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Resilient TB Diagnostics During a Pandemic: Xpert MTB/RIF versus Culture in a Resource-Limited Setting in Taung, South Africa

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INTRODUCTION
Tuberculosis (TB) is a major global health problem infecting millions of people every year. The COVID-19 pandemic has affected health care systems and greatly affected socioeconomic parameters with global focus on fighting this unpredictable pandemic *Mycobacterium tuberculosis* diagnosis was hugely affected. The study presented here investigated the performance of TB GeneXpert and TB culture results during this period to evaluate the effects of COVID-19 on the diagnosis of tuberculosis.

METHODOLOGY
This retrospective study performed using existing data was extracted and evaluated from the NHLS Laboratory Information System (LIS) for samples analysed using Cepheid TB GeneXpert instrument and MGIT for TB culture results during this period. Two consecutive expectorated morning sputum were collected on the same day from the enrolled patients. The minimum acceptable volume of sputum was 2ml in each collection cube. One of the sputum specimens was tested by Xpert MTB /RIF assay in Taung laboratory. The other pair of sputum specimen was tested for TB culture, the sputum specimen were placed on ice packs in a cool box and transported to NHLS Universitas Academic laboratory within 3 days of collection and analyzed.

RESULTS AND DISCUSSION
For TB culture a total of 2520 samples were received for the period of study, 808 samples were received in 2020 and 18% tested positive, 82 % tested negative. In 2021 a decrease of 0.9% was noted on the number of samples received, on diagnosis of TB 16% tested positive which is a 2% increase from 2020 and 84% tested negative which is a 2% increase from 2020. In 2020 the number of samples that tested positive decreased with 4% whereas the number of samples that tested negative for TB culture increased by 4%. Genexpert results for the period of study were a total of 2781 samples were received for analysis, in 2020 88% tested negative and 12% tested positive on the 12% that tested positive 71% was rifampicin sensitive, 21% was trace and 8% was rifampicin resistant. In 2021 a decrease of 6% was noted on the number of samples received for analysis, 84% were negative and 16% were positive of which 71% was rifampicin sensitive, 24% was trace and 5% was rifampicin resistant. A total number 1128 samples were received in 2022 85 % tested negative and 16% was positive of which 85% Was rifampicin sensitive, 16% was trace and 6% was rifampicin resistant.

CONCLUSION
The GeneXpert results performed in NHLS Taung correlate with TB culture results performed in NHLS Univerisitas for the diagnosis of pulmonary tuberculosis during COVID-19 pandemic.

Background
The COVID-19 pandemic is a global outbreak caused by Corona Virus an infectious disease caused by severe acute respiratory syndrome Corona virus 2 (SARS-coV-2) virus (World Health Organization (WHO) 2020). The SARS- CoV2 outbreak has affected health systems and greatly affected socioeconomic parameter (Kant and Tyagi 2021). With global focus on fighting this unpredictable pandemic caused by this new virus the biggest chronic infection killer Mycobacterium tuberculosis was hugely affected from this shift in attention (Kant and Tyagi (2021). An estimated 10.6 million people fell ill with tuberculosis (TB) in 2021an increase of 4.5%from 2020, and 1.6 million people died from TB (including 187 000 among HIV positive people), according to World Health Organizations (WHO) 2022 Global TB report.

Tuberculosis causes immense suffering worldwide especially in underdeveloped and developing countries (Steingart et al., 2015). If diagnosed early most people with TB can be cured if the disease is diagnosed and properly treated, one of the challenges in treating TB is that the bacteria develop resistance to the antibiotics (Steingart et al., 2015). Detecting TB and TB drug resistance quickly is critical for improving health, reducing mortality and minimizing the spread of TB in communities (Steingart et al., 2015).

GeneXpert (Xpert) Mycobacterium tuberculosis (MTB) is a new test that quickly detects the TB and rifampacin resistance at the same time, Mycobacterium culture is generally considered the best available reference standard for diagnosing TB and is the first step in detecting drug resistance, however culture is a relatively complex and slow procedure (Steingart et al., 2015).

