ORIGINAL ARTICLE

Diagnosis of tuberculosis with Xpert® MTB/RIF test in the eastern region of Cuba

Diagnóstico de tuberculosis con ensayo Xpert® MTB/RIF en la región oriental de Cuba

Diagnóstico de tuberculose com ensaio Xpert® MTB/RIF na região leste de Cuba

Ernesto CarmenatesRicardo[I]* iD ,Marilin Pérez Díaz[I] iD

[I]Centro Provincial de Higiene, Epidemiología y Microbiología de Holguín. Holguín, Cuba.

*Corresponding author: e.carmenates95@gmail.com

ABSTRACT

Introduction: tuberculosis infection affects the world despite years of study and technological advances in its diagnosis. The Xpert® MTB/RIF test allows, to a large extent, the identification of Koch bacillus in any pathological sample, and does so with high sensitivity, specificity and speed compared to other methods. **Objective:** to diagnose tuberculosis with the Xpert® MTB/RIF test. **Method:** a cross-sectional study was carried out on 46 analyzed samples (n 46) from the eastern provinces of Cuba with the Xpert® MTB/RIF test, between April and September 2023, by the Centro Provincial de Higiene, Epidemiología y Microbiología de Holguín (Provincial Center of Hygiene, Epidemiology and Microbiology of Holguín).The variables studied were: province of origin, age, sex, type of sample, risk factors, test result and resistance to rifampicin. **Results:** Santiago de Cuba and Guantánamo were the provinces that reported the highest number of cases, with 14 cases each (30.4%).The male shad the highest incidence, 33 cases (71.7%), regardless of the province. The age group of 25 to 34 years was the one with the highest prevalence, with 26.1%.The most affected risk groups were: smokers (37.0%), prisoners (32.6%), adults over 60 years of age (26.6%) and alcoholics (23.9%). **Conclusions:** the introduction of GeneXpert in tuberculosis diagnosis is very effective, due to its high sensitivity and specificity in relation to traditional studies, such as smear microscopy and culture, in addition to the speed in obtaining the result. It also reports on resistance to rifampicin, attributable to the rpoβ gene, which is timely at a moment when multidrug resistance is increasing rapidly.

Keywords: tuberculosis; risk factors; rifampicin resistance; Mycobacterium tuberculosis

RESUMEN

Introducción: la infección por tuberculosis repercute en el mundo a pesar de los años de estudio y avances tecnológicos en su diagnóstico. El ensayo Xpert® MTB/RIF permite, en gran medida, la identificación del bacilo de Koch en cualquier muestra patológica, y lo hace con una alta sensibilidad, especificidad y rapidez con respecto a otros métodos. **Objetivo:** realizar el diagnóstico de tuberculosis con ensayo Xpert® MTB/RIF. **Método:** realizó un estudio transversal en 46 muestras analizadas (n=46) de las provincias orientales de Cuba con ensayo Xpert® MTB/RIF, entre abril y septiembre de 2023, por el Centro Provincial de Higiene, Epidemiología y Microbiología de Holguín. Las variables estudiadas fueron: provincia de procedencia, edad, sexo, tipo de muestra, factores de riesgo, resultado al ensayo y resistencia a la rifampicina. **Resultados:** Santiago de Cuba y Guantánamo fueron las provincias que mayor cantidad de casos reportaron, con 14 casos cada una (30,4 %). El sexo masculino fue el de mayor incidencia, 33 casos (71,7 %), independientemente de la provincia. El grupo de edad de 25 a 34 años fue el de mayor prevalencia, con el 26,1 %. Los grupos de riesgos más afectados fueron: los fumadores (37,0 %), los reclusos (32,6 %), los adultos mayores de 60 años (26,6 %) y los alcohólicos (23,9 %). **Conclusiones**: la introducción del GeneXpert en su diagnóstico es muy efectiva, por su alta sensibilidad y especificidad con relación a los estudios tradicionales, como son la baciloscopia y el cultivo, además de la rapidez en la obtención del resultado. Informa también sobre la resistencia a la rifampicina, atribuible al gen rpoβ, lo que resulta muy oportuno en momentos en que la multidrogorresistencia aumenta aceleradamente.

