Volume 20 Issue 21
Originally issued as F5

Global Journal of Medical Research: F
Diseases
Volume 20 Issue 5 Version 1.0 Year 2020
Type: Double Blind Peer Reviewed International Research Journal
Publisher: Global Journals Inc. (USA)
Online ISSN: 2249-4618 & Print ISSN: 0975-5888

Integrated use of the GeneXpert Platform for TB, HIV and EVD Testing in Liberia

By Kassaye Tekie Desta, John B. Dogba, Julia Toomey Garbo, Dedeh B. Kessely, Candace B. Eastman & Jerry G. Daboi

Abstract- *Background:* The capacity for molecular testing of the Human Immunodeficiency Virus (HIV) Viral load, Tuberculosis (TB) and epidemic- prone disease was very limited in Liberia prior to the Ebola Virus Diseases (EVD) outbreak. The use of point of care and near point of care machines for multiple disease testing of HIV, TB and EVD was adopted as a solution to these challenges. The purpose of this study was to evaluate the integrated use of GeneXpert for the three disease testing.

Methods: A previously collected and reported GeneXpert testing data was used to evaluate the integrated use of the GeneXpert platform for TB, HIV viral load and EVD testing. All the laboratory GeneXpert secondary data available since the machines were installed and started testing were analyzed.

Keywords: *GeneXpert, EVD, HIV, viral load, TB.*

GJMR-F Classification: *NLMC Code: QW 168.5.H6*

Strictly as per the compliance and regulations of:

© 2020. Kassaye Tekie Desta, John B. Dogba, Julia Toomey Garbo, Dedeh B. Kessely, Candace B. Eastman & Jerry G. Daboi. This is a research/review paper, distributed under the terms of the Creative Commons Attribution-Noncommercial 3.0 Unported License http://creativecommons.org/licenses/by-nc/ 3.0/), permitting all non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

Integrated use of the GeneXpert Platform for TB, HIV and EVD Testing in Liberia

Kassaye Tekie Desta [α], John B. Dogba [σ], Julia Toomey Garbo [ρ], Dedeh B. Kessely [ω], Candace B. Eastman [¥] & Jerry G. Daboi [§]

Abstract- Background: The capacity for molecular testing of the Human Immunodeficiency Virus (HIV) Viral load, Tuberculosis (TB) and epidemic- prone disease was very limited in Liberia prior to the Ebola Virus Diseases (EVD) outbreak. The use of point of care and near point of care machines for multiple disease testing of HIV, TB and EVD was adopted as a solution to these challenges. The purpose of this study was to evaluate the integrated use of GeneXpert for the three disease testing.

Methods: A previously collected and reported GeneXpert testing data was used to evaluate the integrated use of the GeneXpert platform for TB, HIV viral load and EVD testing. All the laboratory GeneXpert secondary data available since the machines were installed and started testing were analyzed. Besides; Field observation report on the operation, coordination and impact of the integrated testing programmatic intervention was included.

Results: The integrated testing of HIV Viral load, Mycobacterium Tuberculosis/Rifampicin (MTB/RIF) and EVD using the GeneXpert platform has played a significant role in Liberia. A total of 706 HIV viral load, 3695 MTB/RIF and 2309 EVD GeneXpert tests were conducted since the start of the integrated testing.

Conclusion: The integrated use of the GeneXpert platform for TB, HIV and EVD is very crucial as it helped in enhancing the services and coordinating resources in a sustainable way. Lessons learned from this integration will help to effectively scale up the integrated testing.

Keywords: GeneXpert, EVD, HIV, viral load, TB.

I. Introduction

The EVD outbreak in Liberia began in March 2014 and has had a devastating impact on the health system. The health system was ill- equipped to effectively respond to the epidemic. The laboratory diagnostic service was one of the health services which was affected by the EVD outbreak [1]. During the outbreak, laboratory services like other health services component had to come to a standstill. This was mainly due to the lack of laboratory reagents and consumables. The laboratory system of Liberia in the pre- Ebola era was weak and lagged behind the other component of the health services. Even though the National Diagnostic Unit of Liberia was established in 2009 and laboratory policy was developed in 2011, the laboratory subunits in the Ministry of Health including the National Reference Laboratory, the National Diagnostics Unit and the National Blood Safety Program, were not well coordinated and operated as separate units. The laboratory testing service was limited to hospitals, health centers and clinics. There was no specialized and molecular testing capacity at the national reference laboratory which was providing limited testing services for epidemic-prone diseases such as measles, rubella and yellow fever [2, 3].

The lack of in-country molecular and specialized testing capacity critically affected the epidemic- prone disease testing as well as specialized clinical testing in Liberia. Some of the services which were affected by the lack of the molecular testing capacity were HIV viral load, HIV early infant diagnosis testing, TB, Lassa fever, Dengue, Marburg and other hemorrhagic fevers. It was only at the end of 2013 that the first molecular testing capacity was established at the national reference laboratory of Liberia. Prior to 2013, Liberia used to send HIV 1 specimens to South Africa for polymerase chain reaction molecular testing. The average Turnaround Time (TAT) was 30 to 45 days. The first molecular testing capacity was initiated at the national reference laboratory of Liberia by the coordinated effort of the Clinton Health Access Initiative (CHAI) Liberia office and the National AIDS Control Program (NACP) of Liberia. A standard molecular laboratory for specimen extraction, master mixing and amplification/detection was established for HIV molecular testing. This was funded by the Global Fund. The testing service for HIV was interrupted and the laboratory was dedicated for EVD testing; following the Ebola outbreak in March 2014. This was the only molecular laboratory in Liberia that could be potentially used for EVD testing. The dedication of the molecular laboratory for EVD testing interrupted the HIV clinical molecular testing. During the EVD outbreak; the HIV molecular testing was not restored for more than one year. The interrupted molecular tests include HIV 1 early

Author α: National Diagnostic Unit of Liberia /Clinton Health Access Initiative, Liberia. e-mail: kassayetek@gmail.com
Author σ: National Public Health Institute of Liberia, National Public Health Reference Laboratory.
Author ρ: National AIDS Control Program of Liberia.
Author ω: National Leprosy and Tuberculosis Control Program of Liberia.
Author σ ¥: Africabio Enterprises Inc.
Author §: National Diagnostic Unit of Liberia.
Author σ: University of Ibadan, Department of Veterinary Public Health and Preventive Medicine; Centre for the Control and Prevention of Zoonoses (CCPZ).

