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RESEARCH ARTICLE

COMPARISON OF XPERTMTB/RIF AND GENOTYPE MTBDRPLUS ASSAYS IN THE DETECTION OF TUBERCULOSIS AND RIFAMPICIN RESISTANCE AMONG RETREATMENT SAMPLES IN KENYA.

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Abstract

Background: Tuberculosis (TB) is a major public health problem globally. The National TB program in Kenya has adopted number of new TB diagnostic tools. The present study investigated the performance of XpertMTBRIF and GenoTypeMTBDRplus in the diagnosis of Tuberculosis and rifampicin resistance among retreatment cases.

Methods: A total of 561 TB retreatment sputum samples were subjected to XpertMTBRIF, MGIT culture and GenoTypeMTBDRplus assays. Thereafter, their performance in diagnosis of *Mycobacterium tuberculosis* and detection rifampicin resistance was compared. The sensitivity and specificity of the tests were determined and Receiver operating characteristic (ROC) analysis was performed to compare the diagnostic tools.

Results: The area under the curve (AUC) for XpertMTBRIF MTB detection was 0.81 while that of LPA was 0.85. The AUC for Rifampicin resistance detection was 0.95 and 0.83 for XpertMTBRIF and GenoTypeMTBDRplus respectively. The sensitivity of XpertMTBRIF assay in the detection of MTB was 86.2% while the specificity was 74.9%. GenoTypeMTBDRplus exhibited a sensitivity of 87.8% and the specificity was 84%. On the other hand, XpertMTBRIF exhibited a high sensitivity (91.7%) and specificity (98.5%) in the detection of Rifampicin resistance. GenoTypeMTBDRplus had a sensitivity and specificity of 66.7% and 98.9% respectively. Comparison of the areas under the curve (AUC) for both tests revealed that there is no significant difference ($p=0.16$, $p>0.05$) in the detection of MTB as well as Rifampicin resistance ($p=0.9$, $p>0.05$).

Conclusion: Based on the findings of this study the sensitivity and specificity of the two diagnostic tests, we recommend the use of XpertMTBRIF for surveillance

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since its reagents and operationalization costs are easy to implement.

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Introduction:-

Tuberculosis (TB) continues to cause high morbidity and mortality in developing as well as the developed countries. In the African region, the pandemic is mainly propelled by TB/HIV co-infection since HIV increases the reactivation of latent TB as well as the rapid progression to active infection (Corbett *et al*., 2003). Kenya remains in the list of high TB burden countries(WHO, 2017). According to a prevalence survey carried out in 2016, it was reported that the TB burden in the country is higher than previously thought and currently stands at 558 cases per 100,000 population with approximately 40% of cases missed annually (Ministry of Health, 2016). In order to determine emergence of resistance to first line medicines. Sputum samples from previously treated patients are usually sent for culture and drug susceptibility testing in designated laboratories in the country. Kenya has adopted the new WHO approved molecular technologies which have greatly improved case detection as well as turnaround time in the diagnosis and management of TB (Ministry of Health, 2016). The XpertMTB/RIF introduced in Kenya in 2011 and the GenoTypeMTBDRplus have all been incorporated in the in-country's TB testing algorithm. The two tests have a great ability to detect TB as well drug resistance (Bablishvili *et al*., 2015). Genotype MDRTB*plus* technology also known as Line Probe Assay (LPA) is a qualitative in vitro diagnostic test based on DNA-STRIP technology for the identification of M. tuberculosis complex and its resistance to rifampicin (RMP) and/or isoniazid (INH), while the Xpert MTBRIF assay is based on real-time PCR. However LPA requires several manual steps to prepare DNA template, which could result in the loss of DNA during processing; the technique also involves manual hybridization steps which could decrease the sensitivity of the assay. Nevertheless, the XpertMTBRIF assay only detects RIF resistance while GenoTypeMTBDR*plus* detects both rifampicin and isoniazid (INH) (Rufai *et al*., 2014). Since their introduction in the country, there are no elaborate studies that have been done to compare their performance in our setting. Initially, surveillance was performed using culture and later GenoTypeMTBDRplus was introduced for DNA. Rollout of XpertMTRIF assay across the country is ongoing with plans to make it the first diagnostic test for all. Presumptive and previousely treated TB patients need quick responses of laboratory results for management. In the Kenyan context surveillance using culture and then later introduction of LineProbeAssay/ GenoTypeMTBDRplus has been in place. Further, the current testing algorithm aims at expanding XpertMTBRIF assay services which can readily be available and accessible to the peripheral facilities to ensure that there is access to universal drug susceptibility testing to all bacteriologically confirmed cases of Tuberculosis.

The current study assessed the performance of XpertMTB/Rif and GenoTypeMTBDR*plus* in the diagnosis of tuberculosis and detection of rifampicin resistance among retreatment cases considered as a high risk for developing drug resistant tuberculosis.