Palabras clave: tuberculosis; factores de riesgos; resistencia a rifampicina; Mycobacterium tuberculosis

RESUMO

Introdução: a infecção tuberculosa afeta o mundo apesar de anos de estudo e avanços tecnológicos no seu diagnóstico.O ensaio Xpert® MTB/RIF permite, em grande medida, a identificação do bacilo de Koch em qualquer amostra patológica, e fá-lo com elevada sensibilidade, especificidade e rapidez em comparação com outros métodos. **Objetivo:** diagnosticar tuberculose com o ensaio Xpert® MTB/RIF. **Método:** foi realizado um estudo transversal em 46 amostras analisadas (n 46) das províncias orientais de Cuba com o ensaio Xpert® MTB/RIF, entre abril e setembro de 2023, pelo Centro Provincial de Higiene, Epidemiologia e Microbiologia de Holguín.As variáveis estudadas foram: província de origem, idade, sexo, tipo de amostra, fatores de risco, resultado de exame e resistência à rifampicina. **Resultados:** Santiago de Cuba e Guantánamo foram as províncias que notificaram o maior número de casos, com 14 casos cada (30,4%).O sexo masculino teve a maior incidência, 33 casos (71,7%), independentemente da província.A faixa etária de 25 a 34 anos foi a que apresentou maior prevalência, com 26,1%.Os grupos de risco mais acometidos foram: fumantes (37,0%), presidiários (32,6%), adultos acima de 60 anos (26,6%) e alcoolistas (23,9%). **Conclusões:** a introdução do GeneXpert no seu diagnóstico é muito eficaz, devido à sua alta sensibilidade e especificidade em relação aos estudos tradicionais, como baciloscopia e cultura, além da rapidez na obtenção do resultado.Também relata a resistência à rifampicina, atribuível ao gene rpoβ, que é muito oportuna numa altura em que a resistência a múltiplos medicamentos está a aumentar rapidamente.

Palavras-chave: tuberculose; fatores de risco;resistência à rifampicina; Mycobacterium tuberculose

INTRODUCTION

Tuberculosis (Tb) is an infectious disease caused by Mycobacterium tuberculosis (MTb) that mainly affects the lungs, but can spread throughout the body and damage the kidneys, spine, and brain.[1,2]

Worldwide, Tb is the 13th leading cause of death: in 2021, 1.6 million people died and 10.6 million became ill (6 million men, 3.4 million women and 1.2 million children) so it is estimated that a quarter of the world's population has been infected with the Tb bacillus, of which between 5% and 10% will develop the disease.[3,4,5] Likewise, the number of drug-resistant MTb strains increased by 3% between 2020 and 2021 (with 450,000 new rifampicin-resistant cases).[4]

With the COVID-19 pandemic and socioeconomic inequalities, the burden of those infected increased, especially in the most vulnerable; however, satisfactory evolutions were achieved with therapeutic regimens of 4 to 6 months in 85% of those infected worldwide, and thus transmission could be reduced.[4]

Particularly in the Americas, 215,116 cases of Tb, 32,000 deaths and 4,820 cases of drug resistance (including rifampicin-resistant and multidrug-resistant) were reported in 2021.

In Cuba, the incidence rate in 2021 was 4.3 per 100,000 inhabitants (for a total of 477 cases), and during 2022, 5 new cases of Tb per 100,000 inhabitants were recorded, representing the low incidence of the disease in the country with respect to others in the continent.[6,7] The provinces with the highest rates over the course of 2021-2022 in Cuba were Havana (188 cases), Santiago de Cuba (93 cases) and Granma (57 cases) with 8.8; 9.0 and 7.1 per 100 000 inhabitants, respectively.[8]

As part of the Tb eradication program, GeneXpert kits were distributed in different provinces of the country to ensure the diagnosis of MTb. The Xpert® MTB/RIF assay is a molecular biology assay based on a real-time polymerase chain reaction (PCR-RT) that allows the detection of a segment of MTb DNA: rpoβ. This gene corresponds to the section that detects MTb rifampicin resistance, so the test not only confirms the presence of the mycobacterium, but also determines the resistance to this drug.[9,10] In Holguin, one of these equipments was placed in order to obtain a sensitive, specific and fast diagnosis of samples from the eastern region of Cuba, so it is relevant for the medical-epidemiological knowledge the data registered from this test.

The development of this research responds to the need to choose a method as efficient as the Xpert® MTB/RIF assay (which allows the diagnosis of MTb and MTb with rifampicin resistance in less than two hours, and with a sensitivity between 88 and 99% in pulmonary samples)[9] instead of bacilloscopy, with limited sensitivity, and culture, which takes eight weeks; also valuing the relevance of the accurate diagnosis of drug-resistant strains. Objective: to diagnose tuberculosis with the Xpert® MTB/RIF assay.

