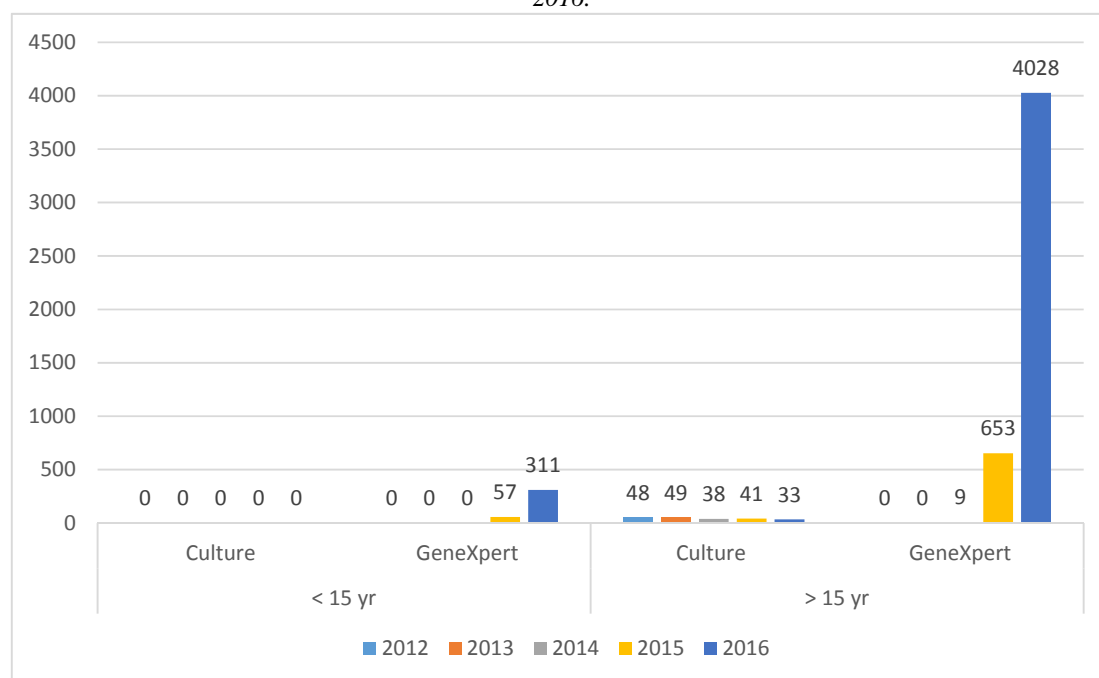
DISCUSSION

There was a general downward trend in TB notification in Kiambu County from 2012 to 2016. This is in keeping with the global trends where TB prevalence is dropping by 1.5% annually. (1) The data for 2015 Q1 was absent (no patients notified). This could have been due to a TIBU data systems upgrade, and explains the sharp drop in 2015.Majority of patients notified were aged 25- 34 years. Children aged 0-4 years were the most affected among those under 15 years of age. There was a steady increase of use of bacteriological confirmation for diagnosis among the notified cases from 2014 likely due to the introduction of GeneXpert.X-Ray was the most utilized diagnostic modality in children while SSM was commonest for adults.

Children aged 0-4 years are entirely dependent on the caregivers, mainly the mothers. The relationship is not just one of providing, but the children spend majority of their time in close proximity to their mothers or caregivers who, if infective with active TB, will likely transmit TB to them. It has been shown in Malawi, looking at children ages 2-4years, that the main risk factors for infection in this age are maternal HIV infection at birth and living in close proximity to a known case of infectious TB (18). In children, the mainstay of diagnosis was clinical. The gold standard for diagnosis of TB in children, prior to 2014 when GeneXpert was introduced into Kiambu was culture. The data shows that no cultures were done during the whole period under study, but this is most likely due to errors of documentation. Once GeneXpert was introduced, it was the gold standard for diagnosis. Again, uptake was poor. In 2016 July, a government directive was issued on the use of GeneXpert(17). Following this, more tests were done, but the number was still very low.