The Xpert MTB /Rif is considered as a great advance over conventional smear and culture in the diagnosis of TB and MDR –TB by simultaneously detecting *M. tuberculosis* and rifampacin resistance bacilli (Geleta et al., 2015).

Problem statement

The purpose of this study is to evaluate the performance of xpert assay compared to conventional sputum smear and culture methods for the diagnosis of pulmonary tuberculosis in Taung laboratory during the COVID -19 pandemic as both TB and COVID-19 are infectious diseases that primarily involve the lungs, as far as clinical manifestations are concerned symptoms such as cough, fever, weakness, malaise and hemoptysis can be seen in both conditions, similar presentations can pose a diagnostic challenge (Tadolini et al., 2020). In order to contain SARS –Cov2 , lockdowns were imposed by countries worldwide , people were forced to stay indoors, resulting in a number of effects the symptom similarity between TB and COVID-19 probably resulted in a delay in suspecting TB as most people could have attributed similar symptoms to COVID-19 and preferred to wait it out (Kant and Tyagi., 2021)

Aim

This study aims to assess the correlation between Xpert MTB/Rif results and TB culture results during COVID-19 pandemic in NHLS Taung Laboratory.

Objectives

- Analyze the Xpert MTB /Rif and TB Culture results collected between 2020 and 2022.
- Compare the results of the Genexpert to TB culture for the period 2020-2022.
- Explore the underlying factors that influence the results.
- Assess the effects of COVID-19 Pandemic on the diagnosis of TB.

Literature review

Tuberculosis (TB) which is caused by Mycobacterium tuberculosis (MTB) complex is a major global health problem infecting millions of people every year with a particular heavier burden in the developing world (Geleta et al., 2015). This has recently been shown that South Africa is one of the 30 high burden tuberculosis countries contributing 87% estimated incident TB cases worldwide, on its own South Africa accounts for 3% of cases globally (Van der Walt., 2018).

Prior to COVID-19, tuberculosis was the leading infectious disease killer globally, in 2019 alone, there were approximately 10.0 million new TB infections and 1.5 million TB deaths globally, over the past decades efforts to curb the TB epidemic have gradually intensified (Zimmer et al., 2022). By the end of 2019, 78 countries were on track to achieve the 2020 End TB goals of reducing TB incidence by 80% and TB mortality by 90% compared with 2015 rates, however the COVID 19 pandemic and lockdown measures have created a massive global setback towards achieving these goals as TB services were disrupted at every level of the health care system (Zimmer et al., 2022).

Diagnosing and detecting active TB and multi-drug resistant (MDR) strains are essential to interrupt transmission of the disease in the community, isolation of the bacteria using Conventional solid culture and drug susceptibility testing is the gold standard, liquid culture and molecular line probe assays were also introduced for rapid detection of MDR-TB, however these methods require long turnaround time, expensive laboratory infrastructure, extensive bio-safety precaution and specialized laboratory personnel seldom found in primary health care facilities in developing countries (Geleta et al., 2015)

Xpert MTB/RIF

Xpert MTB/RIF is a diagnostic test used for the rapid detection of tuberculosis (TB) and its resistance to rifampicin, a common antibiotic used in TB treatment. It is a molecular test that utilizes the polymerase chain reaction (PCR) technique to amplify and detect specific DNA sequences unique to Mycobacterium tuberculosis, the bacterium causing TB (WHO:2017)

The Xpert MTB/RIF test is known for its high sensitivity and specificity in diagnosing TB, even in individuals co-infected with HIV, the test requires sputum samples or other respiratory specimens from patients suspected of having TB

(Chakravorty et al .2017). These samples are placed into a cartridge containing reagents necessary for PCR amplification and detection, once the sample is loaded into the cartridge, it is inserted into the Xpert machine, which automates the entire testing process. Within approximately two hours, the machine provides results indicating whether M. tuberculosis DNA was detected and if any resistance to rifampicin is present (Bodmer and Strohle., 2012).

