Review Article
The Value of GeneXpert MTB/RIF for Detection in Tuberculosis: A Bibliometrics-Based Analysis and Review

Zhiyi Li

Laboratory Medicine, Nanan Hospital, Nanan, Quanzhou 362300, Fujian, China

Correspondence should be addressed to Zhiyi Li; lilangfu1@163.com

Received 5 September 2022; Revised 26 September 2022; Accepted 1 October 2022; Published 15 October 2022

Academic Editor: Li Fu

Copyright © 2022 Zhiyi Li. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

With the continuous development of medical science and technology, especially with the advent of the era of precision diagnosis and treatment, molecular biology detection technology is widely valued and applied as an aid to early diagnosis of tuberculosis. The GeneXpert Mycobacterium tuberculosis Branching (MTB) technology is a suite of semi-nested real-time fluorescent quantitative PCR in vitro diagnostic technologies developed by Cepheid Inc. It targets the rifampicin resistance gene, rpoB, and can detect both MTB and resistance to rifampicin within 2h. This review analyzed the papers related to GeneXpert using bibliometric software CiteSpace and Bibliometrix. A total of 151 articles were analyzed, spanning from 2011 to 2021. This bibliometrics-based review summarizes the history of the development of GeneXpert in tuberculosis diagnosis and its current status. Contributions of different countries to the topic, journal analysis, key paper analysis, and clustering of keywords were used to analyze this topic.

1. Introduction

Bacteriological and immunological detection techniques for tuberculosis require long detection times with poor sensitivity or specificity, which limit the early diagnosis and treatment of tuberculosis. In particular, smear-negative pulmonary tuberculosis, extrapulmonary tuberculosis, and Mycobacterium tuberculosis (MTB) latent infection lack typical clinical manifestations or imaging features. Fewer diagnostic differential techniques have led to a more complex situation in tuberculosis prevention and control. With the continuous development of medical science and technology, especially with the advent of the era of precision diagnosis and treatment, molecular biology detection technology has been widely used in the early diagnosis of tuberculosis. Molecular biology detection technology has the advantages of accuracy, high efficiency, and high throughput, bringing new light to the diagnosis and treatment of tuberculosis and the prevention and control of the epidemic.

MTB nucleic acid amplification techniques usually target IS6110, rpoB, gyrB, IS1081, culture filtrate protein 10 (CFP-10), etc. and are amplified and detected by PCR. In 2017, China published the standard WS288-2017 Tuberculosis Diagnosis, which includes a positive MTB nucleic acid test as one of the diagnostic criteria for tuberculosis. The advent of the GeneXpert MTB/RIF (GeneXpert) cassette test represents a breakthrough in molecular biology of tuberculosis. The GeneXpert assay kit was developed by Cepheid Inc. for use with the GeneXpert instrument. The technique is based on multiplexed semi-nested real-time fluorescence quantitative PCR to detect the MTB rifampicin resistance determining region rpoB gene. It detects the presence of MTB and its resistance to rifampicin directly from the patient’s fresh or frozen sputum within 2h. Studies have shown that the sensitivity of the GeneXpert test is 61.8% to 85.0% and the specificity is 98% to 99% for the examination of respiratory specimens from patients with pulmonary tuberculosis [1–3]. It has a sensitivity of 85% for the detection of sputum specimens from MTB/HIV co-infected patients [4]. It has a sensitivity of 98% for the detection of sputum specimens from patients with sputum smear-positive tuberculosis [4]. It has a sensitivity of 67% for sputum specimens from patients with sputum smear-negative tuberculosis [4]. The use of GeneXpert in the detection of smear-positive TB has been
widely recognized. For suspected MTB/HIV dual infection, the World Health Organization recommends GeneXpert as the preferred test [5]. However, it has also been shown that GeneXpert is less sensitive in detecting specimens with low bacterial content, limiting its use in the detection of smear-negative tuberculosis and extrapulmonary tuberculosis patients [6].

To further improve the sensitivity of the GeneXpert assay, Cepheid has introduced the Xpert Ultra, a second-generation GeneXpert assay system. The assay system has two different multiplicity amplification targets (IS6110 and IS1081) and a larger DNA reaction chamber (from a 25 μL system in GeneXpert to a 50 μL system in XpertUltra) [2]. XpertUltra also incorporates a full suite of nucleic acid amplification and a faster thermal cycle, which enables detection down to 16 CFU/mL compared to 114 CFU/mL for GeneXpert. In a recent prospective study [7], XpertUltra and GeneXpert tested sputum specimens from 137 smear-negative but culture-positive tuberculosis patients with sensitivities of 63% and 46%, respectively. It tested 115 culture-positive sputum specimens from patients with MTB/HIV coinfection with sensitivities of 90% and 77%, respectively. The overall specificity of the XpertUltra and GeneXpert assays was 96% and 98%, respectively. XpertUltra has a slightly lower specificity for relapsed patients compared to primary tuberculosis patients, but its sensitivity in detecting rifampicin resistance is consistent with that of GeneXpert. Currently, GeneXpert and XpertUltra are widely used in dozens of countries.

In recent years, many scholars have worked on the use of GeneXpert for the diagnosis of extrapulmonary tuberculosis. For example, bone tuberculosis lesions have a low number of MTBs in the lesions because they are at the end of the circulation. The traditional culture and smear method has faced the disadvantages of low positive rate and poor timeliness, and the early diagnosis of bone tuberculosis still faces challenges until now. In a study of 201 patients with suspected bone tuberculosis, GeneXpert detected eight more positive cases than the culture method, two of which were rifampicin-resistant patients [8]. Tuberculous pleurisy is the second most common form of extrapulmonary tuberculosis, and the sensitivity and specificity of biochemical, immunologic, and bacteriologic assays are low in ancillary laboratory tests. GeneXpert showed high sensitivity (90.0% and 72.0%) and specificity (100.0% and 100.0%) [9]. In addition, GeneXpert has been used in both urinary tract tuberculosis and tuberculous meningitis. To date, there have been a series of reviews and reviews on the value of the application of GeneXpert. For example, Brown et al. [10] summarized the use of GeneXpert in low and middle-income countries. Sagilli et al. [11] used a review to analyze the relationship between cost and effectiveness of GeneXpert in the diagnosis of tuberculosis. However, no bibliometrics-based review is available to date. In this work, bibliometrics was used in a statistically based analysis of the use of GeneXpert in tuberculosis. Bibliometrics is a quantitative analysis of the literature that provides an understanding of a topic by analyzing the interrelatedness of information in different sections of a paper (e.g., title, keywords, authors, and reference). This analysis technique has been widely used in recent years for systematic reviews of different topics [12–18]. Bibliometric analyses on tuberculosis have focused on the development of the entire field [19–22]. However, the bibliometric analyses of GeneXpert have not been conducted. Therefore, we have paid special attention to the development of GeneXpert techniques in tuberculosis in this bibliometric work.