METHOD

A cross-sectional study of positive cases was carried out from 200 samples analyzed with Xpert®MTB/RIF assay, from April to September 2023, at the Provincial Center of Hygiene, Epidemiology and Microbiology (CPHEM) of Holguin, from patients in Las Tunas, Holguin, Granma, Santiago de Cuba and Guantanamo.

The data are registered in the software that regulated the trial. From this population were excluded the cases with deficiencies in the registry, repeated patients with equal results and the deceased, or that when running the trial had "INVALID" or "ERROR" result. The results were grouped in a Microsoft Access 2010 database created in the processor of the Mycobacterium laboratory of that center.

The dependent variable selected was test positivity, and the independent variables were rifampicin resistance, types of samples, provinces, sex, age groups and risk groups, which were organized according to the guidelines of the National Program and Procedural Standards for the Prevention and Control of Tuberculosis in Cuba (PNCT). To this last variable was added the other aspect, where a series of factors related to the disease fit, which are not written in the program, but some physicians enunciated in the indications as possible relapses and search for resistance to rifampicin.

Sample processing and analysis

Specimen collection, storage and transportation

1. Collect at least 2 mL of unprocessed sputum or other samples, or 1 mL of sputum sediment after digestion, decontamination and concentration.
a) Reject samples with solid particles.
b) Samples with traces of blood should be heparinized.

Unprocessed sputum: keep for a maximum of 3 days at temperatures up to 35 °C, and then between 2 °C and 8 °C for up to 7 days.[9,10]

Sputum sediment: store at 2°C to 8°C for up to 7 days; or dilute 0.25 mL of sputum sediment with 0.583 mL of 100% ethanol and store at 4°C.[11]

Test Procedures

Sputum Sediment Samples
1. Transfer 1.5 mL of sample reagent (sodium hydroxide -NaOH-, pH>12.5) to 0.5 mL of sputum sediment. For higher sample concentrations, add 3 times more of the sample reagent to the sample.
2. Shake 10 to 20 times or use vortex shaker for 10 seconds.

Sputum samples or other specimens
1. Add 2 times the volume of specimen reagent to the sputum or other specimens. Example: for 1 mL of sputum, use 2 mL of specimen reagent.
2. Shake 10 to 20 times or use vortexing shaker for 10 seconds.

For both mixtures: incubate at 20 °C to 30 °C for 15 minutes. Shake again after 5 and 10 minutes.

Preparation of the cartridge

With the aid of a pipette, aspirate the mixture up to the pipette mark. If the volume is insufficient, do not continue with the test.
Dispense slowly into the cartridge.
The rest of the mixture is useful for up to 4 hours stored at 2 °C to 8 °C.[10]

Starting the test

Turn on the GeneXpert instrument system and then the computer, in that order.
The GeneXpert software will start automatically. Click on "Create test".
Scan the cartridge, record the data, and start the assay.[10]

Interpretation of the results

The Xpert® MTB/RIF assay simultaneously detects MTb and its resistance to rifampicin by amplification of the rpoβ gene specific to the MTb complex, which is probed with 5 molecular beacons to detect mutations of the drug resistance determining region. Each beacon is labeled by a different flourophore; that is why the GeneXpert system generates the results from measured fluorescent signals and integrated computational algorithms. The possible results are:

- MTB DETECTED. Rif resistance DETECTED (MTB detected. Rif. resistance DETECTED).
- MTB DETECTED. Rif. resistance NOT DETECTED (MTB detected. Rif. resistance NOT DETECTED).
- MTB DETECTED. Rif resistance INDETERMINATE (MTB detected. Rif resistance INDETERMINATE).
- MTB NO DETECTED (MTB not detected).
- INVALID.
- ERROR.(9,10)

Data collection and processing analysis

Data collection

A database was created in Microsoft Access 2010, where tables were created with the following fields, whose values were taken from the Xpert® MTB/RIF test report:

- Provinces: field that allows selecting the province that sent the sample aided by a search wizard that allows recognizing the provinces from a table that groups this data.
- Date of test: is a Date/Time field where the date on which the sample was tested is recorded.
- Date of birth: is a Date/Time field where the patient's date of birth was recorded from the ID card.
- Ages: this is a calculated field that outputs the age according to the difference between the "Test date" and "Date of birth" fields.
- Sex: in this field the biological sex is reported (F, for female and M, for male).
- Types of samples: field that allows selecting the samples that were sent aided by a search assistant that allows recognizing the types of samples from a table that groups the most frequent samples analyzed.
- Risk groups: multivalue field allowing the selection of more than one risk group aided by a search wizard that allows the recognition of sample types from a table grouping the risk groups determined by the NTP and, in addition to it, the "Others" aspect defined for other indications not mentioned in the NTP.
- Results: field that allows selecting the results issued by the test software assisted by a search assistant, whose values were mentioned in the interpretation of the results.