© 2020 Global Journals

infant diagnosis and HIV viral load testing. Patients on Anti-Retroviral Therapy (ART) should be monitored for treatment response using viral load test [4]. Despite this, developing countries manage patients by CD4 cell counts and clinical staging as result of the expensive equipment and skilled manpower required by the current viral load assays [5].

According to 2013 Liberian Demographic and Health Survey, the prevalence of HIV in the general population aged 15-49 was 2.1% (1.9% HIV 1 and about 0.3% HIV-2). In 2015, an estimated 26,313 adults and 2,339 children were living with HIV respectively. The percentage of eligible people receiving ART were 25.8% only [6]. The lack of capacity for HIV molecular testing, the low testing volume as result of the 2.1% low prevalence of HIV and the poor specimen referral linkage are the fundamental reasons for the adoption of point of care and near point of care devices in Liberia. As a good opportunity to this, the Xpert HIV-1 Viral Load (Cepheid) cartridge was launched in 2014 as a potential point-of-care rapid viral load assay [7]. The release of the EVD and HIV viral load GeneXpert assays from Cepheid in 2014 followed by Ministry of Health of Liberia approval for use in 2015 was a very crucial opportunity for Liberia.

The GeneXpert instrument system is an automated and integrated cartridge-based system for sample purification, nucleic acid amplification and detection of target in clinical specimens using real-time Reverse Transcription Polymerase Chain Reaction (RT-PCR). Several infectious agents can be detected using the technology and appropriate cartridge including EVD, HIV Viral Load, HIV Early Infant Diagnosis (EID), MTB and rifampicin resistant strains. The GeneXpert platform offers module sizes of 1 to 64 which facilitates placement of the technology across the entire health system tier. The GeneXpert can be used outside of central reference laboratories and is ideal when placed at district and even sub-district levels [8].

In July 2017, the HIV-1 viral load cartridge received the World Health Organization (WHO) pre-qualification [7]. The GeneXpert viral load assay is the most needed and market attractive diagnostic tool in resource-constrained settings as result of the minimal training and infrastructure requirement. Country-level validation studies have been conducted on the accuracy of the GeneXpert viral load assays in a variety of settings. All reported correlations between the Xpert HIV-1 viral load assay and gold-standard tests were very high and indicated a very high degree of agreement between Xpert viral load and reference standard viral load values [9]. Despite the recommendations put forward by the WHO consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection, viral load monitoring of ART is not routinely performed in Liberia [10]. The national ART guideline of Liberia also recommends viral load testing for monitoring of treatment failure for all patient categories.

EID was initiated in Liberia in 2013 at the national reference laboratory of Liberia using Roche reagent. However, it was interrupted by EVD outbreak as the molecular laboratory used for EID was dedicated to EVD testing. A decentralized EID testing is very critical in low volume and resource constrained setting. The placement of the GeneXpert machines also considered the EID testing. During 2015, a total of 71,891 pregnant women were tested for HIV and 2122 of them were HIV positive. Out of the 1684 infants born from HIV positive mothers, only 346 were EID tested in 2011 [6].

The GeneXpert MTB/RIF assay on the GeneXpert molecular system, which was endorsed by WHO in 2010, is the first GeneXpert TB assay released for clinical testing in resource-limited settings and the most scaled-up new TB technology [11]. Liberia adopted a 4 modules GeneXpert technology for testing MTB/RIF assay in 2013 with two machines installed at the TB annex hospital and the Ghanta TB/leprosy rehabilitation center. The machines were procured by the Global Fund office in Liberia and the installation and training were conducted by CHAI and the National Diagnostics Unit of Liberia. The GeneXpert technology was introduced as a diagnostic test in individuals suspected of Multi-Drug Resistant (MDR) TB. In 2015, the national TB program TB testing algorism was revised to include GeneXpert for smear-negative TB cases and for HIV associated TB. The Tuberculosis culture and drug susceptibility testing laboratory was not fully operational, and adoption of MTB/RIF assay was very timely to detect MDR suspected cases in Liberia.

According to the WHO report of 2017, the TB incidence in Liberia for the year 2016 was 308/100,000 population. The total number of patients diagnosed with TB was 7180 in 2016. The percentage pulmonary TB case is 70% of all the notified TB cases and only 60% of the pulmonary cases were bacteriologically confirmed. The MDR-TB burden is unknown in Liberia as there has been no national drug resistance survey conducted. According to the 2017 WHO TB report, the estimated MDR/RR-TB was 2.6% in new cases and 18% in previously treated cases respectively. TB diagnosis in Liberia has been mainly based on sputum smear microscopy [12]. The sensitivity and specificity of sputum microscopy are very low.

To improve the TB diagnosis in Liberia, the introduction of GeneXpert technologies with higher sensitivities and specificities is crucial. The pooled sensitivity of GeneXpert MTB/RIF assay is 88% and 68% when used as an initial diagnostic test replacing smear microscopy and as an add-on test following a negative smear-microscopy result respectively. The pooled specificity is 99% in both cases. When used to detect rifampicin resistance, GeneXpert MTB/RIF assay

© 2020 Global Journals

achieved a pooled sensitivity of 95% and a pooled specificity of 98% [13].

One of the lessons learned from the 2014 outbreak of EVD was the importance of rapid and accurate diagnosis of new and re-emerging diseases and the challenges around diagnostic testing to address these diseases. Throughout the 2014-2015 outbreak, EVD testing was limited to sophisticated biocontainment laboratory facilities, leading to challenges with specimen collection, data management and often a prolonged TAT to final results. In an outbreak setting, it was very difficult to manage the high number of specimens with this setup. Poor specimen referral network, lack of trained workforce and poor result reporting system were some of the challenges faced during the EVD outbreak. As a result of these challenges, the need for rapid test, point-of-care and near point of care EVD testing was evolved [14]. It was with this initiative that the GeneXpert EVD assay was developed for use in 2015.

WHO included Cepheid's GeneXpert Ebola test to its list of Ebola diagnostics with emergency use authorization on the 8th May 2015 [15]. Following the WHO acceptance, The GeneXpert Ebola test also received the United States Food and Drug Association (FDA) approval in March 2015 [16]. The Ministry of Health of Liberia approved the EVD assay in September 2015 with support from WHO, Foundation for Innovative New Diagnostics (FIND), Academic Consortium to Combating Ebola in Liberia (ACCEL), United States Centre for Disease Control and Prevention (CDC) and other stakeholders. The GeneXpert for EVD was used at the modular laboratory at Eternal Love Winning Africa (ELWA) in biosafety level three laboratories during the EVD outbreak [17].