2. Material and Data Cleaning

Two kinds of bibliometrics software have been used in this systematic literature review. CiteSpace, developed by Dr. Chaomei Chen, a professor at the Drexel University School of Information Science and Technology [23–26], has been used in this work. CiteSpace 6.1R2 was used to calculate and analyze all documents. In addition, Bibliometrix package of R was used to perform some additional scientometric analysis [27].

Core collection on Web of Science and PubMed has been selected as a database to assure the integrity and academic quality of the studied material. “GeneXpert tuberculosis” has been used as a “Title.” The retrieval period was indefinite, and the date of retrieval was December, 2021. 151 articles were retrieved, spanning from 2011 to 2021 (Supporting Information). The detailed systematic literature search (Preferred Reporting Items for Systematic Reviews and Meta-Analyses, PRISMA) is shown in Figure 1.

3. Developments in the Research Field

3.1. Literature Development Trends. The literature search for this work spanned from 2011 to 2021 and included a total of 151 papers. Among them, article, editorial material, letter, meeting abstract, and review are 109, 2, 7, 31, and 2, respectively. Figure 2 shows the process of annual publication of papers on this topic. It can be seen that although the number of papers is not always increasing, the overall trend is increasing, with an annual growth rate calculated to be 14.44%. 151 papers include a total of 797 authors. Only 7 papers were published by a single author. The average number of authors per paper was 5.28. International collaborations were included in 23.18% of all papers. All papers contained 201 author keywords and 20732 citations.

3.2. Journals and Cited Journals. Table 1 shows the top 7 journals in terms of number of publications in this topic. The most published journal is the multidisciplinary journal PLOS One. The second most published journal is Journal of Clinical Microbiology. In addition, journals related to respiratory and infection also play important roles.

The contribution of different journals in a topic is measured not only by the number of papers it published but also by the frequency of citations of this journal in papers on this topic. Figure 3 shows the top 10 cited journals on the GeneXpert in tuberculosis. The Journal of Clinical Microbiology, ranked second in Table 1, shows a definite dominance in Figure 2 with a total of 347 located citations. PLOS One, ranked first in Table 1, is ranked third in Figure 2, with
a total of 137 located citations. In addition, the European Respiratory Journal and BMC Infectious Diseases, both of which are listed in Table 1, also appear in Figure 2, representing their publication of papers with significant impact in this topic. Some of the other important journals that appear in Figure 2 fall into two main categories. The first includes journals directly related to tuberculosis, such as the International Journal of Tuberculosis and Lung Disease. The other category includes the most prestigious journals in the medical field, such as the Lancet and the New England Journal of Medicine.

Figure 4 shows the chronology of papers published in this topic by the seven journals in Table 1. It can be seen that International Journal of Infectious Diseases was the first journal to publish a paper on this topic. In contrast, Infection and Drug Resistance did not publish a paper on this topic until 2018. Other journals started to engage in this topic between 2013 and 2016.

3.3. Geographic and Author Distribution. Table 2 shows the level of participation of different countries in this topic. It can be seen that Pakistan is the most engaged country in this

Table 1: Top 7 journals that published articles on the GeneXpert in tuberculosis.

| Journal                                      | Articles |
|----------------------------------------------|----------|
| PLOS One                                    | 14       |
| Journal of Clinical Microbiology             | 11       |
| European Respiratory Journal                 | 10       |
| International Journal of Infectious Diseases | 9        |
| BMC Infectious Diseases                      | 8        |
| Respirology                                  | 7        |
| Infection and Drug Resistance                | 4        |

Figure 1: The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) for this study.

Figure 2: Annual publications from 2011 to 2021 searched in WOS and PubMed about the use of GeneXpert in tuberculosis.

Table 2: Level of participation of different countries in this topic.
topic. In addition, China, USA, and South Africa all have a frequency of more than 40 times. From this result, it can be guessed that the level of participation in this topic depends on two main factors. The first group of countries includes traditionally large scientific countries, such as USA and China. Another reason is that the diagnosis of TB has variability in countries with different levels of health and climate. Therefore, some countries will present an active stance in this topic. Table 2 shows the level of participation of different countries and does not represent that these countries present a leadership position in this topic. Therefore, we further analyzed the countries of the corresponding authors. Figure 5 shows the distribution of corresponding authors by country in the papers on this topic. It can be seen that the largest number of corresponding authors is from China. The second highest is Pakistan. Although there are some differences between the results in Figure 4 and the order in Table 2, they basically match. This represents that these countries in Table 2 do play an important role in the development of this topic.

Figure 6 shows the publication chronology of different countries for this topic. It can be seen that USA is the first country to participate in this topic, probably because GeneXpert is developed by a US company. South Africa started to participate in this topic in 2012 and has been active since then. In contrast, both Pakistan and China did not

Table 2: Top 10 countries’ scientific production on the GeneXpert in tuberculosis.

| Country       | Frequency |
|---------------|-----------|
| Pakistan      | 52        |
| USA           | 42        |
| China         | 41        |
| South Africa  | 40        |
| India         | 28        |
| Brazil        | 20        |
| Nepal         | 18        |
| Australia     | 16        |
| Ethiopia      | 15        |
| Vietnam       | 14        |
publish papers on this topic until the beginning of 2016. Among the countries in Table 2, Vietnam was the latest to participate in this topic. However, it is worth noting that this bibliometric analysis only retrieved core collections in WOS. Therefore, this does not necessarily represent the exact time of participation of these countries in this topic.

