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Screening and Managing Latent Tuberculosis Infection in the Workplace: A Model for TB Eradication in Senegal

Asséga Sylvain SAGNA[1]*, Mossane Dominique NDOUR[2], Modou Mbacké GUEYE[3] and Mame Thioro Aïssatou FALL[4]

[1]*Managem group, Boto SA, Kédougou Sénégal.*

[2]*International Committee of the Red Cross, Dakar, Sénégal.*

[3]*Gaston BERGER University de Saint-Louis, Sénégal.*

[4]*West Africa Farms (WAF), Yamane, Louga Sénégal.*

***Correspondence:**
Asséga Sylvain SAGNA, Boto SA, Managem group, Kédougou Sénégal, Tel: +221777213222.

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ABSTRACT

Background: *The elimination of tuberculosis is an increasingly common theme. This study describes the screening and management strategy for latent tuberculosis infection at SCL, with the aim of strengthening the efforts of the health authorities in the eradication of tuberculosis in Senegal.*

Methods: *We have described part of the overall public strategy for combating tuberculosis in SCL. An electronic TB risk questionnaire was used to identify people eligible for testing. The QIAreach QuantiFERON-TB essay was used for interferon gamma detection.*

Results: *A total of 107 workers out of 506 were eligible for testing, with a positivity rate of 50.47%. The main risk factor for latent tuberculosis was the contact with TB patients (59.26%). All positive cases were treated with weekly doses of Rifapentine/Isoniazid for 3 months (3HP). The treatment completion rate was 96.3%, and the most frequent adverse event was nausea. Sun exposure was correlated with a higher frequency of adverse effects, whereas the existence of a comorbidity appeared to be a protective factor.*

Conclusion: *Tuberculosis can be eradicated in Senegal with a low-cost strategy of identifying, screening, and treating people with latent tuberculosis infection. Our experience has proven to be acceptable and compliant with the weekly Rifapentine/Isoniazid regimen for 3 months. These strategies should be supported by regional labor inspectorates and rolled out on a large scale by regional health departments across the country.*

Keywords

Interferon gamma, Rifapentine+Isoniazid, Mycobacterium tuberculosis, Senegal, QIAreach, Quantiferon TB.

Introduction

Tuberculosis is endemic worldwide and is one of the deadliest infectious diseases [1-3]. More than a quarter of the world's population is said to be infected with Koch's bacillus [4-7]. It is a public health issue, especially in Africa, where it causes the highest number of deaths [1]. TB is a disease of poverty, spreading particularly in workplaces located in rural areas [8,9].

To eradicate the disease, WHO recommends strengthening prevention by treating Latent tuberculosis infection [10,11]. Latent tuberculosis infection is a state of persistent immune response to *M. tuberculosis* antigens, without visible clinical signs of active tuberculosis [11,12]. Indeed, most tuberculosis cases result from reactivation of Latent tuberculosis infection [2,11-13]. Treatment of Latent tuberculosis infection would significantly minimize the incidence of tuberculosis disease [14].Testing for LTB Infection increases the certainty that individuals targeted for Tuberculosis Preventive Treatment will benefit better from it. There is, however, no gold standard test for diagnosing LTB infection. All the currently

available tests – TST (tuberculin skin test), IGRA (interferon-γ release assay) and TBST (*M. tuberculosis* antigen-based skin test for LTB infection) – are indirect and require a competent immune response for a valid result [10,15].

Latent tuberculosis infection assessment is usually carried out for particularly exposed people, such as health-care personnel or prison employees [12,16-18].

A distinction is made between people at high risk of exposure to *Mycobacterium tuberculosis* and individuals whose health status increases the risk of developing tuberculosis [3,6]. Increasing the capacity of occupational health services to prevent, diagnose, and treat tuberculosis is a key factor in the fight against this epidemic [19,20].