The statistical analysis of these variables was of absolute frequency and percentages, with the creation of query tables in the program itself, where the dependent variable was used as a reference to obtain results of the positive cases according to the needs of the research:

- Query to find duplicates: it allows knowing the repeated data, taking as reference the province, date of birth, sex and result.
- Query of positive and negative cases by province: Allows knowing the absolute frequency of positive and negative cases, respectively, according to the provinces.
- Query of positive cases by sex.
- Query of positive cases according to age groups.
- Query of risk groups of positive cases.

RESULTS

Overall, the 46 positive samples represented 23.0% of 200 samples applied to the Xpert® MTB/RIF assay between April and September 2023 in the CPHEM of Holguín, whose distributions (according to provinces) were shown in Table 1. It is showed that Santiago de Cuba and Guantánamo are the provinces with the highest number of cases reported from the Xpert MTB/RIF assay, with 14 positive cases each, which constituted 30.4%, individually.

Table 1. Cases studied by provinces applying the Xpert MTB/RIF assay

Provinces	Positive		Negative		Total	
	F. a.	%	F. a.	%	Total	%
Santiago de Cuba	14	30,4	52	33,8	66	33,0
Guantánamo	14	30,4	14	9,10	28	14,0
Holguín	12	26,1	75	48,7	87	43,5
Las Tunas	6	13,0	7	4,55	13	6,50
Granma	0	0	6	3,90	6	3,00
Total	**46**	**23,0**	**154**	**77,0**	**200**	**100,0**

Regarding the study of sample types, all cases were positive from sputum samples. Likewise, no resistance or indeterminate value was detected in terms of rifampicin resistance.

According to Table 2, it was observed that, regardless of the provinces, the disease had the greatest impact on the male sex. The total number of positives in this gender was 33 cases, which represented 71.7%.

Table 2. Cases positive for Mycobacterium tuberculosis by province according to sex using the XPERT MTB/RIF assay.

Provinces	Male		Female	
	F. a.	%	F. a.	%
Santiago de Cuba (N=14)	11	78.6	3	21.4
Guantánamo (N=14)	10	71.4	4	28.6
Holguín (N=12)	9	75.0	3	25.0
Las Tunas (N=6)	3	50.0	3	50.0
Total (N=46)	**33**	**71,7**	**13**	**28,3**

As represented in Table 3, the age groups with the highest number of Tb cases were those between 25 and 34 years (12 cases; 26.1 %), between 45 and 54 years (11 cases; 23.9 %), and those older than 65 years (10 cases; 21.7 %).

Table 3. Cases positive for Mycobacterium tuberculosis by province using the Xpert MTB/RIF assay

Age Groups (in years)	Santiago de Cuba (N=14)		Guantánamo (N=14)		Holguín (N=12)		Las Tunas (N=6)		Total (N=46)	
	F. a.	%	F. a.	%	F. a.	%	F. a.	%	F. a.	%
Between 15 and 24	1	7,14	0	0	0	0	2	33,3	3	6,52
Between 25 and 34	3	21,4	8	57,1	0	0	1	16,7	12	26,1
Between 35 and 44	1	7,14	1	7,14	1	8,33	0	0	3	6,52
Between 45 and 54	4	28,6	1	7,14	5	41,7	1	16,7	11	23,9
Between 55 and 64	3	21,4	1	7,14	3	25,0	0	0	7	15,2
Older than 65	2	14,3	3	21,4	3	25,0	2	33,3	10	21,7

The categorizations of the risk groups in Table 4 were based on the NTP, which includes 16 aspects referring to those patients who have a higher incidence of the disease and therefore require systematic screening. In addition, the "Other" aspect could be seen, which although not part of the NTP, gathers a series of specific elements, for which it was necessary to test the sample (such as relapses and search for resistance to rifampicin).[23]

In the analysis of these data, it was observed that the most prevalent risk groups were smokers (17 cases; 37.0 %), prisoners (15 cases; 32.6 %), adults over 60 years of age (12 cases; 26.6 %) and alcoholics (11 cases; 23.9 %). These data should not be viewed separately because many of these factors coincided in the same case. It is important to highlight the low prevalence of HIV and Tb co-infection (3 cases; 6.52%).