Table 3 shows the top 10 affiliations involved in this topic. South African institutions play an important role, such as the University of Cape Town, Wits University, and Stellenbosch University. Figure 7 shows the network of collaboration between different institutions. As can be seen from the figure, there are 2 main collaborative networks formed by this topic. The first collaborative network is

---

Table 3: Top 10 affiliations that participated in the GeneXpert in tuberculosis.

| Affiliation                               | Articles |
|-------------------------------------------|----------|
| University of Cape Town                   | 13       |
| Capital Medical University                | 12       |
| University California San Francisco       | 8        |
| Makerere University                       | 7        |
| National Health Laboratory Service        | 6        |
| Universidade de São Paulo                 | 6        |
| National Institute of Respiratory Diseases| 6        |
| Stellenbosch University                   | 5        |
| The University of Sydney                  | 5        |
| Wits University                           | 5        |
mens. Zetola et al. [32] specifically focused on the feasibility of ampicillin-resistant strains in sputum smear-negative specimens for the diagnosis of tuberculosis and identification of rifampicin resistance. They measured pulmonary specimens, extrapulmonary specimens, and other health areas. Ioannidis et al. [31] systematically investigated the performance of GeneXpert against current financial crisis coupled with a huge unmet need in the nearly 2 million people who die from TB each year. This study included 253 lung specimens with 47.7% for smear-negative specimens. Based on the results, they concluded that GeneXpert is an accurate, easy-to-apply, and rapid detection technique, especially for sputum-coated positive respiratory samples.

Table 4 shows the top 5 of the most local cited references on GeneXpert in tuberculosis. These papers largely set the stage for the development of this topic. Boehme et al. [34] evaluated the performance of GeneXpert. A total of 1730 samples from patients with suspected drug-sensitive or multidrug-resistant tuberculosis were included in this study. The population included Peru, Azerbaijan, South Africa, and India. A single direct GeneXpert test confirmed 551 of 561 smear-positive tuberculosis cases and 124 of 171 smear-negative tuberculosis cases. Thus, GeneXpert can detect tuberculosis and rifampicin resistance in less than 2 h. Zifodya et al. [1] compared the diagnostic accuracy of Xpert Ultra and Xpert MTB/RIF in the detection of pulmonary tuberculosis and rifampicin resistance in presumptive adult tuberculosis patients. Helb et al. [35] published the first report on MTB/RIF of the Xpert system in 2010. Since our search was performed with GeneXpert as a keyword and only the title was searched, this paper did not appear in the results. Boehme et al. [36] also conducted large-scale tests to validate the feasibility, diagnostic accuracy, and effectiveness of GeneXpert. The effect of GeneXpert was also validated by Marlowe et al. [37]. They had a smaller sample size.

Table 5 and Figure 9 show the clustering analysis of keywords. Tuberculosis is a specific type of inflammatory disease. It is the largest global threat of death caused by a single infectious agent. Tuberculosis can be divided into pulmonary and extrapulmonary tuberculosis, of which about 1/5 are extrapulmonary tuberculosis, which can cause infection and even disease in close contacts by expelling microdroplets containing Mycobacterium tuberculosis through coughing and sneezing. The exact pathogenesis of tuberculosis is still unknown and consists mainly of infection by Mycobacterium tuberculosis, a series of immune responses triggered by the infection in the host, and host disease. In most developing countries, the diagnosis of tuberculosis is still made using relatively outdated tools and methods, including chest radiographs and sputum smear microscopy. The disadvantages of these diagnostic tools are more obvious, such as longer time consumption, higher
false-negative rate, lower positive rate, and inability to promote their application in grassroots organizations on a large scale. These clinical primary health organizations, in turn, have the functional task of making the vast majority of initial diagnoses. Some patients with extrapulmonary tuberculosis do not have a range of clinical symptoms due to *Mycobacterium tuberculosis*, but rather a range of clinical symptoms due to respiratory infections caused by other pathogenic bacteria. There are also some general practitioners and non-tuberculosis specialists who are able to make routine diagnoses but lack a certain amount of expertise in tuberculosis, resulting in longer diagnosis times, more frequent referrals, and other delays in the diagnosis and treatment of tuberculosis.

In 2011, the World Health Organization strongly recommended the GeneXpert MTB/RIF automated molecular identification of *Mycobacterium tuberculosis* and rapid diagnosis of rifampicin resistance as the initial diagnostic method involving multidrug-resistant tuberculosis or AIDS-associated tuberculosis. The GeneXpert assay has gained widespread interest because of its

### Table 4: Top 5 of the most local cited references on GeneXpert in tuberculosis.

| Cited reference | Citations |
|-----------------|-----------|
| Boehme CC, 2010, new engl J med, V363, P1005, DOI 10.1056/NEJMOA0907847 | [47] |
| Steingart KR, 2014, cochrane Db syst rev, DOI 10.1002/14651858.CD009593.PUB3, 10.1002/14651858.CD009593.PUB2 | [34] |
| Helb D, 2010, J clin microbiol, V48, P229, DOI 10.1128/jcm.01463–09 | [32] |
| Boehme CC, 2011, lancet, V377, P1495, DOI 10.1016/s0140-6736(11)60438–8 | [27] |
| Marlowe EM, 2011, J clin microbiol, V49, P1621, DOI 10.1128/jcm.02214–10 | [22] |