Materials and Methods:-

The study was carried out at Kenya Medical Research Institute, Centers for Disease Control Tuberculosis culture laboratory (KEMRI-CDC) Kisumu. The study was reviewed approved by Kenyatta National Hospital-University of Nairobi Ethical Review Committee (KNH-UoN ERC). Sputum samples collected from TB retreatment patients were subjected to, XpertMTB/Rif, GenoTypeMTBDR*plus* assays as well as liquid MGIT culture. Processed specimens were inoculated onto BACTECTMGIT^{TM} 960 broth culture system (BD diagnostics) as described by (Lu, Heeren, & Dunne, 2002). All sputum samples received through courier delivery were processed using the *N*-acetyl-l-cysteine-sodium citrate-NaOH (NALC-NaOH) method. Samples were decanted following centrifugation, and the sediments were resuspended in 3 ml of phosphate buffer solution. Aliquots were prepared from the processed samples to perform, MGIT960 culture, GenoTypeMTBDR*plus* assay as previously described by (Ombura *et al*., 2016). All the processed sputum samples were equally subjected to XpertMTBRIF assay according to the manufacturer's instructions. Data generated by XpertMTRIF, GenoTypeMTBDR*plus* and MGIT culture were recorded on laboratory log books as well as Excel worksheets. The data was coded and analysis was done using STATA version 13. The sensitivity and specificity of the tests were determined with reference to MGIT culture as a gold standard. Receiver operating characteristic (ROC) analysis was performed and the output of the areas under the curve (AUC) for the tests were compared.

Results:-

A total of 561 sputum samples were examined in this study. The mean age of the study participants was 38.7 years with a standard deviation of 15.64. The minimum and maximum ages were 1 and 95 respectively. **Figure 1** gives an insight on the frequency of MTB detection by XpertMTBRIF assay and GenoTypeMTBDRplus (LPA) for the 561 samples tested. Twenty six percent (26.74%, n=150) of the samples tested were positive for MTB by both LPA and XpertMTBRIF assay while 54.9% (n=308) were negative for MTB by both tests. Among the samples that were positive for MTB by XpertMTBRIF assay, 11.76% (n=66) were negative for MTB by LPA. On the other hand, 4.28% (n=24) of samples that were positive by LPA were detected as negative for MTB by XpertMTBRIF assay. Among the samples that were detected as an error 2.3% (n=13) by XpertMTBRIF assay, 1.6% (n=9) and 0.71% (n=4) were detected as negative and positive for MTB by GenoTypeMTBDR*plus* (LPA) respectively.

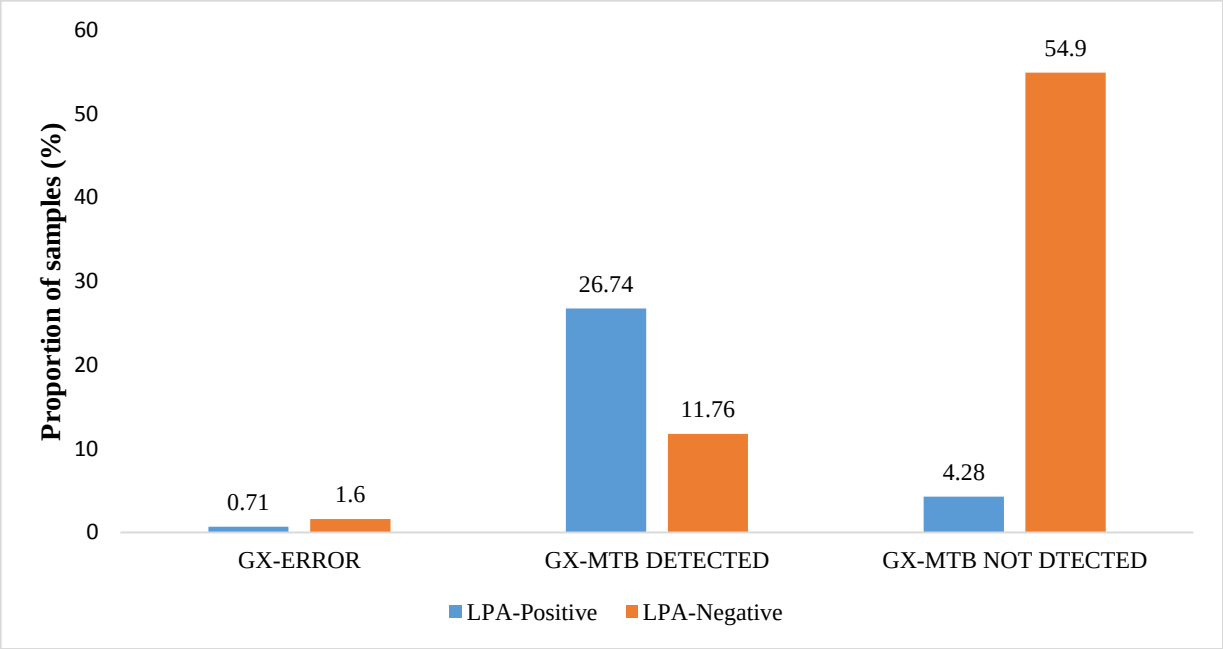

Figure 1:-Comparison of MTB detection frequencies for XpertMTBRIF assay and GenoTypeMTBDRplus.