This reluctance to use diagnostic modalities by clinicians attending to children may be attributed to the difficulty in obtaining specimens. Both culture and GeneXpert require either sputum which children do not readily produce or a gastric washout which is quite invasive. Secondly, children are pauci-bacillary making it difficult for even the obtained samples to yield results. Additionally, there may be inertia among laboratory staff creating off the cuff bottle necks to testing using GeneXpert. That adults aged 25-34 years were the most notified is in keeping with the findings of the Kenya Prevalence Survey that the age most affected by TB are those aged 25-34 (19). TB disproportionately affects persons found in densely populated settings such as slums, transport workers and commuters.

Among adults, clinical diagnosis or bacteriological confirmation were used almost equally to make a diagnosis. The modality mainly used by adults was SSM. In all patients notified in Kiambu County, almost half were diagnosed and started on therapy based on bacteriological confirmation. This is far below The End TB strategy by WHO which recommends that over 90% of TB patients should be diagnosed using WHO-recommended rapid tests. (1) From 2014, there was a steady decline in clinical diagnosis and a commensurate rise in bacteriological confirmation. This could be explained by the introduction of GeneXpert in Kiambu County in 2014.

Generally, though, diagnosis by bacteriological confirmation was low. Of all the diagnostic modalities, X-ray and SSM were the most utilized. Culture, the gold standard for EPTB diagnosis, had low uptake in adults, and was not done in children in the 4-year period. It is only available at the Tuberculosis Central Reference Laboratory and the Kenya Medical Research Institute laboratory and the results are relayed back to the clinician after a period of up to six weeks. This means that it is not a viable option for making the decision on whether to start therapy or not. Due to this delay, it was not routinely done. After the introduction of GeneXpert in Kenya, and its role as the gold standard of diagnosis in children, its uptake remained very low. After government intervention, by December 2016, there was a 5-fold increase in its use in comparison with 2015. This was also reflected the rise in cases of bacteriological confirmation.

LIMITATIONS

Our study had few limitations. The group categorized as clinically diagnosed were not discretely identified in TIBU, but were deduced by virtue of not being bacteriologically confirmed. The sample sizes were different for the different variables due to missing data. For age the effect was not so much as only 27/20132 were missing. For BMI [4000/20132] it was.

STRENGTHS

This study looking at different diagnostic modalities in TB diagnosis is a first of its kind in Kenya. Secondly, TIBU has robust data quality assurance mechanisms. Third, the sample size was large and findings can be confidently generalized to similar counties in Kenya and beyond in regions with similar settings. Finally, the study adhered to the STROBE guidelines (20).

RECOMMENDATIONS

To improve the uptake of diagnostics in the diagnosis of TB in children, methods that are easy to use and at the same time less invasive should be adopted. There needs to be active policy and programmatic direction to guide clinicians to use evidence prior to initiating TB treatment, especially in children. The GeneXpert circular from the ministry seems to have had an impact on its uptake, but further efforts, at county and facility level need to be made to sensitize clinicians on the importance of testing before treating. Increasing the number of GeneXpert capable facilities will also improve access and uptake.

To increase the use of SSM in the county, a special pool of technologists needs to be developed who can be capacity built to specifically handle SSM. Though this will bring about issues of referral chain, it will build clinician confidence, improve SSM sensitivity and increase its general uptake.

CONCLUSION

This study shows that the use of diagnostic modalities in TB diagnosis was low in Kiambu County and in children, diagnosis was mainly clinical. The introduction of GeneXpert into the county as the recommended diagnostic modality did little to improve the rates of bacteriological confirmation. There is therefore need to for further work to explore this finding. Adherence to government directives and greater efforts on clinician sensitization need to be implemented, especially amongst children.

ACKNOWLEDGEMENT STATEMENT

REFERENCES

1. World Health Organization. The End TB Strategy [Internet]. Geneva; 2015. Available from:http://www.who.int/tb/End_TB_brochure.pdf?ua=1

2. DLTLD. Guidelines for Management of Tuberculosis and Leprosy in Kenya. Nairobi; 2013.

3. van Cleeff MRA, Kivihya-Ndugga LE, Meme H, Odhiambo JA, Klatser PR. The role and performance of chest X-ray for the diagnosis of tuberculosis: a cost-effectiveness analysis in Nairobi, Kenya. BMC Infect Dis. 2005;5:111.