### Table 5: Knowledge clusters in the field of GeneXpert in tuberculosis on keyword co-occurrences for each cluster.

| Cluster ID | Size | Silhouette | Keywords | References |
|------------|------|------------|----------|------------|
| 0          | 28   | 0.928      | Assay; resistance; complex; polymerase chain reaction | [28, 38–46] |
| 1          | 27   | 0.906      | Diagnosis; accuracy; GeneXpert MTB/RIF; bactec mgit 960; feasibility | [39, 47–54] |
| 2          | 25   | 0.931      | Performance; xpert MTB/RIF assay; disease; rifampinresistance | [55–61] |
| 3          | 22   | 0.969      | Drug resistance; mutation; epidemiology | [30, 32, 62–64] |
| 4          | 20   | 0.906      | DNA Identification; GeneXpert assay; DNA | [65, 66] |
| 5          | 18   | 0.890      | Microscopy; children; HIV | [67–70] |
| 6          | 17   | 0.988      | Pulmonary tuberculosis; prevalence; impact | [71–78] |
| 7          | 16   | 0.890      | Xpert MTB/RIF; rifampin resistance; rapid diagnosis; specimen | [47, 58, 59, 79–86] |
| 8          | 14   | 0.850      | Extrapulmonary tuberculosis; culture; GeneXpert MTB | [74, 79, 87, 88] |
| 9          | 12   | 0.957      | Cost effectiveness; molecular diagnostic technique; acidamplification test | [89] |

Figure 9: Grouping of keywords for GeneXpert in tuberculosis.
high sensitivity and specificity and its ease and speed of use. The GeneXpert assay is a landmark in the study of tuberculosis.

5. Conclusion

The GeneXpert assay has been widely reported in recent years as a type of nucleic acid assay. The GeneXpert test is more sensitive and accurate than traditional smear and culture methods and can detect Mycobacterium tuberculosis even in the presence of negative sputum smears. It therefore enables early intervention in tuberculosis patients to prevent serious consequences of tuberculosis disease without delaying the optimal treatment of first diagnosed patients. In areas with a high prevalence of TB, the GeneXpert test is important for rapid diagnosis of drug-resistant tuberculosis and for guiding rational clinical use of drugs.

GeneXpert has shown higher sensitivity and specificity than traditional smear and culture in the diagnosis of extrapulmonary tuberculosis such as bone TB, tuberculosis pleurisy, and urogenital tuberculosis. It can also detect rifampicin resistance and make a preliminary determination of MTB or non-MTB in smear-positive patients. In addition, studies on the specific advantages of GeneXpert in terms of timeliness and its impact on the ultimate prognosis and survival of patients are expected. With the increasing number of cases of tuberculosis resistant to other first-line and second-line drugs, such as multidrug-resistant tuberculosis, GeneXpert is not yet able to detect them, so the existing system needs to be improved to cover more drug-resistant loci.

On the other hand, the high cost of testing makes it difficult to scale up these technologies in low and middle-income countries, where a large proportion of tuberculosis patients are located. Therefore, in contrast to the pursuit of technologies with high sensitivity, high specificity, and full automation, it is particularly important to develop molecular biology assays that are suitable for medically disadvantaged areas based on a comprehensive assessment of technical performance and affordability. In addition to economic constraints, these areas often have limited access to timely medical services, especially for molecular biology testing, which requires high laboratory conditions. Therefore, GeneXpert not only needs to improve efficiency and reduce costs, but also needs to develop a rapid detection system to meet the immediate detection needs in remote areas.

Data Availability

The data supporting this review are from previously reported studies and datasets, which have been cited. The processed data are available in the supplementary files.

Conflicts of Interest

The author declares that there are no conflicts of interest.

Supplementary Materials

The supporting information includes the original data used in the bibliometric analysis. (Supplementary Materials)

References

[1] J. Zifodya, J. Kreniske, I. Schiller et al., “Xpert Ultra versus Xpert MTB/RIF for pulmonary tuberculosis and rifampicin resistance in adults with presumptive pulmonary tuberculosis (Review),” Cochrane Database of Systematic Reviews, vol. 2, 2021.
[2] A. W. Kay, L. Gonzalez Fernandez, Y. Takwoingi et al., “Xpert MTB/RIF and Xpert MTB/RIF Ultra assays for active tuberculosis and rifampicin resistance in children,” Cochrane Database of Systematic Reviews, vol. 8, 2020.
[3] A. E. Shapiro, J. M. Ross, M. Yao et al., “Xpert MTB/RIF and Xpert Ultra assays for screening for pulmonary tuberculosis and rifampicin resistance in adults, irrespective of signs or symptoms,” Cochrane Database of Systematic Reviews, vol. 3, 2021.
[4] D. Horne, M. Kohli, J. Zifodya et al., “Xpert MTB/RIF and Xpert MTB/RIF Ultra for pulmonary tuberculosis and rifampicin resistance in adults,” Cochrane Database of Systematic Reviews, vol. 6, 2019.
[5] World Health Organization, Guidance for National Tuberculosis Programmes on the Management of Tuberculosis in Children, World Health Organization, Geneva, Switzerland, 2014.
[6] M. Park and O. M. Kon, “Use of Xpert MTB/RIF and Xpert Ultra in extrapulmonary tuberculosis,” Expert Review of Antiinfective Therapy, vol. 19, no. 1, pp. 65–77, 2021.
[7] S. E. Dorman, S. G. Schumacher, D. Alland et al., “Xpert MTB/RIF Ultra for detection of Mycobacterium tuberculosis and rifampicin resistance: a prospective multicentre diagnostic accuracy study,” The Lancet Infectious Diseases, vol. 18, no. 1, pp. 76–84, 2018.
[8] M. Held, M. Laubscher, L. Workman, H. J. Zar, and R. Dunn, “Diagnostic accuracy of GeneXpert MTB/RIF in musculoskeletal tuberculosis: high sensitivity in tissue samples of HIV-infected and HIV-uninfected patients,” South African Medical Journal, vol. 107, no. 10, pp. 854–858, 2017.
[9] M. Saedd, M. Ahmad, S. Iram, S. Riaz, M. Akhtar, and M. Aslam, “GeneXpert technology,” Saudi Medical Journal, vol. 38, no. 7, pp. 699–705, 2017.
[10] S. Brown, J. E. Leavy, and J. Jancey, “Implementation of GeneXpert for TB testing in low and middle-income countries: a systematic review,” Global Health, Science and Practice, vol. 9, no. 3, pp. 698–710, 2021.
[11] K. D. Sagili, M. Muniyandi, K. S. Nilgiriwala et al., “Cost-effectiveness of GeneXpert and LED-FM for diagnosis of pulmonary tuberculosis: a systematic review,” PLoS One, vol. 13, no. 10, Article ID e0205233, 2018.
[12] Y. Zheng, H. Karimi-Maleh, and L. Fu, “Advances in electrochemical techniques for the detection and analysis of genetically modified organisms: an analysis based on bibliometrics,” Chemosensors, vol. 10, no. 5, 2022.
[13] Q. Zhou, M. Jin, W. Wu, L. Fu, C. Yin, and H. Karimi-Maleh, “Graphene-based surface-enhanced Raman scattering (SERS) sensing: bibliometrics based analysis and review,” Chemosensors, vol. 10, no. 8, 2022.
[14] L. Fu, S. Mao, F. Chen et al., “Graphene-based electrochemical sensors for antibiotic detection in water, food and soil: a
scientometric analysis in CiteSpace (2011–2021),” *Chemosphere*, vol. 297, Article ID 134127, 2022.