This rapid turnaround time allows healthcare providers to initiate appropriate treatment promptly, reducing transmission of TB within communities and improving patient outcomes, additionally identifying rifampicin resistance helps guide appropriate drug choices for effective treatment (Gidado et al., 2019). Xpert MTB/RIF has revolutionized TB diagnosis by providing reliable results quickly and enabling early initiation of appropriate therapy (Gidado et al., 2019)

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Fig 1. Cepheid GeneXpert instrument

2.2.2 Advantages and disadvantages of GeneXpert

Advantages: (Piatek AS et al., 2008)

- High sensitivity and specificity.
- Fast turnaround time results available within 2 hours on number 1 refer fig 1 and fig 2.
- Simultaneous detection of tuberculosis and rifampin resistance on number 1.
- Biological safety compared to traditional culture-based methods Minimal concerns.
- Minimal technical expertise required for implementation.

Disadvantages: (Piatek AS et al ,2008)

- Higher cost per test compared to traditional culture-based methods.
- shelf life of the catridge is limited to 18 months. 2.
- Requires stable power supply and annual calibration. 2.
- Indeterminate results may occur due to lack of genetic material or testing errors.

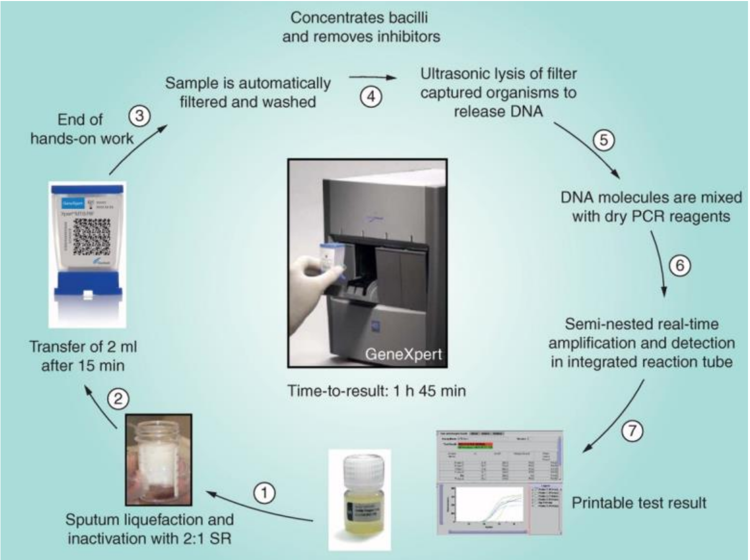

Fig 2: GeneXpert procedure

Interpretation of results

Interpretation of GeneXpert MTB/RIF results depends on whether resistance to Mycobacterium tuberculosis (MTBC) and/or rifampin is detected. If MTBC is detected, it means that tuberculosis infection is likely, and further testing should be done to ensure that. MTBC is not detected it means that tuberculosis infection is unlikely, but other tests may be needed, an indeterminate result means there was an error in the test or there was not enough genetic material in the sample to get a reliable result (Acharya., 2022)

Mycobacterium culture

Mycobacterial culture is a laboratory technique used to grow and identify bacteria belonging to the Mycobacterium genus clinical samples can be used to culture mycobacteria (sputum 102 bacilli/ml-1) culture remains the gold standard for tuberculosis diagnosis (Kenaope et al., 2020). Mycobacterium tuberculosis is typically cultured on solid media where it is further identified and tested for drug susceptibility, thus providing guidance to physicians for effective antimicrobial treatment (Kenaope et al., 2020). Liquid culture systems such as the BACTEC MGIT 960 allow you to detect Mycobacterium tuberculosis in just a few days. The BACTEC MGIT 960 automated culture system monitors oxygen-quenched fluorescence and a signal is detected as soon as mycobacteria grow in the tube (Hasan et al). It was found that MGIT 960 is more effective than his L-J solid medium in rapid detection of mycobacteria and early diagnosis of tuberculosis (Hasan et al., 2013). The VersaTREK system is sensitive to pressure fluctuations. Therefore, we detect the growth of inoculated samples by measuring pressure changes in the broth medium (Espasa et al., 2012). The MB/BacT Alert 3D system uses a colorimetric carbon dioxide sensor to detect M. tuberculosis (Piersimoni et al., 2001). Considering the slow growth of Mycobacterium tuberculosis complex (MTBC), most MTCB-positive cultures develop after at least 1 week, whereas MTCB-negative cultures develop after 8 weeks (Lee et al., 2003).