4. Steingart KR, Henry M, Ng V, Hopewell PC, Ramsay A, Cunningham J, et al. Fluorescence versus conventional sputum smear microscopy for tuberculosis: a systematic review. Vol. 6, Lancet Infectious Diseases. 2006. p. 570–81.

5. Wikman-Jorgensen P, Llenas-García J, Hobbins M, Ehmer J, Abellana R, Queiroga Gonçalves A, et al. Microscopic observation drug susceptibility assay for the diagnosis of TB and MDR-TB in HIV-infected patients: a systematic review and meta-analysis.EurRespirJ[Internet].2014;4(44):973–84.Availablefrom: http://www.ncbi.nlm.nih.gov/pubmed/25186265

6. Hepple P, Novoa-Cain J, Cheruiyot C, Richter E, Ritmeijer K. Implementation of liquid culture for tuberculosis diagnosis in a remote setting: Lessons learned. Int J Tuberc Lung Dis. 2011;15(3):405–7.

7. Yuan LY, Li Y, Wang M, Ke ZQ, Xu WZ. Rapid and effective diagnosis of pulmonary tuberculosis with novel and sensitive loop-mediated isothermal amplification (LAMP) assay in clinical samples: A meta-analysis. J Infect Chemother. 2014;20(2):86–92.

8. World Health Organisation. Rapid diagnostic test and shorter, cheaper treatment signal new hope for multidrug-resistant tuberculosis patients [Internet]. Geneva;2016.Availablefrom:http://www.who.int/mediacentre/news/releases/2016/multidrug-resistant-tuberculosis/en/

9. ZekaAN,Tasbakan S, Cavusoglu C. Evaluation of the GeneXpert MTB/RIF assay for rapid diagnosis of tuberculosis and detection of rifampin resistance in pulmonary and extrapulmonary specimens.J Clin Microbiol. 2011;49(12):4138–41.

10. World Health Organization. Guidelines for intensified tuberculosis case-finding and isoniazid preventive therapy for people living with HIV in resource constrained settings [Internet]. Geneva; 2011.Availablefrom:http://apps.who.int/iris/bitstream/10665/44472/1/9789241500708_eng.pdf

11. National Tuberculosis Leprosy and Lung Disease Program. National Strategic plan for Tuberculosis, Leprosy and Lung Health 2015 – 2018. Nairobi; 2014.

12. KNBS. The 2009 Kenya Population and Housing Census. Home Healthcare Nurse. Nairobi; 2010.

13. Omwenga M. Nairobi -Emerging Metropolitan Region: Development Planning and Management Opportunities and Challenges. In: 46th ISOCARP Congress 2010 [Internet].Nairobi;2010. Available from: http://www.isocarp.net/data/case_studies/1662.pdf

14. National Tuberculosis Leprosy and Lung Disease Program. TB VIPASHO quarterly newsletter [Internet]. Nairobi; 2015.Availablefrom:https://www.chskenya.org/wpcontent/uploads/2015/10/TB-ARC-Vipasho-Jan-June-2015-Edition.pdf

15. World Health Organisation. Frequently Asked Questions on Xpert MTB/RIF assay [Internet].Geneva; Available from: http://www.who.int/tb/laboratory/xpert_faqs.pdf

16. World Health Organisation. Same-day diagnosis of tuberculosis by microscopy [Internet].Geneva; 2011. Available from: http://apps.who.int/iris/bitstream/10665/44603/1/9789241501606_eng.pdf

17. Muraguri N. Use of Genexpert as first diagnostic test. Nairobi; 2016.

18. Khan PY, Glynn JR, Fielding KL, Mzembe T, Mulawa D, Chiumya R, et al. Risk factors for Mycobacterium tuberculosis infection in 2-4 year olds in a rural HIV-prevalent setting. Int J Tuberc Lung Dis. 2016;20(3):342–9.

19. The National Tuberculosis Leprosy and Lung Disease - Program. Kenya Tuberculosis Prevalence Surey 2016. Nairobi; 2016.

20. Von Elm, Erik; Altman, Douglas G; Egger, Matthias; Pocock, Stuart J; Gøtzsche, Peter C; Vandenbroucke JP.The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Lancet [Internet]. 2007, Available from: http://www.thelancet.com/pdfs/journals/lancet/PIIS014067360761602X.pdf