[15] M. Jin, J. Liu, W. Wu et al., “Relationship between graphene and pedosphere: a scientometric analysis,” *Chemosphere*, vol. 300, Article ID 134599, 2022.

[16] Y. Shen, S. Mao, F. Chen et al., “Electrochemical detection of Sudan red series azo dyes: bibliometrics based analysis,” *Food and Chemical Toxicology*, vol. 163, Article ID 112960, 2022.

[17] S. Mao, L. Fu, C. Yin, X. Liu, and H. Karimi-Maleh, “The role of electrochemical biosensors in SARS-CoV-2 detection: a bibliometrics-based analysis and review,” *RSC Advances*, vol. 12, no. 35, pp. 22592–22607, 2022.

[18] Y. Zheng, H. Karimi-Maleh, and L. Fu, “Evaluation of antioxidants using electrochemical sensors: a bibliometric analysis,” *Sensors*, vol. 22, no. 9, 2022.

[19] A. Igwara and C. E. Edosomodu, “Bibliometric analysis on tuberculosis and tuberculosis-related research trends in Africa: a decade-long study,” *Antibiotics*, vol. 10, no. 4, p. 423, 2021.

[20] V. Nafade, M. Nash, S. Huddart et al., “A bibliometric analysis of tuberculosis research, 2007–2016,” *PloS One*, vol. 13, no. 6, Article ID e0199706, 2018.

[21] J. M. Ramos, S. Padilla, M. Masia, and F. Gutierrez, “A bibliometric analysis of tuberculosis research indexed in PubMed, 1997–2006,” *International Journal of Tuberculosis & Lung Disease*, vol. 12, pp. 1461–1468, 2008.

[22] W. M. Sweileh, A. S. AbuTaha, A. F. Sawalha, S. Al-Khalil, S. W. Al-Jabi, and S. H. Zyoud, “Bibliometric analysis of worldwide publications on multi-extensively, and totally drug – resistant tuberculosis (2006–2015),” *Multidisciplinary Respiratory Medicine*, vol. 11, no. 1, 2017.

[23] K. Börner, C. Chen, and K. W. Boyack, “Visualizing knowledge domains,” *Annual Review of Information Science & Technology*, vol. 37, no. 1, pp. 179–255, 2005.

[24] C. Chen, “CiteSpace II: detecting and visualizing emerging trends and transient patterns in scientific literature,” *Journal of the American Society for Information Science and Technology*, vol. 57, no. 3, pp. 359–377, 2006.

[25] C. Chen, “Searching for intellectual turning points: progressive knowledge domain visualization,” *Proceedings of the National Academy of Sciences*, vol. 101, pp. 5303–5310, 2004.

[26] C. Chen, F. Ibehwe-Sanjuan, and J. Hou, “The structure and dynamics of cocitation clusters: a multiple-perspective cocitation analysis,” *Journal of the American Society for Information Science and Technology*, vol. 61, no. 7, pp. 1386–1409, 2010.

[27] M. Aria and C. Cuccurullo, “Bibliometrix: an R-tool for comprehensive science mapping analysis,” *Journal of Informetrics*, vol. 11, no. 4, pp. 959–975, 2017.

[28] D. Hillemann, S. Rüsch-Gerdes, C. Boehme, and E. Richter, “Rapid molecular detection of extrapulmonary tuberculosis by the automated GeneXpert MTB/RIF system,” *Journal of Clinical Microbiology*, vol. 49, no. 4, pp. 1202–1205, 2011.

[29] A. N. Zeka, S. Tasbakan, and C. Cavusoglu, “Evaluation of the GeneXpert MTB/RIF assay for rapid diagnosis of tuberculosis and detection of rifampin resistance in pulmonary and extrapulmonary specimens,” *Journal of Clinical Microbiology*, vol. 49, no. 12, pp. 4138–4141, 2011.

[30] C. A. Evans, “GeneXpert—a game-changer for tuberculosis control?” *PloS Medicine*, vol. 8, no. 7, Article ID e1001064, 2011.

[31] P. Ioannidis, D. Papaventis, S. Karabela et al., “Cepheid GeneXpert MTB/RIF assay for *Mycobacterium tuberculosis* detection and rifampin resistance identification in patients with substantial clinical indications of tuberculosis and smear-negative microscopy results,” *Journal of Clinical Microbiology*, vol. 49, no. 8, pp. 3068–3070, 2011.

[32] N. M. Zetola, S. S. Shin, K. A. Tumedi et al., “Mixed *Mycobacterium tuberculosis* complex infections and false-negative results for rifampin resistance by GeneXpert MTB/RIF are associated with poor clinical outcomes,” *Journal of Clinical Microbiology*, vol. 52, no. 7, pp. 2422–2429, 2014.