When Liberia was declared free of EVD, WHO and ACCEL brought additional GeneXpert machines. The EVD GeneXpert machines have been in use for EVD surveillance testing with limited tests per day. The underutilization of these machines as well as the critical molecular testing challenges of HIV and TB program were the driving force for the integrated use of the GeneXpert platform in Liberia. Despite the effort of the NACP to initiate in-country capacity for HIV molecular testing, the dedication of the HIV molecular laboratory for EVD testing and the expiration of the reagents negatively impacted the HIV molecular testing service in Liberia. The TB program as well couldn't conduct enough tests using the four GeneXpert machines. EID was also considered in the integrated testing as it was interrupted during EVD outbreak. GeneXpert EID testing training was provided together with the HIV viral load GeneXpert training using whole blood but it was not included in our study as there was a prolonged delay in the procurement of HIV EID cartridges, heat block and Dried Blood Spot (DBS) bundles. When EID is fully integrated, DBS will be transported from the 335 prevention of mother to child transmission of HIV sites.

As a result of the above challenges, Liberia started integrated use of the GeneXpert technology in 2015. This was designed with aim of filling the testing gaps of TB and HIV molecular tests and sustain epidemic preparedness and response capabilities for EVD and related outbreak testing. From online search of databases, we realized that our study is the first of its type to evaluate the integrated use of GeneXpert for TB, HIV viral load and EVD. It can be used as a model for using a laboratory platform for multiple disease diagnosis as well as active surveillance for epidemic preparedness. WHO also recommends collaboration and integration as a priority for those countries with currently operational multi-disease testing devices [18]. The objective of this study was to evaluate the impact of integrated use of GeneXpert testing for TB, HIV viral load and EVD and provide recommendations and strategies for scaling up of the services based on the findings of the study.

II. Method

a) *Study setting*

Liberia is a West Africa country with a population of about 4 million. This study was conducted in Liberia from December 2015 to March 2017(15 Months) from secondary data collected from 10 GeneXpert sites. All the sites with the GeneXpert machines installed by the MOH different programs and partners were included in the evaluation study. Redemption hospital, TB annex hospital, Phebe hospital, Liberian government hospital (Buchanan), Liberian government hospital (Tubman burg), John Kennedy (JFK) hospital, Ghanta Leprosy Rehabilitation hospital, Jackson F. Doe hospital, Tellewoyan hospital and J.J Dossen hospital were the sites where the evaluation study was conducted.

b) *Study design*

This was a retrospective study from the GeneXpert testing secondary data combined with observational field feasibility evaluation study of the impact of the integrated testing. A previously collected and reported GeneXpert testing data was used to evaluate the integrated use of GeneXpert platform for TB, HIV viral load and EVD testing. All the laboratory GeneXpert secondary data available since the machines were installed and started testing from December 2015 to March 2017 were analyzed. Data on the GeneXpert EVD, HIV viral load and MTB/RIF testing results, infrastructural and logistical requirements were collected. The study was conducted in Liberia from December 2015 to March 2017(15 Months) using secondary data collected from 10 GeneXpert sites. All the sites with the GeneXpert machines installed by the MOH different programs and partners were included in the evaluation study. Redemption hospital, TB annex hospital, Phebe hospital, Liberian Government Hospital

© 2020 Global Journals

(LGH)Buchanan, LGH (Tubman burg), John F. Kennedy Memorial Hospital (JFK hospital), Ganta Leprosy Rehabilitation hospital, Jackson F. Doe hospital, Tellewoyan hospital and J.J Dossen hospital were the sites where the evaluation study was conducted.

III. Results

The following findings were obtained from the programmatic intervention secondary data and feasibility field observations.

a) Field observation of the GeneXpert sites operation and coordination

To compliment the retrospective secondary analysis of the GeneXpert testing data of the three diseases, field observation on the installation of the GeneXpert machines, specimen collection, training, quality assurance and result reporting was included.

All the GeneXpert machines were installed in facilities by taking into consideration testing volumes, availability of uninterrupted power supply, reliable sample transport system, appropriate result reporting mechanism, existing laboratory network and human resource capacity. For site selection of instrument placement in the country, the MOH Laboratory team and partners considered epidemiological data on EVD, HIV viral load and TB, current EVD isolation facilities, HIV and TB Clinics and testing centers. To determine the suitability of the sites, the GeneXpert pre-installation checklists were used. In addition to the above-mentioned factors, GeneXpert instrument placement also took into consideration clinical and testing sites with high burden priority for EVD surveillance, HIV viral load and TB and clinical and testing sites that currently provide isolation facilities and/or care and treatment services for EVD, HIV viral load and/or TB. This will help to maximize patient outcomes and cost effectiveness. Before the installation of the GeneXpert machines at the health facilities, pre-installation assessment was done. Following the assessment, laboratory refurbishments were done. Four instruments were procured by the Global Fund for the TB program and eleven were available for EVD testing only. Altogether, 15 machines were used for this integration at ten facilities. Because of the high surveillance testing burden, Tapita hospital, Phebe hospital and Redemption hospital have each 4, 2 and 2 GeneXpert machines respectively. All instruments were fully integrated; allowing expanded testing by all sites as required.

All the laboratory staff involved in the integrated testing were trained for MTB/ RIF, HIV 1 viral load and EVD testing. The training for MTB/RIF and HIV 1 viral load was provided by CHAI Liberia. The training for EVD testing was conducted by FIND in collaboration with WHO and ACCEL. The training was conducted for five days. It covered practical skills about the operation of the GeneXpert system, principle of the test, interpretation of the assay, quality assurance, data management and troubleshooting. Pre and post-tests were also administered prior and after the training respectively.

Specimen collection for the three-diseases testing followed a standard procedure that ensured the safety of the staff at the GeneXpert site, avoided cross-contamination and minimized workload at the GeneXpert site laboratory. Sputum was processed at the TB sputum processing area and it was added into the cartridge at the site of processing. The cartridge was taken to the GeneXpert laboratory for analysis. ART nurses and laboratory technicians drew whole blood for HIV 1 viral load testing into a standard 4ml Ethylenediamine Tetra-acetic Acid (EDTA) tube. This specimen was taken to the GeneXpert laboratory and centrifuged. From the centrifuged specimen, 1 ml plasma sample was transferred to the HIV 1 viral load cartridge. For the EVD testing, the EDTA whole blood EVD specimens were inactivated at the collection site isolation unit. The inactivated specimen was taken to the GeneXpert laboratory. Processing of this inactivated specimen in the laboratory is considered safe and wearing full personal equipment is not required. An aliquot of the inactivated blood sample was then pipetted into the GeneXpert EVD cartridge and tested as per Cepheid's manufacturer instruction.

