Study of the Diagnostic Delay of Tuberculosis in Spain☆

Estudio del retraso diagnóstico de la tuberculosis en España

To the Editor,

Tuberculosis (TB) control is based on early case detection, initiation and completion of treatment, effective contact tracing, and the appropriate diagnosis and treatment of tuberculous infection in people at risk of developing disease.[1] The longer a patient with pulmonary TB remains undiagnosed or untreated, the greater the chances of disease transmission and epidemic outbreaks.[2,3]

The main objectives of this study were to analyze the diagnostic delay of TB in Spain, to determine the associated factors, and to determine to what extent delays are attributable to the patient and to the health system. An observational, prospective, multicenter study was conducted in Spain in patients diagnosed with TB during the period 2015–2017 and listed in the registry of the Integrated Tuberculosis Research Program (PII-TB) of the Spanish Society of Pulmonology and Thoracic Surgery (SEPAR). "Delay attributable to the patient" (DP) was defined as the time from the onset of symptoms to the request for health care by the patient; "delay attributable to the health system" (DS) was the time from the request for assistance to the start of treatment; and "overall diagnostic delay" (OD) was calculated as DP plus DS.[4] The median diagnostic delay was calculated for each group. Variables associated in the univariate analysis with $p<0.15$ were included in a multivariate model, and adjusted odds ratios (OR) and their 95% confidence intervals (CI) were calculated, $p<0.05$ being considered significant.

Overall, 657 cases were analyzed (52% bacilliferous). Median OD for all cases was 62 days and 61 days for bacilliferous cases. DP was 29 days and DS was 11 days. The OD was attributed to the patient in 82.6% cases and to the system in 17.4%. Factors associated with diagnostic delay, defined as greater than the median delay relative to the study variables, are described in Table 1.

The greater delay observed among foreign patients is probably due to a reluctance to consult the health system because of language barriers, or cultural, social or legal factors[5]; similar results were obtained in Italy and Portugal.[6,7]

The increased delay in the outpatient system compared to the emergency department may be due to the decreased incidence of TB in recent years,[8] because physicians may be less likely to consider this diagnosis. It may also reflect better access to emergency departments.

Drug use appears as a factor associated with less delay, as there may be higher diagnostic suspicion in this group.[9]

Our results were similar to others published not only in Spain,[10,11] but also in neighboring countries.[12,13] The greater delay when exudates and biopsies are used for diagnosis, as in pleural tuberculosis, is noteworthy. These times to diagnosis must be reduced by implementing new diagnostic techniques.[14,15]

We conclude that the diagnostic delay of TB in Spain is still prolonged, while the greater part of the delay is attributable to the

Table 1
Factors associated with diagnostic delay in all study cases. Univariate and multivariate analysis of the study variables.

Variables	Total delay		Univariate analysis		Multivariate analysis	
	≤62 days n=338 (51.4%)	>62 days n=319 (48.6%)	OR (95% CI)	p value	OR (95% CI)	p value
Country of origin						
Others	98 (29.0%)	124 (38.9%)	1,557 (1,125–2,156)	0.008	1,638 (1,114–2,409)	0.012
Native	240 (71.0%)	195 (61.1%)	Ref.		Ref.	
Drugs						
No	305 (90.2%)	304 (95.3%)	Ref.		Ref.	
Yes	29 (8.6%)	12 (3.8%)	0.415 (0.208–0.829)	0.013	0.461 (0.217–0.979)	0.044
ND	4 (1.2%)	3 (0.9%)	0.752 (0.167–3.390)			
Place seen						
Hospital emergency department	206 (60.9%)	122 (38.2%)	Ref.		Ref.	
Primary care	63 (18.6%)	95 (29.8%)	2,546 (1,725–3,758)	<0.001	2,325 (1,539–3,512)	<0.001
Area specialist	39 (11.5%)	65 (20.4%)	2,814 (1,784–4,439)	<0.001	2,132 (1,295–3,509)	0.003
Others	23 (6.8%)	28 (8.8%)	2,056 (1,133–3,728)	0.018		
ND	7 (2.1%)	9 (2.8%)	2,171 (0.789–5,977)	0.134		
HIV						
No	294 (87.0%)	297 (93.1%)	2,441 (1,222–4,876)	0.011	2,773 (1,288–5,969)	0.009
Yes	15 (4.4%)	10 (3.1%)	1,611 (0.566–4,583)	0.371		
ND	29 (8.6%)	12 (3.8%)	Ref.		Ref.	
Diagnostic sample type						
Sputum	241 (71.3%)	197 (61.8%)	1,539 (1,110–2,132)	0.010		
BAS/BAL	72 (21.3%)	77 (24.1%)	1,176 (0.816–1,694)	0.219		
Exudate	51 (15.1%)	19 (6.0%)	2,806 (1,617–4,868)	<0.001	2,074 (1,134–3,795)	0.018
Gastric aspirate	3 (0.9%)	4 (1.3%)	1,418 (0.315–6,386)	0.468		
Tissue biopsies	32 (9.5%)	72 (22.6%)	2,787 (1,779–4,367)	<0.001	2,447 (1,475–4,060)	0.001
Others	36 (10.7%)	28 (8.8%)	0.807 (0.480–1,357)	0.249		
Site						
Pulmonary	258 (76.3%)	242 (75.9%)	0.975 (0.681–1,395)	0.480		
Pleural	75 (22.2%)	20 (6.3%)	4,263 (2,534–7,173)	<0.001	3,667 (2,116–6,353)	0.001
Disseminated	18 (5.3%)	20 (6.3%)	1,189 (0.617–2,292)	0.363		
Extra-pulmonary only	22 (6.5%)	64 (20.1%)	3,605 (2,161–6,014)	<0.001		

patient. Interventions to correct this situation must be based on disseminating knowledge about the disease, both among the general population and among health professionals, and improving access to health services.