Advantages and disadvantages of Mycobacterial culture

Advantages – (Pfyffer GE, Brown-BA, Wallace RJ Jr, 2007)

- High sensitivity and specificity
- Can be used to identify the species of mycobacteria and perform drug susceptibility testing (DST).
- Can be used to monitor patient response to treatment.

Disadvantages (Pfyffer GE, Brown-BA, Wallace RJ Jr, 2007)

- Slow turnaround time, with results available in weeks rather than hours .
- Requires a biosafety level 3 laboratory and trained personnel to handle infectious samples.
- Requires a large volume of sputum sample (at least 5 mL) for optimal sensitivity.
- Contamination can occur during the culture process, leading to false-positive results.
- Cannot differentiate between active and latent TB infection.

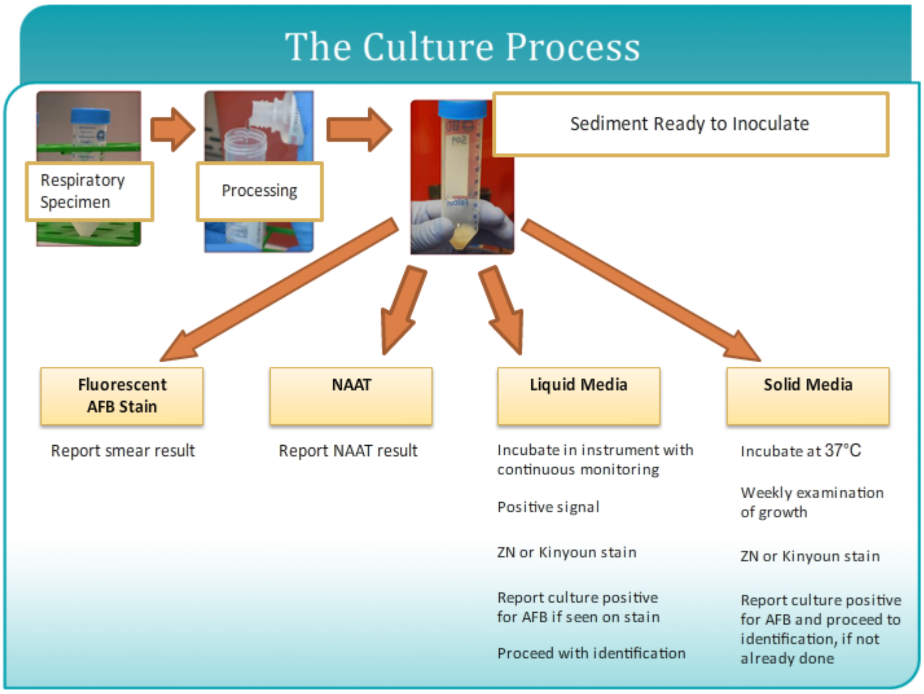

Fig 3: The culture process

Reporting of results

It is important to the clinician to be provided with an interim report as soon as the culture is positive and acid fast bacilli are observed, this preliminary information should be reported with an indication that more information will follow (Baoyu et al., 2022). The preliminary report should be updated when an identification is available. At a minimum, the report should indicate if a MTBC or a NTM has been identified. There is currently no clear guidance on when to issue a negative report. Typically, a final negative culture will be reported at six to eight weeks (Baoyu et al., 2022).