As part of ensuring the quality assurance of the integrated testing, job aids and standard operating procedures were developed. Besides temperature monitoring check list of the GeneXpert room as well as the refrigerators were also developed. A supervision checklist, result recording registers and instrument maintenance logs were used to regularly monitor the GeneXpert sites for addressing instrument failure, troubleshooting support and monitoring of testing error rates. The GeneXpert cartridge is also provided with sample processing control and probe check internal controls which monitor the adequacy of the specimen and the presence of PCR inhibitors respectively.

b) GeneXpert assay secondary data results

A total of 706 HIV 1 viral load, 3695 MTB/RIF and 2309 EVD GeneXpert tests were conducted since the start of the integrated testing in December 2015 to March 2017 (Table 1). This makes the total number of tests conducted for the three diseases 6710. These tests were conducted at the 10 GeneXpert sites located in 8 of the 15 counties in Liberia (Fig 1). The Turn Around Time TAT for the three diseases was one day. Because of the screening and isolation units that were established in Phebe and Redemption hospitals during the EVD outbreak, the two hospitals effectively used the GeneXpert machines for TB, HIV viral load and EVD.

© 2020 Global Journals

Table 1: Integrated GeneXpert testing for HIV viral load, EVD and MTB/RIF

GeneXpert facility	Number of HIV 1 Viral load tests conducted	Number of MTB/RIF tests conducted	Number of EVD tests	Total number of tests conducted
Redemption Hospital	427	556	217	1200
TB Annex Hospital	45	2208	0	2253
Phebe Hospital	19	277	2091	2387
LGH, Buchanan	20	247	0	267
JFK Hospital	145	0	1	146
LGH, Tubman burg	0	25	0	25
Ghanta Rehab Hospital	0	169	0	169
Jackson F. Doe Hospital	22	82	0	110
Tellewoyan hospital	8	40	0	48
J.J.Dossen hospital	20	91	0	91
Total tests conducted	706	3695	2309	6710



Figure 1: Location of the GeneXpert machines for the integrated testing for HIV 1 viral load, MTB/RIF and EVD

1. HIV 1 GeneXpert viral load testing results

A total of 706 HIV1 viral load tests were conducted from December 2015 to March 2017. The viral load tests have been conducted in five major hospitals where the highest number of HIV patients were enrolled for care and treatment. The hospitals included JFK, Redemption, Jackson F.Doe, J.J Dossen and Liberian Government hospital (LGH) in Buchanan (Table 2).

© 2020 Global Journals

Table 2: HIV 1 viral load tests conducted using GeneXpert (December 2015 to March 2017)

GeneXpert testing facilities	HIV 1 Not detected	Invalid result	No result	Total HIV Viral load tests	Viral load <1000 copies/ml	Viral load >1000 copies/ml	% HIV Viral suppression
Redemption Hospital	88	4	5	427	137 (33%)	186 (67%)	33%
TB Annex Hospital	5	1	1	45	9 (21%)	25 (79%	21%
Phebe Hospital	2	0	0	19	6 (32%)	11 (68%)	32%
LGH, Buchanan	2	0	0	20	13 (80%)	4 (20%)	80%
JFK Hospital	20	0	0	145	31 (21%)	96 (79%)	21%
Jackson F. Doe Hospital	3	2	0	22	1(5%)	16 (95%)	5%

For patients who are on ART, their viral load will decline and become less than 1000 copies/ml if they are responding to ART. In this study, the viral load suppression rate among viral load tested individuals was very low (Fig 2). This may be attributed to treatment interruption or ARV drug resistance.

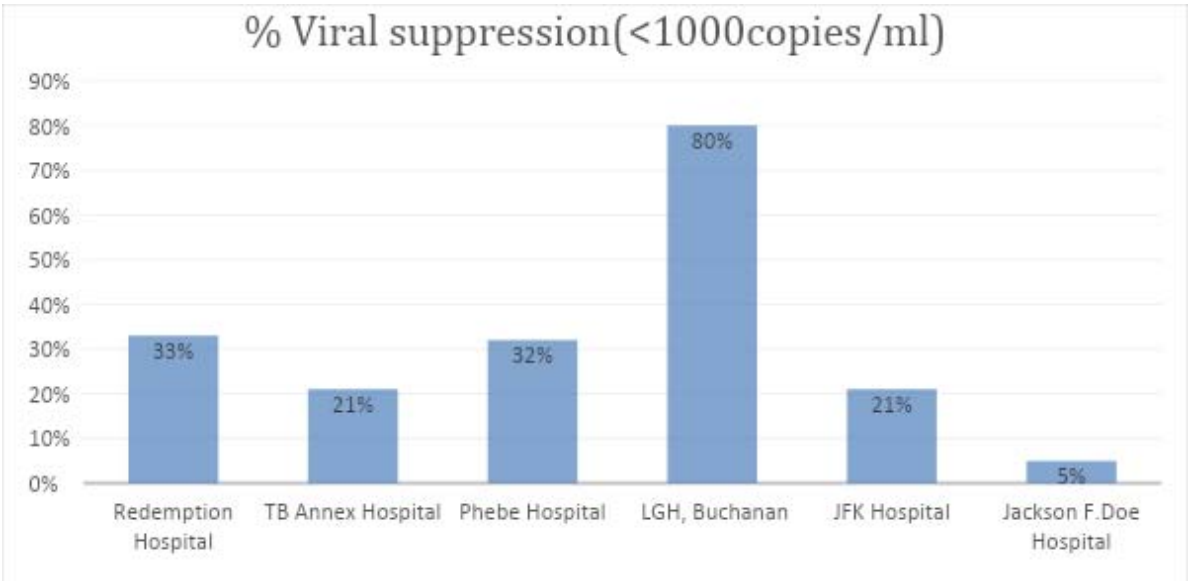


Figure 2: Percentage (%) of viral suppression

2. GeneXpert MTB/RIF testing results

Out of the ten sites with integrated testing, only the four site machines were procured for MTB/RIF by the NLTCP of Liberia. The number of MTB/RIF tests conducted from December 2015 to March 2017 is 3695. The number of RIF resistant MTB detected was high in TB Annex hospital and Redemption hospital. Phebe hospital showed the highest error rate followed by J.J Dosen hospital (Table 3).