[33] E. Bunsow, M. J. Ruiz-Serrano, P. L. Roa, M. Kestler, D. G. Viedma, and E. Bouza, “Evaluation of GeneXpert MTB/ RIF for the detection of *Mycobacterium tuberculosis* and resistance to rifampin in clinical specimens,” *Journal of Infection*, vol. 68, pp. 338–343, 2014.

[34] C. C. Boehme, P. Nabeta, D. Hillelmann et al., “Rapid molecular detection of tuberculosis and rifampin resistance,” *New England Journal of Medicine*, vol. 363, no. 11, pp. 1005–1015, 2010.

[35] D. Helb, M. Jones, E. Story et al., “Rapid detection of *Mycobacterium tuberculosis* and rifampin resistance by use of on-demand, near-patient technology,” *Journal of Clinical Microbiology*, vol. 48, no. 1, pp. 229–237, 2010.

[36] C. C. Boehme, M. P. Nicol, P. Nabeta et al., “Feasibility, diagnostic accuracy, and effectiveness of decentralised use of the Xpert MTB/RIF test for diagnosis of tuberculosis and multidrug resistance: a multicentre implementation study,” *The Lancet*, vol. 377, pp. 9776, pp. 1495–1505, 2011.

[37] E. M. Marlowe, S. M. Novak-Weekley, J. Cumpio et al., “Evaluation of the Cepheid Xpert MTB/RIF assay for direct detection of *Mycobacterium tuberculosis* complex in respiratory specimens,” *Journal of Clinical Microbiology*, vol. 49, no. 4, pp. 1621–1623, 2011.

[38] M. Saeed, S. Iram, S. Hussain, A. Ahmed, M. Akbar, and M. Aslam, “GeneXpert: A new tool for the rapid detection of rifampicin resistance in mycobacterium tuberculosis,” *Journal of Pakistan Medical Association*, vol. 67, pp. 270–274, 2017.

[39] E. Aliasgar, P. Anil, F. Sabur Natasha et al., “An Optimal Diagnostic Strategy for Tuberculosis in Hospitalized HIV-Infected Patients Using GeneXpert MTB/RIF and Alere Determine TB LAM Ag.” *Journal of Clinical Microbiology*, vol. 58, pp. 010322–e1120, 2020.

[40] K. W. To, K. M. Kam, D. P. C. Chan et al., “Utility of GeneXpert in analysis of bronchoalveolar lavage samples from patients with suspected tuberculosis in an intermediate-burden setting,” *Journal of Infection*, vol. 77, no. 4, pp. 296–301, 2018.

[41] L. Rindi, G. Ali, B. Fabiani, G. Fontanini, and C. Garzelli, “Detection of *Mycobacterium tuberculosis* from paraffin-embedded tissues by *GeneXpert MTB/RIF,*” *Tuberculosis*, vol. 106, pp. 53–55, 2017.

[42] J. Ruan, Z. Wang, and S. Xu, “Application of GeneXpert MTB/ RIF assay in the diagnosis of bacteriologically-negative pulmonary tuberculosis,” *International Journal of Clinical and Experimental Medicine*, vol. 13, pp. 7766–7772, 2020.

[43] L. Nakirungi, H. Nankabirwa, and M. Lamorde, “Tuberculosis diagnosis in resource-limited settings: Clinical use of GeneXpert in the diagnosis of smear-negative PTB: a case report,” *African Health Sciences*, vol. 13, pp. 522–524, 2013.

[44] Ó. Herrérez, M. A. Asencio-Egea, M. Huertas-Vaquero et al., “Estudio de coste-efectividad del diagnóstico microbiológico de tuberculosis mediante geneXpert MTB/RIF,” *Enfermedades Infecciosas Microbiología Clínica*, vol. 35, pp. 403–410, 2017.

[45] Y. Mechal, E. Benaida, N. El mirimar et al., “Evaluation of GeneXpert MTB/RIF system performances in the diagnosis of
extrapulmonary tuberculosis,” BMC Infectious Diseases, vol. 19, no. 1, 2019.

[46] M. F. T. Pinto, R. Steffen, A. Entringer, A. C. C. D. Costa, and A. Trajman, “Budget impact of the incorporation of GeneXpert MTB/RIF for diagnosis of pulmonary tuberculosis from the perspective of the Brazilian Unified National Health System, Brazil, 2013-2017,” Cadernos de Saúde Pública, vol. 33, no. 9, Article ID e00214515, 2017.

[47] K. Guenouhi, N. Harir, A. Ouardi et al., “Use of GeneXpert Mycobacterium tuberculosis/rafampicin for rapid detection of rifampicin resistant Mycobacterium tuberculosis strains of clinically suspected multi-drug resistance tuberculosis cases,” Annals of Translational Medicine, vol. 4, 2016.

[48] K. Shakeel, S. Iram, M. Akhtar, S. Hussain, H. Maryam, and A. Anwar, “Diagnostic validation of rapid molecular detection of Mycobacterium tuberculosis in pus samples by GeneXpert,” JPMA. Pakistan Journal of Medical Association, vol. 68, pp. 33–37, 2018.

[49] J. L. Davis, L. M. Kawamura, L. H. Chaisson, L. M. Kawamura, L. H. Chaisson et al., “Impact of GeneXpert MTB/RIF on patients and tuberculosis programs in a low-burden setting. A hypothetical trial,” American Journal of Respiratory and Critical Care Medicine, vol. 189, no. 12, pp. 1551–1559, 2014.

[50] E. Walters, P. Goussard, C. Bosch, A. C. Hesseling, and R. P. Gie, “GeneXpert MTB/RIF on bronchoalveolar lavage samples in children with suspected complicated intrathoracic tuberculosis: a pilot study,” Pediatric Pulmonology, vol. 49, no. 11, pp. 1133–1137, 2014.

[51] L. Muñoz, R. Moure, N. Porta et al., “GeneXpert® for smear-negative pulmonary tuberculosis: does it play a role in low-burden countries?” Diagnostic Microbiology and Infectious Disease, vol. 75, no. 3, pp. 325–326, 2013.