Correlation between GeneXpert and TB culture

A study conducted by Uppe et al., (2020) compared the diagnostic yield of GeneXpert MTB/RIF and TB MGIT culture in extra pulmonary –TB cases, the study found that GeneXpert MTB/RIF had a higher sensitivity (39.33%) than TB MGIT culture (28%). Another study by Piatek AS et al 2018 compared the diagnostic accuracy of GeneXpert and mycobacterial culture in detecting TB and drug resistance in gold miners in south Africa the study found that GeneXpert had a higher sensitivity (98. %) than Mycobacterial culture (89%).

Effects of COVID-19 pandemic on TB diagnostic services

The COVID-19 pandemic has had a significant impact on tuberculosis (TB) diagnostic services globally (Jacjues et al., 2020). The pandemic has disrupted TB care and service delivery, causing delays in TB diagnoses and treatment (Ayinalem et al., 2022) A study conducted in South Africa evaluated the influence of the COVID-19 pandemic on TB diagnostics at primary health clinics (PHCs) in the eThekwini district. The study found that the SARS-CoV-2 outbreak significantly affected both tuberculosis indicators, with a 45% reduction in diagnostic investigations and a 40% reduction in confirmed cases of TB during the lockdown period (Jacques et al., 2020). The COVID-19 pandemic has also strained public health services, including TB prevention and control services. Widespread disruptions to healthcare during the COVID-19 pandemic may have delayed TB diagnoses (Keertan et al., 2022). Modelling work suggests that if the COVID-19 pandemic led to a global reduction of 25% in expected TB detection for 3 months, then we could expect a 13% increase in TB deaths, bringing us back to the levels of TB mortality that we had 5 years ago (Keertan et al.,2022).

Material and Methods

Study design

This was a cross sectional observation and quantitative study.

Study area and period

The study used retrospective data collected extracted from Taung NHLS which serves Taung District Hospital in North-West province of South Africa.

Ethical consideration

The study does require approval from Health Sciences Research Ethics Committee because the samples were collected from humans, permission was requested from NHLS Academic Affairs and Research office manager and laboratory manager.

Materials and methods

This was retrospective study using existing data TB results that were processed between 2020 and 2022 during COVID-19 pandemic. Data was retrieved from the NHLS Laboratory Information system (LIS) TrakCare under Module-Reporting- Monthly statistics then results listing. Data was printed individually according to test e.g GeneXpert, TB auramine and TB culture. The LIS takes days to compile the report depending on the quantity of results in that month the bigger the data the longer it takes to produce the report in PDF format.

Specimen Collection

Data extracted was collected as follows, two consecutive expectorated morning sputum were collected on the same day from the enrolled patients. The minimum acceptable volume of sputum was 2ml in each collection cube. One of the sputum specimens was tested by Xpert MTB /RIF assay in Taung laboratory. The other pair of sputum specimen was tested for TB auramine microscopic examination and cultured for isolation of TB bacilli by conventional methods. Specimens for TB culture were stored at appropriate temperature after collection. The sputum specimen were placed on ice packs in a cool box and transported to NHLS Universitas Academic laboratory within 3 days of collection and analyzed.

Xpert MTB/RIF assay

In generating this retrospective data, sputum samples were treated with sample reagent (SR) containing NaOH and isopropanol. The SR is added using a 2 to 1 ratio of the sputum sample, homogenized and incubated for 15 min at room temperature. The treated sample was transferred into the cartridge, the cartridge was loaded into the GeneXpert instrument and an automatic process completes the remaining assay steps.

Mycobacterial culture

Digestion for decontamination of sputum was performed by N-acytyl L-Cysteine (NALC) sodium Hydroxide method. Inoculation was done on slide and stained using auramine o stain. Both Lowenstein-Jensen (LJ) and MGIIT 960 culture media were inoculated for 6 weeks on MGIT and 8 weeks on LJ culture. a culture was considered positive if MTB growth was confirmed on either LJ and MGIT media a culture was considered negative if no growth was confirmed on both LJ and MGIT media or if one culture result was negative and the other contaminated if both LJ and MGIT demonstrated contamination.