© 2020 Global Journals

Table 3: MTB/RIF tests conducted on the integrated GeneXpert (December 2016 to March 2017)

Facility	MTB not detected	MTB detected/RIF not detected	MTB detected & Rif resistant	MTB detected/Rif indeterminate	Error	No result	Invalid	MTB/RIF Total tests
Redemption Hospital	357	155	15	7	5	13	4	556
TB Annex Hospital	689	326	72	16	9	0	12	1124
Phebe Hospital	191	65	2	0	15	2	2	227
LGH, Buchanan	109	106	3	3	3	22	1	247
JFK Hospital	0	0	0	0	0	0	0	0
LGH, Tubmanburg	14	6	0	0	5	0	0	25
Ganta Rehab Hospital	81	81	2	0	2	12	1	169
Jackson F. Doe Hospital	68	10	1	3	0	0	0	82
Telewoyan Hospital	0	0	0	0	0	0	0	0
J.J.Dosen Hospital	55	27	1	1	7	0	0	91

The Liberian government hospital in Buchanan and the Ganta rehabilitation center recorded 51% MTB positivity rate. The MTB/RIF test was not started in three hospitals. The positivity rate of MTB in Redemption hospital and TB Annex hospital were 33% and 36% respectively (Fig 3)

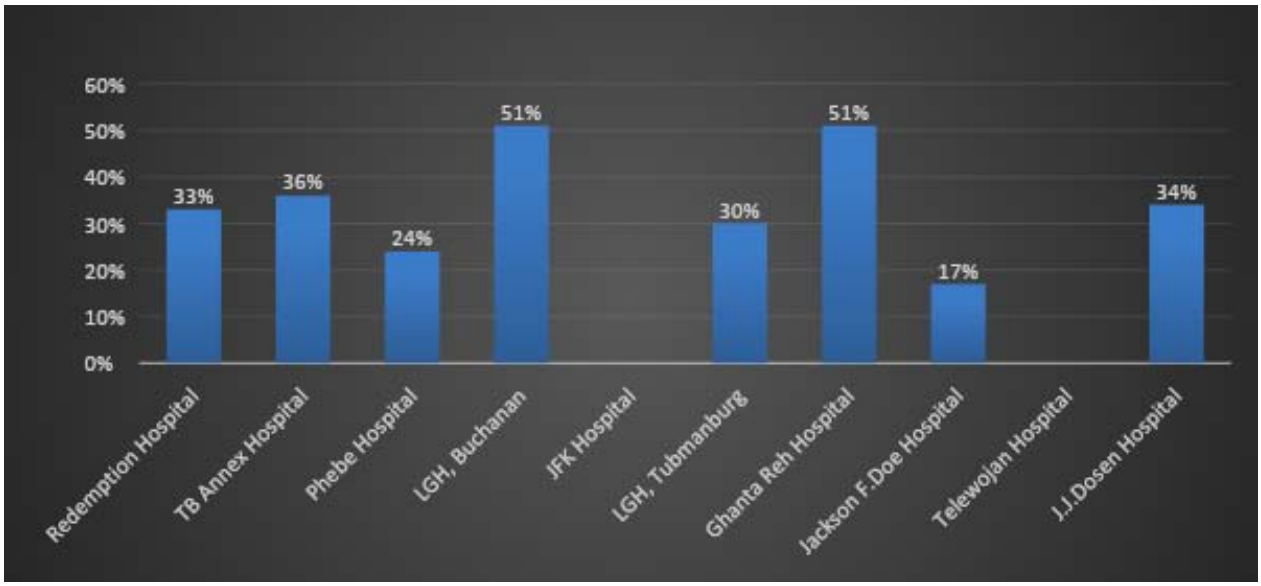


Figure 3: MTB positivity rate

The GeneXpert utilization rate was 38% for TB annex hospital. Although high number of TB suspected cases in the country and the high number of GeneXpert MTB/RIF cartridges available at the central stores, the GeneXpert machines were underutilized (Fig 4).

© 2020 Global Journals

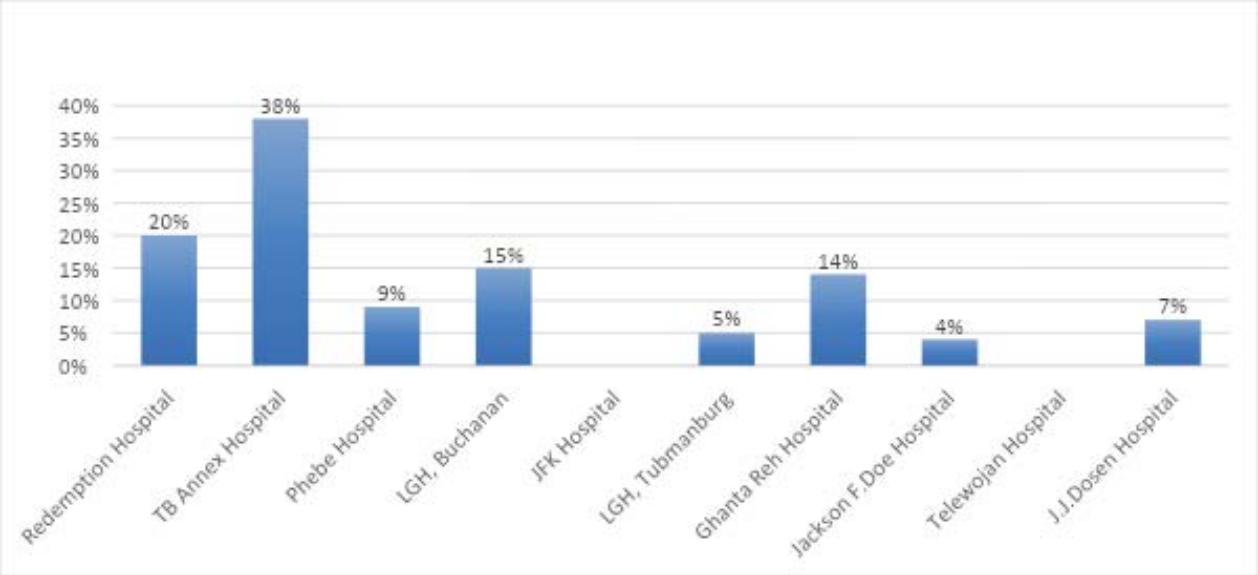


Figure 4: GeneXpert utilization rate for MTB/RIF

The above utilization rate was calculated with the assumption of 3 runs per day per machine and consideration of 20 working days per month. The highest utilization rate is for TB annex hospital which is only 38 % and the utilization rate in other facilities is as low as 4% and even in some facilities the MTB/RIF test was not started despite the fact that training was conducted and the cartridges were available in the facilities (Fig 4). The utilization rate for HIV viral load was by far lower than the utilization rate of MTB/RIF. The HIV viral load utilization rate of Redemption hospital, John F. Kennedy memorial hospital and TB Annex hospital was 15%, 7% and 2% respectively. The HIV viral load utilization rate for the other facilities was 1%.