Table 3. Mycobacterium tuberculosis positive cases according to risk groups using the Xpert MTB/RIF assay

Risk groups	Santiago de Cuba (N=14)		Guantánamo (N=14)		Holguín (N=12)		Las Tunas (N=6)		Total (N=46)	
	F. a.	%	F. a.	%	F. a.	%	F. a.	%	F. a.	%
Smoker	9	64,3	4	28,6	2	16,7	2	33,3	17	37,0
Inmate/ex-convict	8	57,1	4	28,6	2	16,7	1	16,7	15	32,6
Adult over 60 years old	3	21,4	3	21,4	4	33,3	2	33,3	12	26,1
Alcoholism	6	42,9	2	14,3	2	16,7	1	16,7	11	23,9
Radiographic lung lesions	6	42,9	0	0	1	8,33	0	0	7	15,2
Contact of TBp BAAR +	3	21,4	2	14,3	1	8,33	1	16,7	7	15,2
HIV or other immunodeficiencies	1	7,14	1	7,14	1	8,33	0	0	3	6,52
Chronic diseases	2	14,3	0	0	0	0	0	0	2	4,35
Social cases	2	14,3	0	0	0	0	0	0	2	4,35
Malnutrition	0	0	0	0	0	0	1	16,7	1	2,17
Diabetes	0	0	0	0	0	0	1	16,7	1	2,17
Health care worker	0	0	0	0	0	0	1	16,7	1	2,17
Others	0	0	6	42,9	4	33,3	2	33,3	12	26,1

DISCUSSION

According to the 2022 Cuban Health Statistical Yearbook, Santiago de Cuba is one of the provinces with the highest case notification rates (second in the country and first in the eastern region), which corresponded with the analysis of this study; not so Guantánamo, which had the same number of diagnosed cases as Santiago (14 positive cases, which represented 30.4%). However, in 2022, Granma had a notification rate of 7.1 per 100,000 inhabitants (the third in the entire country and the second in the eastern region with the highest number of Tb cases) that did not even yield positivity, which drew attention in this investigation.[8]

One of the objective causes of this last trial could be the result of the number of samples sent to the CPHEM of Holguin to perform the Xpert® MTB/RIF test, and that instead, were sent directly to the National Reference Laboratory (LRN) for confirmation; other reasons may be the type of sample (extrapulmonary samples, specifically), or samples from patients under 5 years old or patients with HIV (whose samples are usually paucibacillary), and that because they did not reach the sensitivity threshold of the test, they were not positive.

Pulmonary samples are the most recommended samples for the Xpert® MTB/RIF assay. However, they account for 90% of the samples sent to the laboratory and show sensitivity results up to 99% for this assay. In HIV patients, this sensitivity can drop to 79 %, and in children to 65 %. On the other hand, the sensitivity of extrapulmonary samples decreases: tissues and lymph nodes, 85 %; cerebrospinal fluid, 79.5 %; and pleural fluid less than 50 %.[9] This is why the above-mentioned is the reason why all positive cases were sputum.

Rifampicin is an indispensable drug and the first line of treatment against Tb, so resistance to it is a poor prognostic factor. Monoresistance to rifampicin is rare and is almost always linked to resistance to other drugs (e.g., isoniazid), and is therefore considered multidrug resistant.[9] It is therefore of vital importance to recognize and study it in antibiogram and molecular biology assays of MTb strains.

In relation to Table 2, in the 2022 Cuban Health Statistical Yearbook (regardless of the fact that the representation is national), the results coincide in terms of the male gender as the most affected by MTb.[8] Likewise, in an article by Acosta Sánchez, et al.,[12] since it was carried out in Santiago de Cuba, and on the basis that cases analyzed by Xpert® MTB/RIF assay were studied, the same results were found in terms of the male gender in the variable sex with the highest prevalence of cases.