Results and discussion

The study assessed the correlation between Xpert MTB/Rif results and TB culture results during COVID-19 pandemic as shown in table 1. For GeneXpert a total number of samples received was 2781 from 2020-2022.

Table 1. Comparison of results from GeneXpert and culture

	2020		2021		2022	
Samples received	GeneXpert	TB culture	GeneXpert	TB culture	GeneXpert	TB culture
Average	853	808	800	780	1128	828
positive	12%	18%	16%	16%	15%	14%
Negative	88%	82%	84%	84%	85%	86%

From 2020 to 2021 a decrease of 6% on number of GeneXpert sample received was noted and it increased by 32% in 2022. For TB culture a total of 2520 samples were received, from 2020 to 2021 a decrease of 14% was noted and a decrease of 9% from 2020 to 2022. Overallmore GeneXpert samples were received during the period of study with 9% difference to TB culture.

Figure 4 shows the TB culture results for the period of study 2020-2022, 808 samples were received in 2020 and 18% tested positive, 82 % tested negative. In 2021 a decrease of 0.9% was noted on the number of samples received, on diagnosis of TB 16% tested positive which is a 2% increase from 2020 and 84% tested negative which is a 2% increase from 2020.

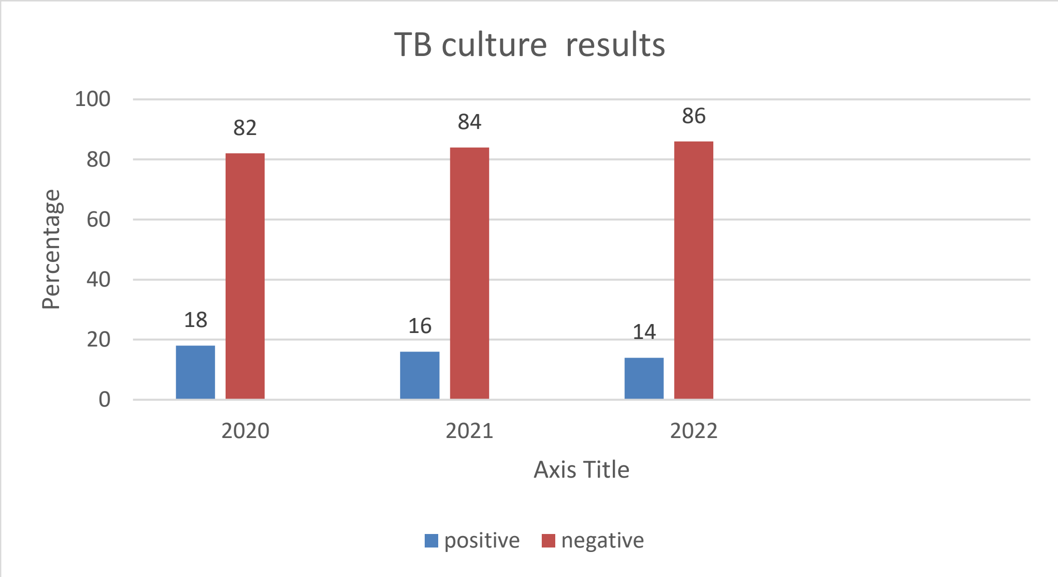

Figure 4: TB culture results.

In 2020 the number of samples received for testing decreased by 3% also the number of samples that tested positive decreased with 4% whereas the number of samples that tested negative for TB culture increased by 4%. GeneXpert results for the period of study are represented by table 1, a total of 2781 samples were received for analysis, in 2020 88% tested negative and 12% tested positive on the 12% that tested positive 71% was rifampicin sensitive, 21% was trace and 8% was rifampicin resistant as shown in fig 5.