In Senegal, the Ministries of Labor and Health, through the regional labor inspectorates, are inviting companies to implement workplace TB control programs. With this in mind, we have decided to expand our control strategy to include TB risk assessment, diagnosis and management of LTB infection.

This article describes the elements of this strategy at the Société de Cultures Légumières (SCL), to strengthen the local health authority's guidelines in tuberculosis elimination.

Material and Method

Diagnostic screening for Latent tuberculosis infection is part of the overall public strategy to combat tuberculosis disease at SCL, an agri-food company, specialized in the production, packaging, and marketing of fresh vegetables. The company is located in the region of Saint-Louis, North of Senegal.

We carried out a total of 4 public talks and awareness sessions with SCL workers, focusing on tuberculosis risk factors, transmission mode, clinical signs, and treatment.

We then conducted a three-day health caravan (2023 January 18 to 20) during which an electronic tuberculosis risk assessment questionnaire (TBRISK) was administered to workers, to classify them into 3 groups: Low risk, High risk, and Very high-risk.

We used the *QIAreachR QuantiFERON-TB* (QIAreach QFT) to detect the interferon gamma in blood samples from people at high risk of tuberculosis.

The QIAreach QFT assay is an in vitro diagnostic test using a peptide cocktail simulating ESAT-6 and CFP-10 proteins to stimulate cells in heparinized whole blood. Detection of interferon gamma (IFN-γ) by nanoparticle fluorescence is used to identify in vitro responses to these peptide antigens that are associated with Mycobacterium Latent tuberculosis infection.

The Very high-risk group received chest X-ray and sputum cytobacteriological examination; and the Low risk received counseling. A 3HP scheme of Rifapentin 900 mg/Isoniazid 900was administered once a week for 3 months to workers whose QIAreach QFT was positive [10,15].

Two groups were spontaneously formed: one group which opted for directly observed therapy and another one which preferred home self-administration of the treatment. The data analysis was carried out on Epi info 7.0 and Excel 2016.

It was a public health program for disease screening and management in accordance with the Senegalese Ministry of Health and Social Actions guidelines. Participation in the program was based on free and informed consent.

Results

A total of 506 workers were met under this program, men accounted for 54.3%. The average age was 36.4 years, with extremes ranging from 18 to 65 years. 107 workers (21.1%) were classified as being at high risk of TB, 8.9% at very high risk, and 69.9% at low risk.

The main risk factor for latent tuberculosis was the contact with TB patients (59.26%), followed by exposure to certain dusts (37.04%), and the presence of an immunosuppressive disease (9.26%).

The average age of high-risk workers was 37. The sex ratio was 1.7. The breakdown by occupation is shown in Figure 1.

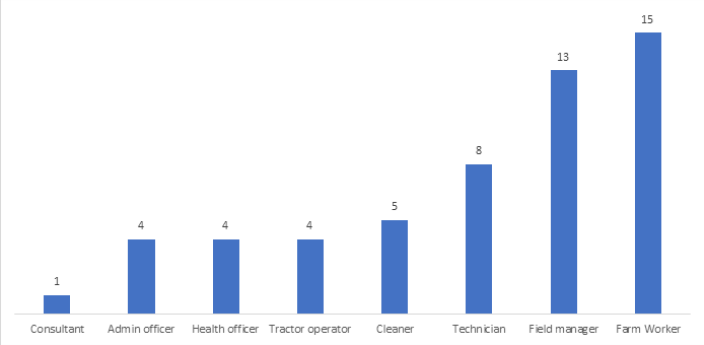

Figure 1: Breakdown of latent TB-positive workers based on occupation.

The comorbidity rate was 10.3%. Hypertension was the major comorbidity, with a prevalence of 2.8%. There were also 2 ulcer syndromes, 1 Behçet disease, 1 Lupus, and 1 HIV positive.

54 cases of Latent tuberculosis infection were confirmed by QIAREACH, i.e. 50.47% of all workers were classified as high-risk. All those workers received pre-treatment counseling. The therapeutic assessment consisted of a thorough physical examination.