The performance of XpertMTBRIF assay in the detection of MTB was compared to MGIT culture results as presented in **Figure 2**. There was a concurrence of 18.9% (n=106) between XpertMTBRIF assay and MGIT on samples that were detected as positive for MTB. The XpertMTBRIF assay detected MTB in 17.5% (n=98) of samples that were negative for MTB by MGIT culture. Forty nine percent 49.9%, (n=280) of the samples were negative for both XpertMTBRIF and MGIT culture. Among the culture positive samples, 2.3% (n=13) were negative for MTB by XpertMTBRIF assay. Culture contamination rate was generally low but within the acceptable limit (5.17%). However, MTB was detected by XpertMTBRIF assay in (1.4%) of samples which had growth of non-Tuberculous mycobacterium (MOTT) on culture.

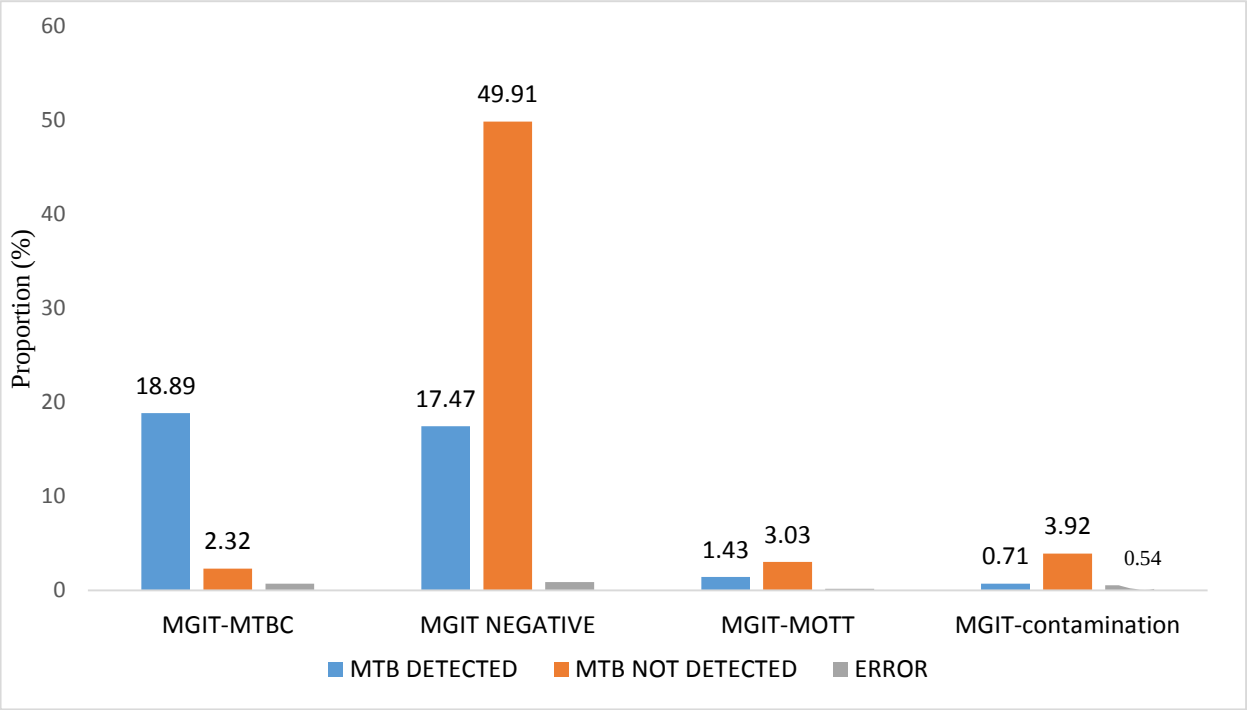

Figure 2:-Comparison of MTB detection frequencies for XpertMTBRIF assay and MGIT culture results.

Figure 3 outlines the comparison of LPA with MGIT culture results for the 561 samples tested. Generally, 19.3% (n=108) of the samples were positive for MTB for both diagnostic tests whereas 57.4% (322) were identified as negative for MTB by both tests. Two percent (2.7%, n= 15) of samples that were culture positive were identified as negative for MTB by LPA while 10.8 % (n=61) were negative by culture but positive for MTB by LPA. A number of sputum samples (1.3%, n=7) in which MOTT were isolated on culture tested positive for MTB by LPA.