IV. Discussion

The integrated testing of HIV1 Viral load, MTB/RIF and EVD using the GeneXpert platform has played a significant role in Liberia. Even though the first GeneXpert for MTB/RIF was installed in 2013, It was underutilized, and the MTB/RIF was interrupted. The reasons for the interruption were the expiration of the MTB/RIF cartridges at the end of 2013 and the EVD outbreak of 2014 in Liberia. As result of the integrated use of the GeneXpert machines, HIV viral load testing was re-initiated in December 2015 after one year of interruption by the EVD outbreak. The WHO Liberia office and ACCEL procured GeneXpert machines for EVD surveillance in 2015. It was few weeks after the EVD assay was prequalified by WHO.

Liberia diagnosed its first cases of Ebola in March 2014. Liberia was declared free of Ebola for the first time in May 2015. However, the country faced another outbreak in June 2015, was declared free of transmission on September 2015, experienced three more cases in November 2015 and was again declared Ebola-free on January 2016.The magnitude as well as the frequent re-emergence of the EVD outbreak indicated the need for building sustained diagnostics to support surveillance and emergency preparedness. This can be achieved by building the capacity of clinical laboratory in such a way to shift in addressing any occurrence or re-occurrence of epidemic as well as emerging diseases [17]. EVD machines were installed in some EVD isolation facilities in 2015 at the time when the outbreak was declining. No positive EVD result was detected from the GeneXpert machines and they have been in use for surveillance and readiness in case of future re-occurrence. The MOH of Liberia NLTCP, NACP and CHAI took this as a golden opportunity to use the EVD machines in an integrated way to test MTB/RIF and HIV viral load. The GeneXpert machines were procured by NLTCP have also been used for EVD and viral load testing. It was with this context that the three tests were integrated. 2309 EVD tests were conducted since the start of the integration in December 2015 to March 2017. Liberia was declared free of EVD during this interval and there was no positive EVD result. The integrated approach helped in active surveillance. In all the sites where the three-disease testing was integrated, the international partners working in laboratory strengthening trained enough local manpower who can run EVD molecular tests in their absence. Running the GeneXpert by Liberian nationals makes the preparedness and response to any future outbreak very sustainable. The integrated use of GeneXpert platform at EVD isolation facilities has strengthened preparedness and early response capabilities for future EVD outbreaks in Liberia [17].

According to the 2013 WHO integrated guidelines, HIV viral load testing for patients on ART is crucial for monitoring treatment response [19]. Despite this, Liberia has not successfully initiated a steady viral

© 2020 Global Journals

load testing until the Ebola outbreak in 2014. Viral load testing was interrupted during the EVD in 2014 due to the HIV molecular laboratory been converted to test EVD. With technical support from CHAI, reagent support from WHO, the Global Fund and the National Diagnostics Unit Viral load test was started successfully at Redemption hospital, TB annex hospital, JFK hospital, Phebe hospital, Jackson F. Doe and the Liberian Government hospital in Grand Basa on four- modules GeneXpert machines procured for MTB/RIF and EVD testing. The WHO guidelines for integrating HIV and TB services in Liberia was implemented before the EVD outbreak [20]. The NLTCP, in collaboration with the NACP of Liberia, has- integrated TB/HIV services in 24.9% of the 551 functional health facilities in the country [21]. The efforts to initiate viral load testing at the National Reference Laboratory and the St. Joseph Catholic hospital was interrupted by the EVD outbreak. After the first EVD outbreak, all the HIV 1 Viral load reagents and consumables were expired. The PCR machine at the Catholic hospital was damaged during the outbreak. The HIV viral load test was interrupted for more than one year. The HIV real time PCR machines, reagents and consumables requested by NACP to be procured by the Global Fund to restore the service were delayed for more than six months. The only opportunity to restore the HIV viral load testing in Liberia was to use the MTB/RIF and EVD GeneXpert machines in an integrated manner. The integrated approach helped the program to initiate viral load for treatment monitoring.

In 2014, the Joint United Nations Program on HIV/AIDS and partners launched the 90–90–90 targets which refer to the pathway by which 90% of all people living with HIV will know their HIV status, 90% of all people with diagnosed HIV infection will receive sustained antiretroviral therapy to achieve 90% viral suppression of those treated by 2020 [22].

The GeneXpert utilization rate of HIV viral load was low in almost all of the GeneXpert sites. The poor specimen referral linkage from the 55 sites which offer ART services in Liberia to the GeneXpert testing sites was one of the reasons. The low HIV viral load request by the ART clinicians was the other reason for the underutilization of the GeneXpert viral load test. A study conducted on multi-disease GeneXpert testing in Zimbabwe demonstrated higher utilization of the HIV viral load cartridges than our findings [8]. Our study findings also indicated a very low viral load suppression percentage that could have been resulted from poor adherence to treatment.

The integrated approach is also helpful for the NLTCP of Liberia as MTB/RIF tests were conducted at facilities where the GeneXpert was installed for EVD testing. The NLTCP procured excess cartridges for the four machines in the entire country. The expiration dates of the cartridges were very short and the integration helped the TB program to utilize the cartridges before they expired. A result of this integrated use, 3695 MTB/RIF tests were conducted during the study period. The utilization rate of MTB/RIF is very low in Liberia compared to the utilization rate of the 21-high burden countries [23].

The current algorism of the NLTCP of Liberia is using the GeneXpert MTB/RIF as an initial diagnostic test in individuals suspected of MDR i.e. treatment failure cases only. The NLTCP should revise the algorithm to increase the utilization of the GeneXpert MTB/RIF cartridges and consider replacing AFB microscopy with GeneXpert for case finding in high burden areas. Our study findings also indicated a high positivity rate for MTB/RIF compared to the positivity rate of the sputum microscopy at each facility. As far as resources are available, using the MTB/RIF assay for all patients except for follow up patients can increase the detection rate and is crucial in prevention of the spread of the disease as TB suspects are diagnosed earlier. The 2013 WHO guidelines on MTB/RIF GeneXpert included a conditional recommendation for GeneXpert MTB/RIF as the initial diagnostic test in all adults with suspected TB, acknowledging resource implications [11]. Besides, the NLTCP has to regularly sensitize clinicians to increase the utilization of GeneXpert and to strengthen sputum sample transportation system from peripheral to the GeneXpert sites.