All accepted the treatment; however, 72.22% accepted it immediately and 27.78% hesitated. Hesitation was due to fear that the treatment's side effects may affect work performance (40% of cases), and fear of swallowing tablets (26.67% of cases) See Figure 2.

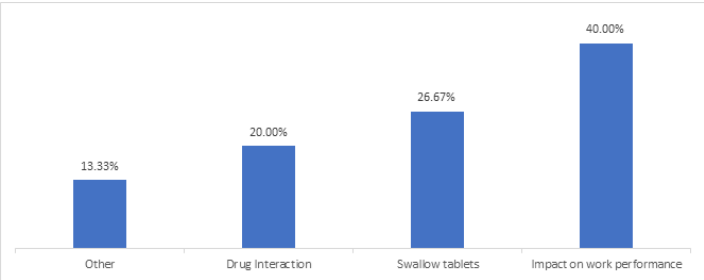

Figure 2: Reasons for reluctance to take treatment.

13 workers (24.07%) spontaneously and freely opted for directly observed therapy, and the health personnel agreed to support them.

The treatment completion rate was 96.3%. Two patients discontinued treatment after the 4th dose due to severe epigastralgia despite adjuvant therapy. 32 workers (59.26%) of those on treatment, reported one or more adverse effects. 2 required an anti-ulcer medication. Figure 3 summarizes the adverse events observed during treatment.

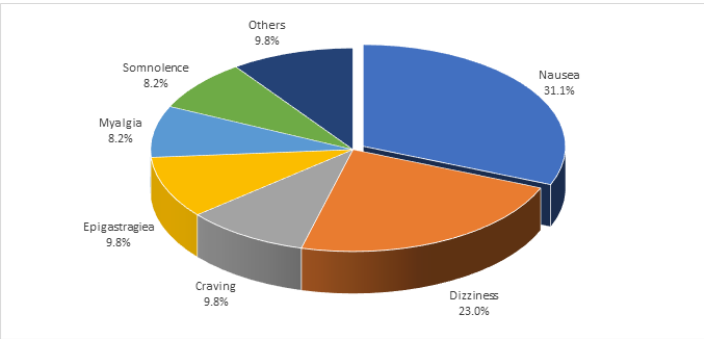

Figure 3: Ratio of treatment-related adverse events.

61.5% of workers who received directly observed therapy experienced one or more adverse effects, compared with 58.5% of those who took the treatment at home. However, the difference was not statistically significant (Table 1).

Table 1: Existence of adverse effects based on treatment option.

Directly observed therapy	Adverse effects		
	Yes	No	Total
Yes	08 (61.5%)	05 (38.5%)	13 (100%)
No	24 (58.5%)	17 (41.5%)	41 (100%)
Total	32 (59.2%)	22 (40.7%)	54 (100%)

P = 0.5

60% of women who received treatment experienced at least one adverse event, compared with 58.8% of men. However, this difference was not significant.

Among workers with comorbidity, 31.3% experienced an adverse reaction, compared with 71% of workers without comorbidity. This difference was statically significant. The existence of a comorbidity appeared to be a protective factor OD 0.18 [0.05 - 0.6] table 2.

Table 2: Adverse effects according to the existence or absence of comorbidity.

Comorbidity	Adverse effects		
	Yes	No	Total
Yes	05 (31.3%)	11(78.7%)	16 (100%)
No	27 (71%)	11 (29%)	38 (100%)
Total	32 (59.3%)	22 (40.7%)	54 (100%)

P<0.005

81.8% of workers exposed to the sun as part of their professional activities experienced adverse effects, compared with 43.7% of those who were not exposed to the sun. This difference was statistically substantial. Sun-exposed workers were 5.8 OD times more likely to experience an adverse reaction than non-exposed workers as shown in table 3.