[52] N. Rakotosamimanana, S. G. Lapierre, V. Raharimanga et al., “Performance and impact of GeneXpert MTB/RIF® and Loopamp MTBC Detection Kit® assays on tuberculosis case detection in Madagascar,” BMC Infectious Diseases, vol. 19, no. 1, 2019.

[53] Y. Deng, Y. F. Duan, S. P. Gao, and J. M. Wang, “Comparison of LAMP, GeneXpert, mycobacterial culture, smear microscopy, TSPOT.TB, TBAg/PHA ratio for diagnosis of pulmonary tuberculosis,” Current Medical Science, vol. 41, no. 5, pp. 1023–1028, 2021.

[54] Y.-Y. Zhou, J.-C. Shi, N. Pan et al., “The value of GeneXpert MTB/RIF in bronchoalveolar lavage fluid in the diagnosis of smear-negative pulmonary tuberculosis,” Investigacion Clinica, vol. 62, no. 1, pp. 28–36, 2021.

[55] S. Walusimbi, F. Bwanga, A. De Costa, M. Haile, M. Joloba, and S. S. Malinga, “Meta-analysis to compare the accuracy of GeneXpert, MODS and the WHO 2007 algorithm for diagnosis of smear-negative pulmonary tuberculosis,” BMC Infectious Diseases, vol. 13, no. 1, p. 507, 2013.

[56] Q. Zhang, Q. Zhang, B. q. Sun et al., “GeneXpert MTB/RIF for rapid diagnosis and rifampicin resistance detection of endobronchial tuberculosis,” Respirology, vol. 23, no. 10, pp. 950–955, 2018.

[57] N. Hiruy, M. Melese, D. Habte et al., “Comparison of the yield of tuberculosis among contacts of multidrug-resistant and drug-sensitive tuberculosis patients in Ethiopia using GeneXpert as a primary diagnostic test,” International Journal of Infectious Diseases, vol. 71, pp. 4–8, 2018.

[58] O. Sánchez-Cabral, C. Santillán-Díaz, Á. P. Flores-Bello et al., “GeneXpert® MTB/RIF assay with transbronchial lung cryobiopsy for Mycobacterium tuberculosis diagnosis,” Annals of Translational Medicine, vol. 8, 2020.

[59] N. K. Cuong, N. B. Ngoc, N. B. Hoa, V. Q. Dat, and N. V. Nhung, “GeneXpert on patients with human immunodeficiency virus and smear-negative pulmonary tuberculosis,” PLoS One, vol. 16, no. 7, Article ID e0253961, 2021.

[60] P. Garg, A. Goyal, V. D. Yagnik, S. Dawka, and G. R. Menon, “Diagnosis of anorectal tuberculosis by polymerase chain reaction, GeneXpert and histopathology in 1336 samples in 776 anal fistula patients,” World Journal of Gastrointestinal Surgery, vol. 13, no. 4, pp. 355–365, 2021.

[61] D. Habte, M. Melese, N. Hiruy et al., “The additional yield of GeneXpert MTB/RIF test in the diagnosis of pulmonary tuberculosis among household contacts of smear positive TB cases,” International Journal of Infectious Diseases, vol. 49, pp. 179–184, 2016.

[62] A. K. Alame-Emame, C. Pierre-Audigier, O. C. Aboumegone-Biyougo et al., “Use of GeneXpert remnants for drug resistance profiling and molecular epidemiology of tuberculosis in libreville, Gabon,” Journal of Clinical Microbiology, vol. 55, no. 7, pp. 2105–2115, 2017.

[63] M. Saeed, S. Hussain, S. Riaz et al., “GeneXpert Technology for the diagnosis of HIV-associated tuberculosis: Is scale-up worth it?” Open Life Sciences, vol. 15, no. 1, pp. 458–465, 2020.

[64] H. Kazemian, J. Kardan Yamschi, A. Bahador et al., “Efficacy Of Line Probe Assay In Detection Of Drug-Resistant Pulmonary Tuberculosis In Comparison With GeneXpert And Phenotypic Methods In Iran And Genetic Analysis Of Isolates By MIRU-VNTR,” Infection and Drug Resistance, vol. 12, 2019.

[65] E. Aninagyei, R. Ayivor-Djanie, J. Attoh, M. P. Dakorah, M. N. Ganko, and D. O. Acheampong, “Molecular detection of Mycobacterium tuberculosis in blood stained sputum samples using GeneXpert PCR assay,” Diagnostic Microbiology and Infectious Disease, vol. 100, Article ID 115363, 2021.

[66] S. Shenai, D. Amisano, K. Ronacher et al., “Exploring alternative biomaterials for diagnosis of pulmonary tuberculosis in HIV-negative patients by use of the GeneXpert MTB/RIF assay,” Journal of Clinical Microbiology, vol. 51, no. 12, pp. 4161–4166, 2013.

[67] P. Tang, P. Xu, W. Shu et al., “Additional benefits of GeneXpert MTB/RIF assay for the detection of pulmonary tuberculosis patients with prior exposure to fluoroquinolones,” Infection and Drug Resistance, vol. 12, pp. 87–93, 2018.

[68] D. Gebretsadik, N. Ahmed, E. Kebede, M. Mohammed, and M. A. Belete, “Prevalence of tuberculosis by automated GeneXpert rifampicin assay and associated risk factors among presumptive pulmonary tuberculosis patients at ataye district hospital, north east Ethiopia,” Infection and Drug Resistance, vol. 13, pp. 1507–1516, 2020.

[69] W. S. Stevens, L. Scott, L. Noble, N. Gous, and K. Dheda, “Impact of the GeneXpert MTB/RIF technology on tuberculosis control,” Microbiology Spectrum, vol. 5, no. 1, p. 5, 2017.

[70] Y. Pang, Y. Shang, J. Lu et al., “GeneXpert MTB/RIF assay in the diagnosis of urinary tuberculosis from urine specimens,” Scientific Reports, vol. 7, no. 1, p. 6181, 2017.