During the implementation of the integrated use of the GeneXpert platform, the GeneXpert system has two basic internal controls which monitor the instrument, cartridge content and system contents for each test conducted. The sample adequacy control ensures that sufficient sample is added to the cartridge in a detectable amount. The sample processing control checks for PCR inhibition caused by cross contamination during specimen preparation in the laboratory [24]. Despite the above-mentioned controls provided with in the cartridges, there was no External Quality Assessment (EQA) proficiency panel provided from any source.

The testing turnaround time obtained from the GeneXpert site laboratories registers indicated patient test reporting time in hours compared to the conventional tests which provided results in days. The GeneXpert technology provides result in an average of 2 hours and allows for single specimen testing to overcome potential delays of batching compared to the conventional molecular testing.

An estimated 26,313 adults and 2,339 children were living with HIV in 2015 respectively. The population of Liberia is about 4,000,000. The prevalence of HIV in the general population aged 15-49 is 2.1%. Out of the estimated 26,313 adults and 2,339 children who were living with HIV in 2015, only 8000 were enrolled on ART [6]. Considering the burden of TB, a total of 7,119 patients in Liberia were diagnosed with TB in 2016 including 857 children. The estimated incidence and the

© 2020 Global Journals

estimated prevalence of TB in Liberia for the year 2016 was 300 per 100,000 population and 490 per 100,000 population respectively [13]. With the current national testing algorism of the NLTCP and NACP, strategic placement of one 4 module GeneXpert machines for the integrated tests of the three diseases in the six counties where GeneXpert testing machine is not installed is very helpful. Together with the existing 15 GeneXpert machines, the testing need of the three diseases can be met. These took into consideration the weak specimen referral system, the bad road condition and the lack of infrastructure in the health facilities in Liberia. Any national algorism changes in line with WHO recommendation can be accommodated by these strategic placements of the GeneXpert machines.

Challenges of the integration

- The procurement of the GeneXpert supplies and cartridges was not well coordinated. Proper forecasting and quantification of cartridges, calibrators and other accessors must be conducted on regular basis.
- The short expiration date of EVD and HIV viral load cartridges resulted in shortage of cartridges and interruption of testing service.
- HIV 2 is known to be prevalent in West African region. GeneXpert assay for detection of HIV2 has not been developed yet.
- The was no strong specimen referral system for HIV viral load and MTB/RIF.
- Regular calibration of the machines was one of the challenges as there was no in-country authorized service provider.
- Failure of air conditioners in some facilities contributed to high error rates.
- There was underutilization of the GeneXpert plat form in some sites. This was due the weak specimen referral system and the limited number of isolation units to screen and take EVD specimen.
- There was lack of coordination of the three programs as there was no focal person designated to coordinate the integration at facility and at national level.
- Data connectivity has not been implemented yet.

V. Recommendations

Integrated use of the GeneXpert technology will improve patient outcomes if it is implemented within the context of strong and well-coordinated programs and systems of the three diseases. The following recommendations are provided based on the findings of the study.

- Guidelines, policy and strategy for scaling up the GeneXpert technology to support integrated diagnostics for EVD, HIV and TB should be developed. This helps to coordinate activities and to designate the role and responsibilities. This should include decentralized testing throughout the country and building local capacity to address epidemics.
- Strong collaboration should be developed between the NLTCP of Liberia, the NACP of Liberia and the National Public Health Institute of Liberia in resource mobilization and coordination of the integrated testing.
- Training should be provided to clinicians to use the proper national algorism for each disease. This will ensure effective utilization of the cartridges, minimize wastes and expiry and maximize/improve patient outcome.
- Proper monitoring and evaluation of the integrated testing services regularly using appropriate indicators should be considered.
- The role and responsibility of implementing partners for each disease testing should be defined and coordinated by MOH to ensure sustainability in the absence of partners.
- Master trainers and trainers of trainees should be identified, trained and availed.
- Master-list of instruments should be compiled and updated regularly to keep track of all instruments in-country, including serial numbers, installation dates, supporting partners, calibration dates, maintenance and trained users.
- Training modules should be defined and approved by MOH, including pre and post-training assessment of competencies as well as mentorship with monitoring and evaluation plan.
- Establishment hotline system for remote support and implementing connectivity tools like the GxAlert should be considered.
- Regular quantification and forecasting of cartridges based on history of consumption and/or epidemiological data should be conducted.
- EQA panels were not available for proficiency testing for GeneXpert EVD, Viral load and MTB/RIF. The development of low-cost panels should be considered.
- Enhanced adherence counselling should be provided to patients with viral load higher than 1000copies/ml.

VI. Conclusions

Integrated use of the GeneXpert platform significantly improved the testing services for HIV viral load and MTB/RIF testing. It increased access to viral load testing for monitoring treatment failure. It also helped to utilize the EVD GeneXpert machines and sustain the epidemic preparedness and response. Despite the integrated approach, the utilization rate of the GeneXpert machines in the country is very low. There is lack of coordination of logistics, weak specimen referral system, expiry and stockout problems and lack

© 2020 Global Journals

of connectivity. The high cost of the cartridges to support continuous testing is a challenge. The three disease programs and partners should coordinate and effectively implement the integrated use and scale up the services. Each step of the integration should be monitored regularly. This is crucial in sustaining the EVD surveillance testing capacity in Liberia and help the TB and HIV programs in meeting the 90-90-90 targets for both diseases by 2030. The significant reduction in turnaround time is a critical advantage in the GeneXpert usage.

Declaration

Ethics approval and consent to participate

Permission to use the existing data from programs and GeneXpert sites database was provided by the NACP of Liberia, the National Leprosy and Tuberculosis program (NLTCP) of Liberia as well as the health facilities where the GeneXpert machines are used for multiple testing (S1 Text).

Consent for publication

Not Applicable

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on request.

Competing interests

The authors declare that they have no conflict of interest which may have inappropriately influenced them in writing this article.

Funding

This work was not funded by any institution or organization.

Authors' contributions

Conceptualization: Kassaye Tekie Desta

Data curation: Kassaye Tekie Desta, Jerry G Daboi, Dedeh B. Kessely and Julia Toomey Garbo & Candace B. Eastman

Formal analysis: Kassaye Tekie Desta and John B. Dogba

Methodology: Kassaye Tekie Desta

Writing – original draft: Kassaye Tekie Desta.