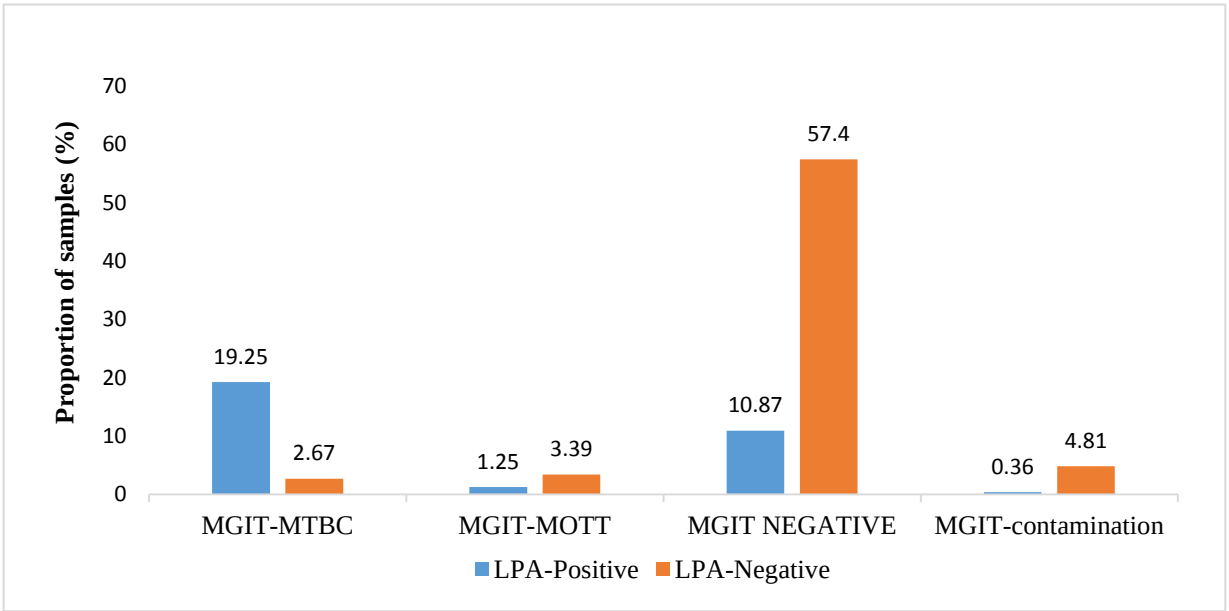

Figure 3:-Comparison of GenoTypeMTBDR*plus* (LPA) MTB detection rate versus MGIT culture results

Detection of Rifampicin resistance for MTB positive samples by LPA and XpertMTBRIF assay is presented in **Table 1**. Overall, 2.3% (n=13) of the total samples (N=561) were identified as Rifampicin resistant by both diagnostic tests while 23.7% (n=133) were flagged as Rifampicin susceptible by both diagnostic platforms. Out of

18 samples detected as Rif resistant by XpertMTBRIF assay, 27.8% (n=5) were identified as Rifampicin susceptible by LPA. There was a concurrence of 72.2% (n=13) on both diagnostic tools for samples in which Rifampicin resistance was detected.

Xpertmtbrif rif resistance results	**LPA-Susceptibility results for Rifampicin**			
	N/A	R	S	Total
Detected	0	13	5	18
	0.0%	72.22%	27.78%	100%
Intermediate	1	0	0	1
	100%	0.00%	0.00%	100%
N/a	316	1	26	343
	92.13%	0.29%	7.58%	100%
Not detected	66	0	133	199
	33.17%	0.00%	66.83%	100
Total	383	14	164	562
	68.27	2.50%	29.23%	100%

Table 1:-Comparison of Rifampicin susceptibility test results for XpertMTBRIF assay and GenoTypeMTBDRplus (LPA).
Key: R=Rifampicin resistant, S= Rifampicin susceptible, N/A=Not applicable

Comparison of MGIT culture and XpertMTBRIF assay susceptibility results are presented on **Table 2.** Out of 18 samples that tested positive for Rifampicin resistance by XpertMTBRIF assay, 11 (61.1%) were Rifampicin susceptible by MGIT-DST. There was a disparity between XpertMTBRIF and MGIT DST tests where 6 (33.3%) samples that were flagged as Rifampicin susceptible by MGIT whereas XpertMTBRIF assay identified them as Rifampicin resistant. A total of 12 MTB positive samples were identified as Rifampicin resistant by culture. Both tests agreed on 89 (44.7%) of samples in which Rifampicin resistance was not detected.

Table 2:-Comparison of Rif susceptibility test results for XpertMTBRIF and MGIT DST

Xpert mtbrif rif resistance detection	**MGIT culture & DST results Rifampicin**			
	N/A	R	S	Total
Detected	1	11	6	18
	5.56%	61.1%	33.3%	100%
Intermediate	1	0	0	1
	100%	0.0%	0.0%	100%
N/a	327	0	16	343
	95.34%	0.0%	4.66%	100%
Not detected	109	1	89	199
	54.77%	0.50%	44.7%	100%
Total	438	12	111	561
	78.07%	2.1%	19.8%	100%

Key: R=Rifampicin resistant, **S**= Rifampicin susceptible N/A=Not applicable
Rifampicin susceptibility results for LPA was compared to MGIT culture results. **Table 3** illustrates the frequency of Rifampicin resistance detection by both diagnostic tests. A total of 14 samples were flagged as Rifampici resistant by LPA while 12 were detected by MGIT. Eight samples (57%) that were Rifampicin resistant by LPA, were similarly detected as Rifampicin resistant by MGIT culture DST. However, 4 (29%) of the samples that were detected as Rifampicin resistant by LPA were identified as Rifampicin susceptible by MGIT culture DST. Ninety-three MTB positive samples were negative for Rifampicin resistance by both diagnostic tools.
Table 3:- Rifampicin susceptibility test results for LPA and MGIT DST