The relationship between sex and the disease is not well elucidated, but it is almost universal that the male sex represents the broadest spectrum of patients with Tb, to such an extent that even with age, the prevalence is lower in women.[13-19] Some reports point to epidemiological differences based on the association of this phenomenon with physical, emotional and psychological overload of males in the family and social environment. As an example, it should be noted that the largest prison population is male.[20]

As shown in the Cuban Health Statistical Yearbook of 2022, and in relation to the results of Table 3, it is these age groups where Tb has the greatest impact.[8] However, age alone does not define that Tb is produced and developed, so adjacent to this factor, other factors that disadvantage the body's defense mechanisms should be grouped. On the other hand, it is necessary to recognize that according to the Demographic Yearbook of Cuba of 2021, the median age is 42.3 years, which justifies the results of this study due to the direct proportionality of the population at risk, the cases sent and positive cases according to age groups.[21,22,23]

In comparison with the results offered in Table 4, articles such as those by Romero García, et al.[24] also mentioned being deprived of freedom (overcrowding factor), old age and alcoholism as the most common risk factors in the genesis of the disease; however, smoking did not even cause any impact during the five-year study period. In another study, Grave de Peralta, et al.[25] did mention smoking, followed by chronic obstructive diseases.

In Cuba, one in five persons aged 15 years and older (representing 21.6% of the population) is an active smoker, which is alarming despite the low Tb rate compared to other countries. Smoking can paralyze the respiratory cilia and hinders the expulsion of mucus from the airways; in turn, it decreases the phagocytic capacity of alveolar macrophages and induces a decrease in the formation of antibodies, making the person more likely to become ill.[26,27]

The prison population becomes ill because most of them come from strata that are high consumers of tobacco, alcohol and drugs, and are usually homeless and mentally ill: elementary circumstances that make them vulnerable to becoming ill with Tb.[28]

Old age constitutes a risk factor due to the unquestionable aging of the immune system, as well as of the other defense mechanisms of the organism.[29]

Alcoholism, in addition to being a psychosocial problem (related to family and work conflicts), can cause anemia, malnutrition and directly affect the immune system, with the consequent depression of the patient's defenses.[29]

Some limitations intercepted the investigation. The methodological limitations were justified by the fact that the samples, and in essence the extrapulmonary samples, if they had traces of blood or were of high protein origin, formed a clot. This clot was able to trap mycobacterium, which could justify that these samples could be negative to the Xpert MTB/RIF assay, because solid particles are discarded for processing. So, if the assay did not completely detect the rpoβ gene in the entire sample, the detection threshold was insufficient for the software to interpret the sample as positive.

On the other hand, sputum sediment samples could also not be worked because the centrifuge is defective, which implies that sputum samples must be worked without processing; this means that the study was less sensitive because the objective of this procedure is based on the capture and recovery of only concentrated Mycobacterium tuberculosis bacilli, thus helping to limit contamination of personnel by proportion of the sample to be analyzed.

The limitations of bias were appreciated by the defective indications: either essential data were missing, such as the identity card (from which the reference for the calculation of age was taken) or the age itself; also, the indication should have shown some data related to symptoms and signs of the patients that favored the analysis of clinical variables; and with respect to the variable of risk groups, it should have shown precisely which risk groups were identified and if they were not found in those grouped in the NTP, they should have justified the reason for sending them. For this reason, it is recommended to follow the instructions of model 64-31-04 of the Cuban Ministry of Public Health: Request for TB analysis in biological samples, for the formulation of a suitable indication.

CONCLUSIONS

Tuberculosis is an infectious disease that constitutes a health problem in the world. Socioeconomic inequalities contribute to its spread. The introduction of GeneXpert in its diagnosis is very effective due to its high sensitivity and specificity in relation to traditional studies, such as smear microscopy and culture, in addition to the rapidity in obtaining the result. It is an automated molecular assay that identifies the Mycobacterium tuberculosis complex and induces the suspicion of atypical mycobacterium. It also provides information on rifampicin resistance, attributable to the rpoβ gene, which is very timely at a time when multidrug resistance is increasing rapidly.

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The authors declare that there are no conflicts of interest.

Author contributions:

Ernesto Carmenates Ricardo: conceptualization, data curation, formal analysis, research, supervision, validation, visualization, writing original draft, writing-revision and editing.

Marilin Pérez Díaz: data curation, formal analysis, research, methodology, *Writing-review and editing:*.

Complementary file (Open Data):

Base de datos sobre diagnóstico de tuberculosis con ensayo Xpert® MT/BRIF en la región oriental de Cuba