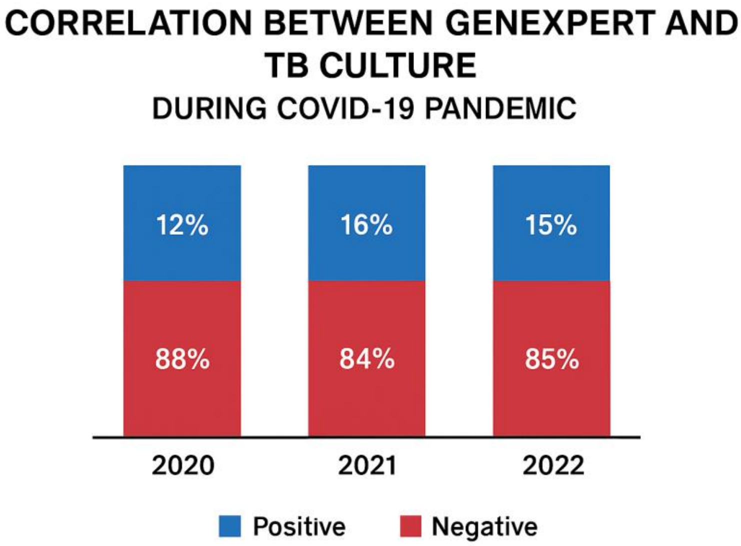

Figure 5: GeneXpert results

In 2021 a decrease of 6% was noted on the number of samples received for analysis, 84% were negative and 16% were positive of which 71% was rifampicin sensitive, 24% was trace and 5% was rifampicin resistant. A total number 1128 samples were received in 2022 85 % tested negative and 16% was positive of which 85% Was rifampicin sensitive, 16% was trace and 6% was rifampicin resistant.

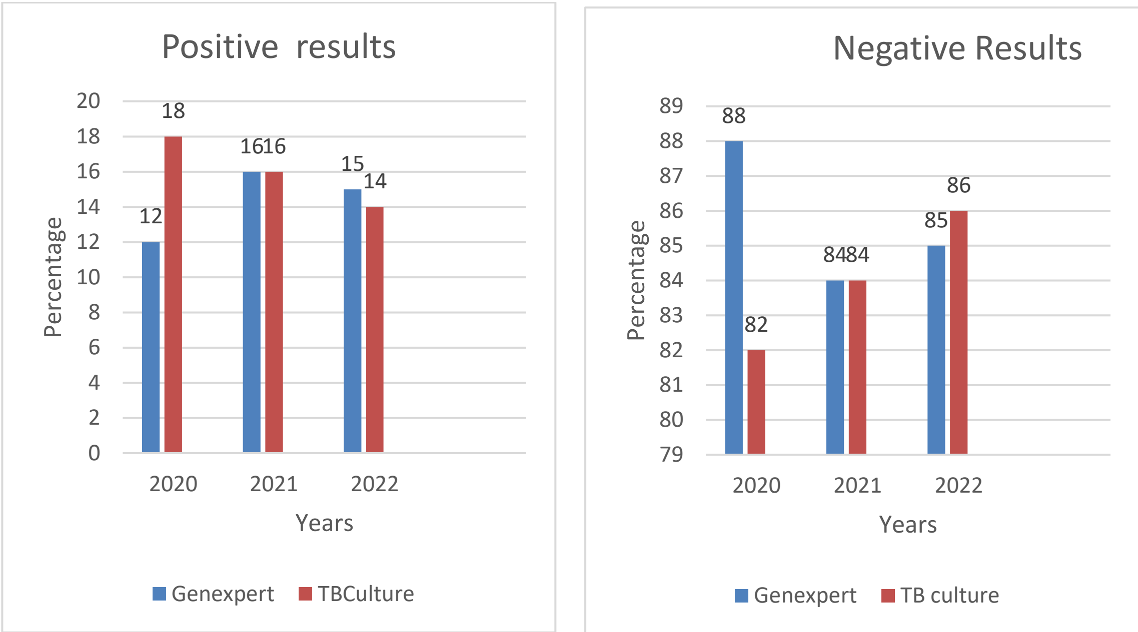

Figure 7: A: Positive-B: Negative results (Comparison of TB results)