LPA- RIF resistance detection	**MGIT culture & DST results for Rifampicin**			
	N/A	R	S	Total
N/A	368	1	14	383
	96.08%	0.26%	3.66%	100%
R	2	8	4	14

	14.29%	57.14%	28.57%	100%
S	68	3	93	164
	41.46%	1.83%	56.71%	100%
Total	438	12	111	561
	78.07%	2.14%	19.79%	100%

Key: R=Rifampicin resistant, **S**= Rifampicin susceptible

Receiver operating characteristic (ROC) analysis was performed on MTB detection rates for XpertMTBRIF assay and GenoTypeMTBDRplus (LPA). The area under the curve (AUC) for XpertMTBRIF assay was 0.8053 with a standard error of 0.0188 and a 95% confidence interval (CI) of 0.7705-0.8377. The AUC for LPA is 0.8591 with a standard error of 0.0172 and a 95% confidence interval of 0.82761-0.88690. Test for equality of the area under the curve (AUC) for the two diagnostic tests yielded a chi 2 value of 1.95 and a p value of 0.1626. The resulting ROC curve with MGIT culture results as a reference for MTB detection is as shown on **Figure 4**. The corresponding sensitivity and specificity for XpertMTBRIF assay is 86.18% and 74.89% respectively with a positive likelihood ratio (LR+) of 3.43 and a negative likelihood ratio (LR-) of 0.1846. On the other hand, the sensitivity and specificity of LPA is 87.80% and 84.02% respectively whereas the LR+ and LR- are 5.5 and 0.15 respectively.

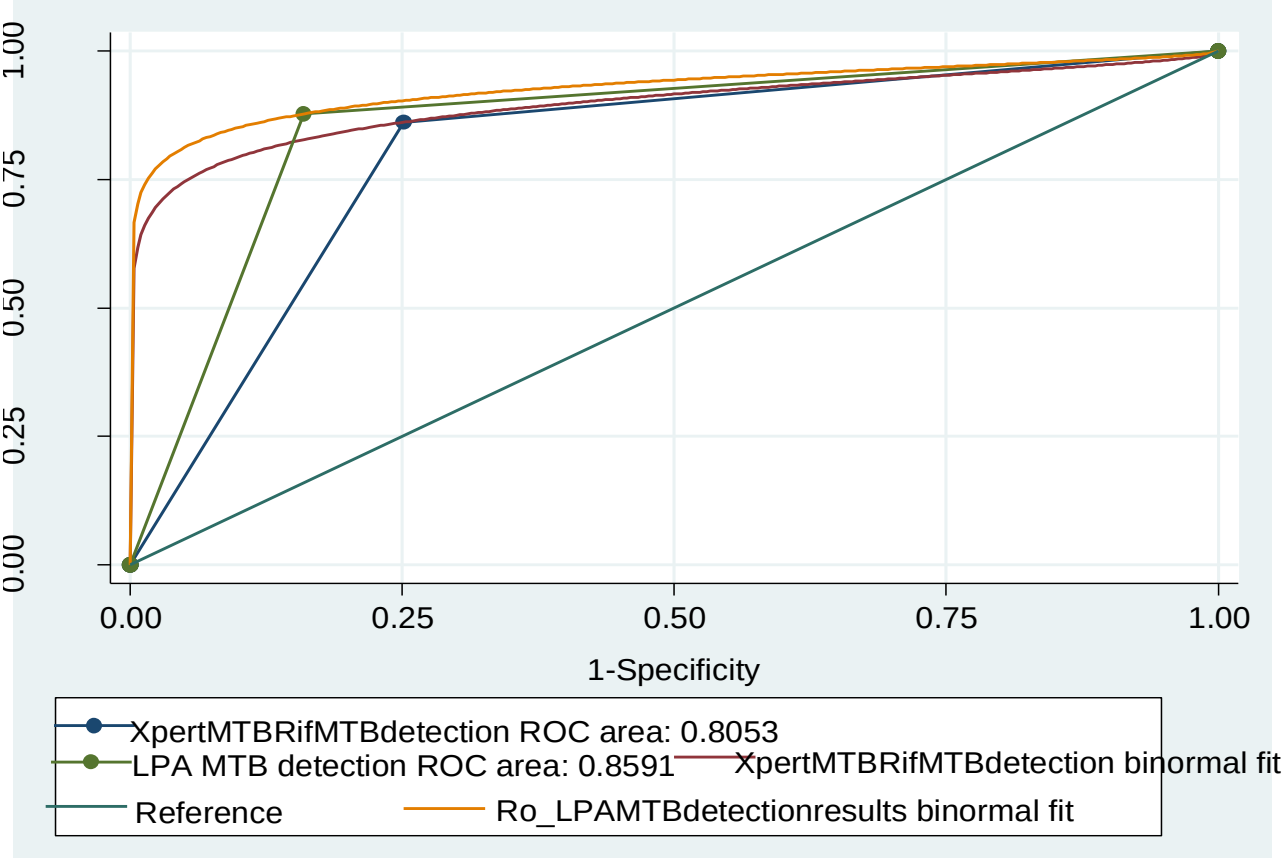

Figure 4:-Receiver operating characteristic (ROC) curve for MTB detection rates by XpertMTRIF assay and GenoTypeMTBDRplus (LPA).