Writing – review & editing: John B. Dogba, Julia Toomey Garbo, Dedeh B. Kessely, Candace B. Eastman and Jerry G Daboi

Acknowledgments

The researchers would like to express their deepest gratitude to the National Leprosy and Tuberculosis Control Program of Liberia, National AIDS Control program of Liberia and The National Reference Laboratory of Liberia for allowing the use the Laboratory data for the research. We also thank all the laboratory staff and clinicians at the GeneXpert testing facilities.

References Références Referencias

1. Ministry of Health of Liberia. Investment Plan for Building a Resilient Health System in Liberia; In response to the Ebola Virus Disease Outbreak of 2014 – 2015. 2015; 1:72 https://au.int/sites/default/files/newsevents/workingdocuments/27027-wd-liberia-_investment_plan_for_building_a_resilient_health_system.pdf
2. Kennedy SB, Dogba JB, Wasunna CL, Sahr P, Eastman CB, Bolay FK, et al. Pre-Ebola virus disease laboratory system and related challenges in Liberia. African Journal of Laboratory Medicine. 2016; 5:1-5.
3. Kennedy SB, Wasunna CL, Dogba JB, Sahr P, Eastman CB, Bolay FK, et al. The laboratory health system and its response to the Ebola virus disease outbreak in Liberia. African Journal of Laboratory Medicine. 2016; 6:1-5.
4. Roberts T, Cohn J, Bonner K and Hargreaves. Scale-up of routine viral load testing in resource-poor settings: current and future implementation challenges. Clin Infect Dis 2016; 62: 1043–48.
5. Madlen N, John R, Ramya K, Sophie H, Madhukar P and Shrikala B. Use of the GeneXpert tuberculosis system for HIV viral load testing in India. The Lancet, 2017:5(8). 754-755.
6. Liberia HIV&AIDS response progress 2015 report. National AIDS and STI Control Program of Liberia.2016; 22-42. http://www.unaids.org/en/file/110934/download?token=5fJHV6Hq
7. World Health Organization. WHO prequalification of in vitro diagnostics public report. 2017; World Health Organization, Geneva, Switzerland. http://apps.who.int/iris/bitstream/handle/10665/259238/WHO-EMP-RHT-PQT-2017.09-eng.pdf
8. Ndlovu Z, Fajardo E, Mbofana E, Maparo T, Garone D, Metcalf C, et al. (2018) Multi- disease testing for HIV and TB using the GeneXpert platform: A feasibility study in rural Zimbabwe. PLoS ONE 13(3): e0193577. https://doi.org/10.1371/journal.pone.0193577
9. Nash M, Huddart S, Badar S, Baliga S, Saravu K, Pai M. 2018. Performance of the Xpert HIV-1 viral load assay: a systematic review and meta-analysis. J Clin Microbiol 56: e01673-17. https://doi.org/10.1128/JCM.01673-17.
10. World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Recommendations for a public health approach. Geneva, Switzerland, 2013. http://apps.who.int/iris/bitstream/10665/85321/1/9789241505727_.pdf

© 2020 Global Journals

11. WHO. Automated real-time nucleic acid amplification technology for rapid and simultaneous detection of tuberculosis and rifampicin resistance: Xpert MTB/RIF system for the diagnosis of pulmonary and extrapulmonary tuberculosis in adults and children. Policy Update. 2013. http://apps.who.int/iris/bitstream/handle/10665/112472/9789241506335_eng.pdf
12. World Health Organization (WHO). Global Tuberculosis report 2016. World Health Organization, Geneva: 2017; WHO press. http://www.who.int/tb/publications/global_report/gtbr2017_main_text.pdf
13. World Health Organization. Updated: Xpert MTB/RIF implementation manual technical and operational 'how-to': practical considerations. Geneva, Switzerland. 2014. http://www.who.int/tb/publications/
14. Broadhurst MJ, Brooks TJ and Pollock NR. Diagnosis of Ebola Virus Disease: Past, Present, and Future. Clinical microbiology reviews. 2016; 29(4):773-793.
15. World Health Organization. Emergency use assessment and listing for Ebola virus disease IVDs, public report, product: Xpert Ebola assay. 2015. http://www.who.int/diagnostics_laboratory/160324_final_public_report_ea_0023_021_00.pdf
16. US Food and Drug Administration. Emergency use authorization, Xpert Ebola assay; letter of authorization. U.S. food and Drug Administration, Rockville,MD. 2015. http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm - ebola. 2015.
17. Raftery P, Condell O, Wasunna C, Kpaka J, Zwizwai R, Nuha M, et al. (2018) Establishing Ebola Virus Disease (EVD) diagnostics using GeneXpert technology at a mobile laboratory in Liberia: Impact on outbreak response, case management and laboratory systems strengthening. PLoS Negl Trop Dis 12(1): https://doi.org/10.1371/journal.pntd.0006135
18. WHO 2017. Considerations for adoption and use of multi-disease testing devices in integrated laboratory networks. http://www.who.int/tb/publications/2017/considerations_multidisease_testing_devices_2017/en/
19. World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Recommendations for a public health approach. Geneva, Switzerland 2013. http://apps.who.int/iris/bitstream/eng.pdf
20. WHO policy on collaborative TB/HIV activities Guidelines for national programmes and other stakeholders, 2012: 1-36. http://www.who.int/tb/pub-lications/2012/tb_hiv_policy_9789241503006/en/
21. Liberia. Ministry of Health and Social Welfare 2012 annual report. 2013; 33-36 https://www.medbox.org/lr-studies-reports/liberia-ministry-of-health-and-social-welfare-2012-annual-report/ preview
22. UNAIDS. Ending AIDS. Progress towards the 90-90-90 targets. 2017. http://www.unaids.org/en/resources/documents/2017/20170720_Global_AIDS_update_2017
23. Cazabon D, Pande T, Kik S et al. Market penetration of Xpert MTB/RIF in high tuberculosis burden countries: A trend analysis from 2014 – 2016.Gates Open Research. 2018, 2:35. (doi: 10.12688/gatesopenres.12842.1)
24. Semper AE, Broadhurst MJ, Richards J, Foster GM, Simpson AJH, Logue CH, et al. Performance of the GeneXpert Ebola Assay for Diagnosis of Ebola Virus Disease in Sierra Leone: A Field Evaluation Study. PLOS Medicine. 2016; 13(3). e1001980. doi:10.1371/journal.pmed.1001980 https://dash.harvard.edu/bitstream/handle/1/26860324/4811569.pdf

© 2020 Global Journals