[71] W. Reechaiwichitkul, A. Phetsuriyawong, P. Chaimane, and P. Ananta, “Diagnostic Test of Sputum Genexpert MTB/RIF for Smear Negative Pulmonary Tuberculosis,” Southeast Asian Journal of Tropical Medicine and Public Health, vol. 47, pp. 457–466, 2016.

[72] H. A. A. Al-Darraj, H. A. Razak, K. P. Ng, F. L. Altice, and A. Kamarulzaman, “The diagnostic performance of a single GeneXpert MTB/RIF assay in an intensified tuberculosis case
finding survey among HIV-infected prisoners in Malaysia,” *PLoS One*, vol. 8, no. 9, Article ID e73717, 2013.

[73] M. G. B. F. de Faria, R. L. d. P. Andrade, A. J. G. Camillo et al., “Efeitividade do GeneXpert® no diagnóstico da tuberculose em pessoas que vivem com HIV/aids,” *Revista de Saúde Pública*, vol. 55, 2021.

[74] T. Tang, F. Liu, X. Lu, and Q. Huang, “Evaluation of GeneXpert MTB/RIF for detecting *Mycobacterium tuberculosis* in a hospital in China,” *Journal of International Medical Research*, vol. 45, no. 2, pp. 816–822, 2017.

[75] T. Z. Berra, A. T. I. Bruce, Y. M. Alves, A. C. V. Ramos, C. L. Giacomet, and R. A. Arcâncio, “Impact of the GeneXpert® MTB/RIF rapid molecular test on tuberculosis detection: temporal trends and vulnerable territories,” *Revista Latino-Americana de Enfermagem*, vol. 29, Article ID e3441, 2021.

[76] M. Das, D. Pasupuleti, S. Rao et al., “GeneXpert and community health workers supported patient tracing for tuberculosis diagnosis in conflict-affected border areas in India,” *Tropical Medicine and Infectious Disease*, vol. 5, 2019.

[77] A. J. Meyer, C. Atuheire, W. Worordria et al., “Sputum quality and diagnostic performance of GeneXpert MTB/RIF among smear-negative adults with presumed tuberculosis in Uganda,” *PLoS One*, vol. 12, no. 7, Article ID e0180572, 2017.

[78] N. T. B. Phuong, N. T. Anh, N. Van Son et al., “Effect of two alternative methods of pooling sputum prior to testing for tuberculosis with genexpert MTB/RIF,” *BMC Infectious Diseases*, vol. 19, no. 1, p. 347, 2019.

[79] C. Marouane, S. Smaoui, S. Kammoun, L. Slim, and F. Messadi-Akrout, “Evaluation of molecular detection of extrapulmonary tuberculosis and resistance to rifampicin with GeneXpert® MTB/RIF,” *Medecine et Maladies Infectieuses*, vol. 46, no. 1, pp. 20–24, 2016.

[80] M. Tadesse, G. Abebe, K. Abdissa et al., “GeneXpert MTB/RIF assay for the diagnosis of tuberculous lymphadenitis on concentrated fine needle aspirates in high tuberculosis burden settings,” *PLoS One*, vol. 10, no. 9, Article ID e0137471, 2015.

[81] N. Taylor, R. L. Gaur, E. J. Baron, and N. Banai, “Can a simple flotation method lower the limit of detection of *Mycobacterium tuberculosis* in extrapulmonary samples analyzed by the GeneXpert MTB/RIF assay?” *Journal of Clinical Microbiology*, vol. 50, no. 7, pp. 2272–2276, 2012.

[82] A. S. Khan, S. Ali, M. T. Khan et al., “Comparison of GeneXpert MTB/RIF assay and LED-FM microscopy for the diagnosis of extra pulmonary tuberculosis in Khyber Pakhtunkhwa, Pakistan,” *Brazilian Journal of Microbiology*, vol. 49, no. 4, pp. 909–913, 2018.

[83] H. Sh. Moussa, F. S. Bayoumi, and A. M. Ali, “Evaluation of GeneXpert MTB/RIF assay for direct diagnosis of pulmonary tuberculosis,” *Saudi Medical Journal*, vol. 37, no. 10, pp. 1076–1081, 2016.

[84] E. M. Mokaddas, S. Ahmad, and H. S. Eldeen, “GeneXpert MTB/RIF is superior to BBD max MDR-TB for diagnosis of tuberculosis (TB) in a country with low incidence of multidrug-resistant TB (MDR-TB),” *Journal of Clinical Microbiology*, vol. 57, no. 6, 2019.

[85] H. A. Terzi, O. Aydemir, E. Karakece, M. Koroglu, and M. Altindis, “Comparison of the GeneXpert (R) MTB/RIF Test and Conventional Methods in the Diagnosis of Mycobacterium tuberculosis,” *Clinical Laboratory*, vol. 65, pp. 1–6, 2019.

[86] R. Bajrami, G. Mulliqi, A. Kurti, G. Lila, and L. Raka, “Comparison of GeneXpert MTB/RIF and conventional methods for the diagnosis of tuberculosis in Kosovo,” *The Journal of Infection in Developing Countries*, vol. 10, no. 04, pp. 418–422, 2016.

[87] E. Mokaddas, S. Ahmad, and H. Eldeen, “Performance comparison of GeneXpert MTB/RIF and ProbeTec ET tests for rapid molecular diagnosis of extrapulmonary tuberculosis in a low TB/MDR-TB incidence country,” *Medical Principles and Practice*, vol. 30, no. 3, pp. 277–284, 2021.

[88] A. M. Elbrolosy, R. H. El Helbawy, O. M. Mansour, and R. A. Latif, “Diagnostic utility of GeneXpert MTB/RIF assay versus conventional methods for diagnosis of pulmonary and extra-pulmonary tuberculosis,” *BMC Microbiology*, vol. 21, no. 1, p. 144, 2021.

[89] L. H. Chaisson, M. Roermer, D. Cantu et al., “Impact of GeneXpert MTB/RIF assay on triage of respiratory isolation rooms for inpatients with presumed tuberculosis: a hypothetical trial,” *Clinical Infectious Diseases*, vol. 59, no. 10, pp. 1353–1360, 2014.