Figure 7 illustrate the comparison of Xpert MTB/RIF results and TB culture results during the COVID-19 pandemic. In 2020 there was a 6% difference in comparability between GeneXpert and TB culture results, TB culture had 6% more positive results than GeneXpert and TB culture had 6% more negative results this is not in keeping with current literature as it is known that GeneXpert is more sensitive and specific than TB culture (Najjingo et al., 2019). In 2021 the comparability of both tests was good as the number of positives was equal to the number of negative results. In 2022 the comparability of test results was good with 1%, GeneXpert had 1% more positive results and TB culture had had 1 more negative result. On overall the comparability of both results was good as what was positive on GeneXpert was also positive on TB culture even the susceptibility testing was corresponding RIF sensitive on GeneXpert was RIF sensitive on TB culture.

Discussion

This study evaluated the correlation between Xpert MTB/RIF assay results and conventional TB culture during the COVID-19 pandemic in Taung, South Africa. The results indicate a generally strong concordance between the two diagnostic methods across the three-year study period (2020–2022), despite disruptions in healthcare services caused by the pandemic.

For GeneXpert, 12–16% of samples tested positive for TB during the study period, with the majority showing rifampicin sensitivity. TB culture results mirrored these findings, with positivity rates ranging from 14–18%, confirming that GeneXpert remains a reliable molecular diagnostic tool even under pandemic constraints. These findings align with previous studies, which have shown high sensitivity and specificity of Xpert MTB/RIF compared to conventional culture methods, particularly in settings with high TB burden (Steingart et al., 2015; Gidado et al., 2019; Piatek et al., 2018).

The slight discrepancies observed in 2020, where TB culture reported 6% more positives than GeneXpert, could be attributed to variations in sample quality, transportation delays, or low bacterial load, as indicated by the trace results in GeneXpert testing. By 2021 and 2022, the concordance improved, suggesting stabilization in diagnostic practices and laboratory efficiency despite ongoing COVID-19 restrictions.

The COVID-19 pandemic affected healthcare-seeking behaviors and sample submission patterns, evidenced by a decrease in the number of specimens received in 2020 and 2021. Similar observations have been reported globally, where lockdowns and fear of SARS-CoV-2 infection led to delays in TB diagnosis and care (Jacques et al., 2020; Keertan et al., 2022). Nonetheless, the diagnostic performance of both GeneXpert and TB culture was not compromised, confirming that these methods are robust and can provide accurate results even during periods of health system disruption.

The study also highlights the advantage of GeneXpert in providing rapid results, including rifampicin resistance profiling, which is crucial for initiating timely and effective treatment. Although TB culture remains the gold standard, it requires longer turnaround times, specialized laboratory infrastructure, and biosafety precautions (Hasan et al., 2013; Pfyffer et al., 2007). GeneXpert therefore offers a practical alternative for decentralized and resource-limited settings, especially when rapid TB detection is critical during overlapping epidemics such as COVID-19.

Overall, the findings suggest that Xpert MTB/RIF can be reliably used in conjunction with TB culture to support accurate diagnosis and treatment decision-making, even under pandemic constraints. The comparability of rifampicin susceptibility results further strengthens confidence in the utility of GeneXpert for guiding TB management in high-burden settings.

Conclusion

The Xpert MTB/RIF assay demonstrates strong correlation with conventional TB culture results for pulmonary tuberculosis diagnosis in Taung during the COVID-19 pandemic. Despite disruptions in sample submission and healthcare access caused by the pandemic, the diagnostic performance of both methods remained consistent. GeneXpert offers the advantages of rapid detection and rifampicin resistance identification, supporting timely initiation of TB treatment and complementing conventional culture methods.

These findings underscore the resilience and reliability of molecular diagnostics like GeneXpert in resource-limited settings during public health emergencies. Maintaining access to TB diagnostic services during crises such as the COVID-19 pandemic is essential to prevent delays in diagnosis and treatment, ultimately reducing morbidity, mortality, and transmission within the community.

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