Receiver operating characteristic (ROC) analysis was performed on Rifampicin resistance detection results from both XpertMTBRIF assay and LPA with MGIT DST as a reference. The AUC for XpertMTBRIF assay was 0.952 with a standard error of 0.0417 and 95% CI between 0.9308-0.9681. The resulting sensitivity and specificity were 91.67% and 98.52% respectively. In this instance, the XpertMTBRIF assay correctly classified 98.57% of the Rifampicin resistant samples. The LR+ ratio was 71.89 while the LR- was 0.0844. The AUC for LPA was 0.8279 with a standard error of 0.0711 and 95% CI between 0.7932-0.8575. The sensitivity and specificity for LPA

Rifampicin resistance detection was 66.67% and 98.91% respectively. The GenoTypeMTBDRplus (LPA) correctly classified 98.22% of Rifampicin resistant samples in comparison to MGIT culture results. The LR+ was 61 while the LR- was 0.34. **Figure 5** illustrates the corresponding ROC curves and the reported AUC. Test for equality between the AUC generated a p=0.9548 (p>0.05).

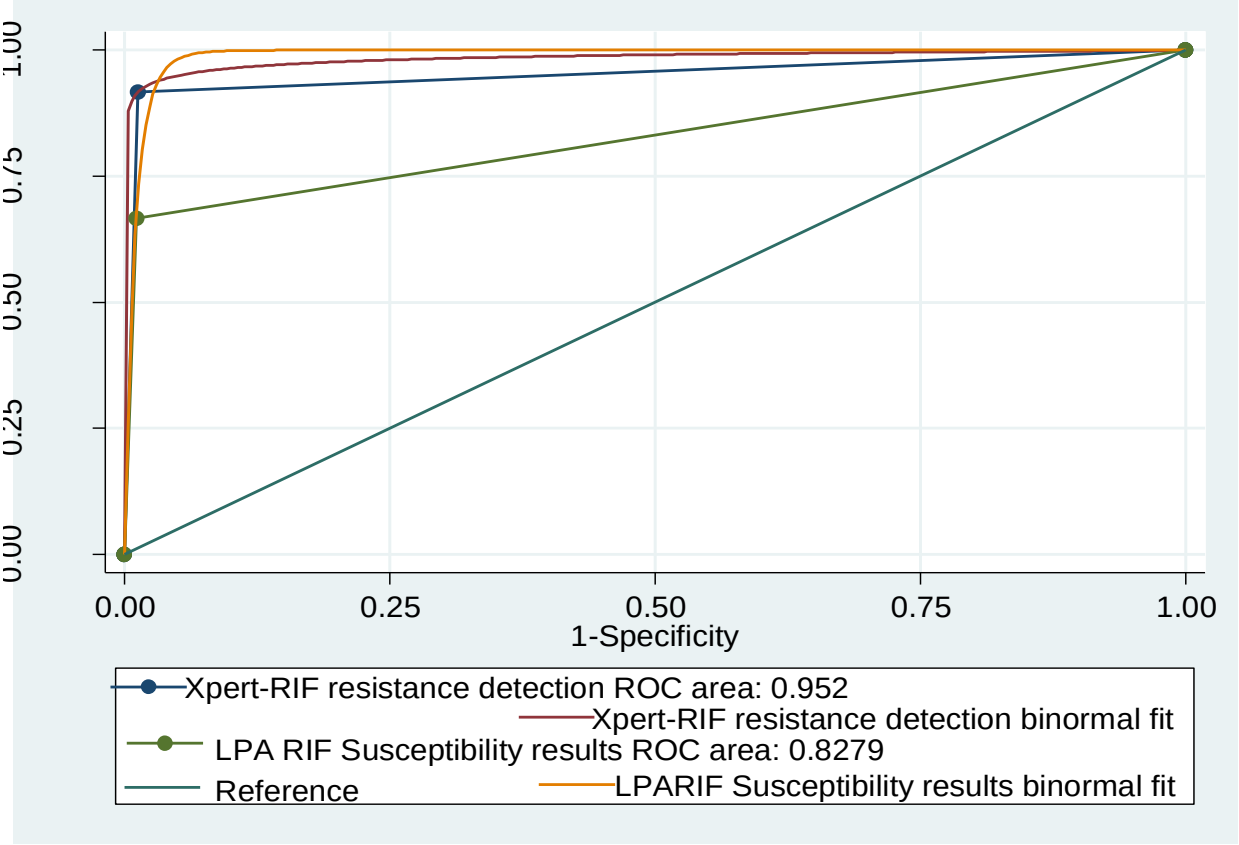

Figure 5:-Receiver operating characteristic curve (ROC) for XpertMTBRIF Assay and LPA Rifampicin resistance detection.