Table 3: Adverse effects based on sun exposure.

Sun Exposure	Adverse effects		
	Yes	No	Total
Yes	18 (81.8%)	04 (18.2%)	22 (100%)
No	14 (43.7%)	18 (56.3%)	32 (100%)
Total	32 (59.3%)	22 (40.7%)	54 (100%)

P<0.005

With a 24-month follow-up, no major health events possibly related to the antibiotic therapy were observed.

Discussion

There is a real risk of tuberculosis in the workplace [20,21]. Rates of infection with LTB infection range from 31.2% in Ethiopia and 49% in Uganda to 55.2% in South Africa.

High prevalence of LTB infection has been reported in at-risk populations such as miners (89%), and from 62% to 84% in healthcare workers in high incidence countries [22].

Highly exposed occupations are not the only ones for whom tuberculosis disease is a health issue [23]. Agri-food companies which employ large numbers of workers [24,25] are the most affected in terms of tuberculosis related morbidity and mortality; hence the need for specific management [9,26,27]. Identifying persons at risk by means of a questionnaire makes it possible to identify and target people with Latent tuberculosis infection, as suggested by learned societies [6,10,28].

As in many series, Latent tuberculosis infection in our study population involved young people, mostly male [29]. This is the most active social class with a 10% risk of developing tuberculosis in their lifetime, and a 5% risk within 10 years [13]. In contrast to many series where the main high-risk factor was HIV (7), we mainly found contagious tuberculosis.

The chosen treatment regimen (Rifapentine/Isoniazid) considers treatment effectiveness, acceptability, compliance, and recommendations of the senegalese National Tuberculosis Control Program [4,12,30,31]. Indeed, the new recommendation of the National

Tuberculosis Controllers Association and CDC, 2020 considers it as the first option ahead of daily Isoniazid 300mg for 6 to 9 months [28]. This protocol has proven to be efficient, but compliance, side effects, and treatment follow-up limit its acceptability [2,4,11,30].

The administration of a 3-month-preventative treatment to our workers showed no resistance. The pre-test awareness approach used, the questionnaire administered to select candidates for latent TB testing, and the pre-treatment counseling resulted in 100% agreement for treatment and a 96.3% completion rate. This achievement is higher than those described in the literature [28,32,33].

Compliance in our study was very good, similar to that found in Norway in 2018 [34]; better than that found by Sterling and Amos in their studies [4,35] where completion rates were 82.1% and 68% respectively. In all three cases, this medication compliance was higher than other regimens management methods for latent tuberculosis [4,11,28].

In fact, the Rifapentine/Isoniazid combination once a week for 3 months provides better compliance with equal efficiency compared with the 2 other main options: 9 months of Isoniazid once weekly, and 3 months of Isoniazid daily [4,5,11,30].

There were no serious adverse effects. As in other studies, directly observed therapy showed no major adverse effects [29,34,35]. Nor did gender influence the occurrence of adverse effects. However, sun exposure was found to be associated with a significant frequency of adverse events. This seemed to be a specific to SCL but was not a reason to stop treatment. The existence of a comorbidity was a protective factor against the development of adverse effects. This differed from what D. Jarraya [36] found in the study carried out in Tunisia.

Conclusion

Tuberculosis disease can be eradicated in Senegal. However, this requires screening and management of people at risk. The strategy developed at the SCL has demonstrated the effectiveness of a simple and low-cost approach involving awareness sessions and a TB risk questionnaire to identify the patients initially.

The treatment mode of a weekly dose of Rifapentine/Isoniazid is accepted and no resistance or cultural barriers were noted. A thorough physical screening as a pre-therapeutic check-up and monitoring method reduces the constraints associated with accepting this treatment.

Regional labor inspectorates should encourage companies to step up their tuberculosis control programs by screening for and treating Latent tuberculosis infection. As for regional health departments, they should support companies' actions and take the same steps along with public services.

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