Appendix A. Annex. PIITB Research Group:

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Enabling a Community Approach to Respiratory Diseases: The HACER COPD Project☆

Habilitando el Abordaje en la Comunidad de las Enfermedades Respiratorias (HACER) EPOC

To the Editor,

Over the past few decades, frequent changes in recommendations for the diagnosis and treatment of chronic obstructive pulmonary disease (COPD) and the growing number of available treatments have led to clinical scenarios of varying complexity that cannot always be resolved by the current guidelines.[1,2] This situation is particularly acute in the area of primary care (PC), where numerous diseases from different specialist areas are evaluated with limited time and resources. As a result, the PC physician often encounters clinical scenarios not addressed by the current recommendations, complicating the management of COPD patients.[3,4] In response to this situation, the Spanish Society of Pulmonology and Thoracic Surgery (SEPAR) has launched an initiative entitled "Enabling a Community Approach to Respiratory Diseases: the HACER COPD project", as a way to facilitate the management of COPD in this care setting.

The objective of HACER COPD was to design 2 pocket cards that physicians could use for quick reference, containing a simplified therapeutic scheme for stable COPD and the management of exacerbations, with clinical criteria for referral to the respiratory medicine department if necessary. To develop these cards, SEPAR contacted the major PA scientific societies and invited them to a face-to-face meeting. The working group consisted of a representative from each PA society, including the Spanish Society of Family and Community Medicine (semFYC), the Spanish Society of Primary Care Physicians (SEMERGEN), and the Spanish Society of General and Family Physicians (SEMG), the SEPAR COPD area coordinator, and a member of the SEPAR executive committee, who acted as group coordinator. The SEPAR secretary's office took care of technical and administrative needs. The representatives of each society were asked to develop 2 simple algorithms for stable COPD and exacerbations that would be discussed during the meeting, held in Madrid on October 30, 2019 at SEPAR headquarters, with the aim of agreeing on a final version.

The HACER COPD algorithm for the management of stable disease is shown in Fig. 1a. The top of the card addresses diagnosis and the need to meet 3 criteria (exposure, symptoms, and bronchial obstruction). The treatment section of the card contains a reminder of the need for adequate non-pharmacological treatment, including smoking cessation, exercise, and influenza and pneumococcal vaccinations. Pharmacological interventions are represented in the card by a 3-step scale, based on dyspnea and exacerbations as the main therapeutic objectives in the community. The

card reminds users that therapeutic adherence, inhalation technique, and the influence of comorbidities on clinical presentation should be taken into account during treatment escalation. The card includes the option of starting with 1 or 2 bronchodilators, depending on the degree of dyspnea. Referral to respiratory medicine is advised if the patient does not achieve stability with the maximum inhaled treatment, due to either exacerbations or dyspnea. Finally, the card includes the modified Medical Research Council scale currently recommended for the assessment of dyspnea[1,2] as a reminder.

The HACER COPD algorithm for the management of exacerbations is shown in Fig. 1b. The clinical approach described for the diagnosis of exacerbation underlines the need to rule out other diseases that may cause increased respiratory symptoms. The algorithm then seeks to determine the potential severity of the exacerbation according to saturation measured using pulse oximetry. The card recommends that patients with exacerbations of acute or chronic respiratory failure should be referred to a hospital. For patients with normal oxygenation, a therapeutic algorithm is established in which underlying inhaled treatment is maintained and intensified with short-acting bronchodilators, administering oral corticosteroids and adding antibiotics if sputum is purulent, with an assessment after 48–72 h. Finally, the card includes a reminder of dosing guidelines for oral corticosteroids and the main antibiotics available in PA.

Schemes for COPD management need to maintain a delicate balance between being exhaustive but complex, or simpler but incomplete. Both approaches have their advantages and disadvantages. HACER COPD is intended to be a simple strategy that strikes a balance between correct treatment in PA and referral of patients to respiratory medicine. This algorithm uses dyspnea as the initial classifier and determinant of bronchodilator therapy in stable disease. Dyspnea is the main reason for COPD patients seeking help; this is the most limiting symptom of the disease and carries implications for prognosis.[5,6] Nevertheless, HACER COPD contains some controversial areas; for example, certain markers such as blood eosinophils and bronchial reversibility have not been included. As a result, the therapeutic escalation schedule is simpler than those currently proposed. Another aspect of the algorithm that might raise questions is the idea of mild exacerbation, which, instead of being defined in detail, has been left to medical judgment. The committee understands that mild exacerbations would be those that respond well to inhalers, without the need for oral steroids or antibiotics, in line with current guidelines.

The aim of this simplified algorithm is to provide practical solutions to the early management of COPD in the PA setting. The variables it uses are easily measurable and listed in an order that is logical and easy to remember. Although COPD is a complex, heterogeneous disease, we believe that this simplified approach complies with current recommendations and, because of its simplicity, will help more COPD patients gain access to the right treatment. Sometimes, less is more.