Discussion:-

The rapid detection of TB and Rifampicin resistance by XpertMTBRIF facilitates timely initiation of treatment for patients hence reducing the TB transmission cycle. GenoTypeMTBDR*plus* can detect resistance to Isoniazid (INH) which is also known to be significant in terms of patient treatment outcomes (Naidoo, Du Toit, et al., 2014). In the current study, the sensitivity of XpertMTBRIF assay in the detection of MTB was 86.2% while the specificity was 74.9%. On the other hand, GenoTypeMTBDRplus (LPA) exhibited a sensitivity of 87.8% and the specificity was 84%. Both diagnostic tests exhibited excellent sensitivity and specificity in the detection of Tuberculosis among retreatment samples. The results obtained in this study are consistent with those reported in other studies (Bablishvili *et al*., 2015; Opota *et al*., 2016). The XpertMTBRIF assay had a higher sensitivity of 91.7% for detection of Rifampicin resistance compared to GenoTypeMTBDR*plus* which had 66.7%. Other studies have reported that XpertMTBRIF demonstrated more accuracy in the detection of Rifampicin susceptibility for discrepant isolates compared with GenoTypeMTBDRplus (Rahman *et al*., 2016). The specificity for Rifampicin resistance detection was nearly similar for both tests i.e. 98.5% and 98.9% for XpertMTBRIF and GenoTypeMTBDR*plus* respectively. The main advantage with the XpertMTBRIF assay is the ability to detect Rifampicin resistance within 2 hours compared to the GenoTypeMTBDR*plus* which takes up to 5 days (Bablishvili *et al*., 2015). A visual look at the Receiver operating characteristic curves (ROC) reveals that the two molecular diagnostic tools are of valuable utility in the detection of MTB as well as Rifampicin resistance (Figure 4 & Figure 5 respectively). The area under the curve (AUC) for XpertMTBRIF MTB detection was 0.81 while that of LPA was 0.85. Both tests are good in the detection of MTB. The AUC for Rifampicin resistance detection was 0.95 and 0.83 for XpertMTBRIF and GenoTypeMTBDRplus (LPA) respectively. Nevertheless, comparison of the areas under the curve (AUC) for both

tests revealed that there is no significant difference (p=0.16, p>0.05) in the detection of MTB as well as Rifampicin resistance (p=0.9, p>0.05) (Blakemore *et al*., 2010) using either technique.

According to a study carried out to compare XpertMTB/RIF assay and GenoTypeMTBDR*plus* DNA probes for detection of mutations linked to Rifampicin resistance, the agreement of XpertMTB/RIF and GenoTypeMTBDR*plus* with LJ-DST for detection of Rifampicin susceptibility was found to be 93.5% and 92.4%, respectively (Rahman *et al*., 2016). The study also reported a 92.4% overall agreement of the two molecular methods for the detection of Rifampicin susceptibility. Results from another study demonstrated that XpertMTBRIF had an excellent ability to detect Rifampicin resistance (Sharma *et al.,* 2014). A study that compared the utility of XpertMTB/RIF & GenotypeMDRTBplus in the diagnosis of bone and joint tuberculosis reported the sensitivity of XpertMTB/RIF for detecting Rifampicin resistance at 100%, and the sensitivities of GenotypeMDRTB*plus* in the detection of Rifampicin and Isoniazid (INH) resistance were 83.3% and 85.7%, respectively (Gu *et al.*, 2015).

Findings from this study also point to the possibility of co-infection of some patients with MTB and MOTT. XpertMTB/RIF assay detected MTB in 1.43% (n=8) of MOTT positive samples while LPA detected 1.25% (n=7) of the samples. This results are critical for the management of these patients in order achieve the desired cure rates. Co-infection with MTB and MOTT has also been documented in other studies (Sekadde *et al*., 2013).

The introduction of new Tuberculosis diagnostic technologies has greatly improved the detection of Tuberculosis and drug resistance. The turnaround time towards initiation on treatment for patients has also improved contributing positively to the overall quality of TB services in the country. Evidence also show that the XpertMTBRIF assay detects with high specificity the extra-pulmonary TB (EPTB) cases with smear-positive non-respiratory samples such as cerebrospinal fluid and tissues (Maynard-Smith, Larke, Peters, & Lawn, 2014). Rapid and accurate results from such techniques has made it possible to reduce TB associated mortality (Naidoo, et al., 2014).

Conclusion:-

Overall, findings from this study indicates that XpertMTBRIF assay and GenoTypeMTBDR*plus* are excellent TB molecular diagnostic tools. There is no significant difference in the detection of MTB as well as Rifampicin resistance. These platforms have enabled the rapid confirmation of cases and increased access to universal Drug Sensitivity Testing. On the other hand, the cost of implementing and sustaining these technologies is high and requires more funds which may be prohibitive in resource limited settings.

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References:-

1. Bablishvili, N., Tukvadze, N., Avaliani, Z., Blumberg, H. M., & Kempker, R. R. (2015). Acomparison of the Xpert® MTB/RIF and GenoType®MTBDRplus assays in Georgia. *International Journal of Tuberculosis and Lung Disease*, *19*(6), 676–678. https://doi.org/10.5588/ijtld.14.0867
2. Blakemore, R., Story, E., Helb, D., Kop, J., Banada, P., Owens, M. R., … Alland, D. (2010). Evaluation of the analytical performance of the Xpert MTB/RIF assay. *Journal of Clinical Microbiology*, *48*(7), 2495–501. https://doi.org/10.1128/JCM.00128-10
3. Corbett, E. L., Watt, C. J., Walker, N., Maher, D., Williams, B. G., Raviglione, M. C., & Dye, C. (2003). The Growing Burden of Tuberculosis. *Archives of Internal Medicine*, *163*(9), 1009. https://doi.org/10.1001/archinte.163.9.1009
4. Gu, Y., Wang, G., Dong, W., Li, Y., Ma, Y., Shang, Y., … Huang, H. (2015). Xpert MTB/RIF and GenoType MTBDRplus assays for the rapid diagnosis of bone and joint tuberculosis. *International Journal of Infectious Diseases*, *36*, 27–30. https://doi.org/10.1016/j.ijid.2015.05.014
5. Lu, D., Heeren, B., & Dunne, W. M. (2002). Comparison of the automated Mycobacteria Growth Indicator Tube system (BACTEC 960/MGIT) with Löwenstein-Jensen medium for recovery of mycobacteria from clinical specimens. *American Journal of Clinical Pathology*, *118*(4), 542–545. https://doi.org/10.1309/65KN-2M7E-7MNN-X0TA
6. Maynard-Smith, L., Larke, N., Peters, J. A., & Lawn, S. D. (2014). Diagnostic accuracy of the Xpert MTB/RIF

assay for extrapulmonary and pulmonary tuberculosis when testing non-respiratory samples: A systematic review. *BMC Infectious Diseases*, *14*(1). https://doi.org/10.1186/s12879-014-0709-7

7. Ministry of Health, Kenya N.-P. T. P. survey R. (2016). Survey Report.
8. Naidoo, P., du Toit, E., Dunbar, R., Lombard, C., Caldwell, J., Detjen, A., … Beyers, N. (2014). A Comparison of Multidrug-Resistant Tuberculosis Treatment Commencement Times in MDRTBPlus Line Probe Assay and Xpert® MTB/RIF-Based Algorithms in a Routine Operational Setting in Cape Town. *PLoS ONE*, *9*(7), e103328. https://doi.org/10.1371/journal.pone.0103328
9. Ombura, I. P., Onyango, N., Odera, S., Mutua, F., & Nyagol, J. (2016). Prevalence of drug resistance mycobacterium tuberculosis among patients seen in coast provincial general hospital, Mombasa, Kenya. *PLoS ONE*, *11*(10), 1–12. https://doi.org/10.1371/journal.pone.0163994
10. Opota, O., Senn, L., Prod'hom, G., Mazza-Stalder, J., Tissot, F., Greub, G., & Jaton, K. (2016). Added value of molecular assay Xpert MTB/RIF compared to sputum smear microscopy to assess the risk of tuberculosis transmission in a low-prevalence country. *Clinical Microbiology and Infection*, *22*(7), 613–619. https://doi.org/10.1016/j.cmi.2016.04.010
11. Rahman, A., Sahrin, M., Afrin, S., Earley, K., Ahmed, S., Rahman, S. M. M., & Banu, S. (2016). Comparison of Xpert MTB/RIF assay and genotype MTBDRplus DNA probes for detection of mutations associated with rifampicin resistance in mycobacterium tuberculosis. *PLoS ONE*, *11*(4), 1–11. https://doi.org/10.1371/journal.pone.0152694
12. Report, G. T. (2017). *TUBERCULOSIS*.ISBN 978-92-4-156551-6Global tuberculosis report 2017. Geneva: World Health Organization; 2017. Licence: CC BY-NCSA 3.0 IGO.
13. Rufai, S. B., Kumar, P., Singh, A., Prajapati, S., Balooni, V., & Singh, S. (2014). Comparison of xpert MTB/RIF with line probe assay for detection of rifampin-monoresistant mycobacterium tuberculosis. *Journal of Clinical Microbiology*, *52*(6), 1846–1852. https://doi.org/10.1128/JCM.03005-13
14. Sekadde, M. P., Wobudeya, E., Joloba, M. L., Ssengooba, W., Kisembo, H., Bakeera-kitaka, S., & Musoke, P. (2013). Evaluation of the Xpert MTB / RIF test for the diagnosis of childhood pulmonary tuberculosis in Uganda : a cross-sectional diagnostic study. *BMC Infectious Diseases*, *13*(1), 1. https://doi.org/10.1186/1471-2334-13-133.