

## Factors affecting time delay to treatment in a tuberculosis control programme in a sub-Saharan African country: the experience of The Gambia

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### SUMMARY

**SETTING:** Rural and urban health centres in The Gambia, West Africa.

**OBJECTIVES:** To estimate the time delay between onset of symptoms and initiation of treatment and identify the risk factors influencing the delay in patients with tuberculosis (TB).

**DESIGN:** Structured interviews with newly diagnosed TB patients aged over 15 years presenting to TB control staff in four health centres.

**RESULTS:** A total of 152 TB patients were interviewed. The median delay from onset of symptoms to commencement of treatment was 8.6 weeks (range 5–17). Delay to treatment was independent of sex, but was shorter in young TB patients. The median delay was longer

in rural than in urban areas (12 weeks [range 8.5–17] vs. 8 [4–12],  $P < 0.01$ ) and in those who did not attend school, but this effect disappeared after adjusting for age and area of residence. Patients who reported haemoptysis as one of their initial symptoms had shorter delays to treatment. There was no relation between duration of delay to treatment and cure rate, but longer delay did increase the risk of death.

**CONCLUSION:** Starting TB patients on treatment as early as possible plays a major role in reducing disease transmission in the community. Key to this is increasing awareness of the signs and symptoms of TB and ensuring easy access to diagnostic facilities and treatment.

**KEY WORDS:** tuberculosis; diagnosis; delay; TB control

ONE OF THE MAIN objectives of tuberculosis control is to reduce tuberculosis transmission in the community through early detection of smear-positive pulmonary tuberculosis (TB) cases and rapid administration of a full course of treatment.<sup>1</sup> As active case-detection is difficult on a large scale and requires the investment of extensive human and financial resources for a relatively poor yield of cases, most TB control programmes in developing countries use passive case-finding, relying on suspect TB cases to present to health services.<sup>2</sup>

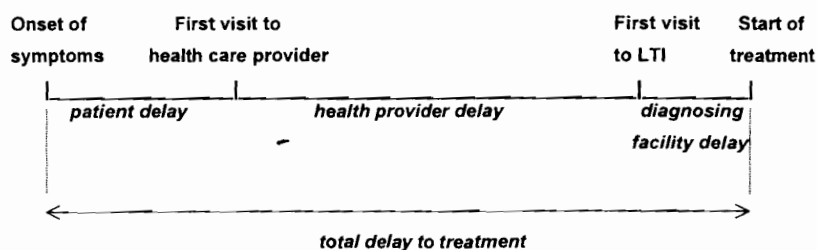
Delays in diagnosis and start of effective treatment increase morbidity and mortality from TB as well as the risk of transmission in the community.<sup>3,4</sup> Delays in diagnosis of TB have been reported in both industrialised and developing countries and vary considerably, from 6.2 weeks in Australia<sup>5</sup> to 12 weeks in Botswana<sup>6</sup> and 16 weeks in Ghana.<sup>7</sup> A number of factors have been identified that appear to influence delay in diagnosis and start of treatment. These include the individual's perception of disease, the severity of the disease, access to health services, and the expertise of the health personnel.<sup>8</sup> Operational research

directed at increasing our knowledge of the factors affecting delay to treatment has an important role to play in improving the quality and effectiveness of national TB programmes. In this paper, we present data from a study investigating the factors affecting the time period between the onset of symptoms and the initiation of treatment in adult TB patients in The Gambia, a country with a well established, decentralised TB control programme and low human immunodeficiency virus (HIV) prevalence. The study is part of a series of collaborative projects between the Gambian Department of State for Health and the UK Medical Research Council (MRC), directed at improving TB control and treatment in The Gambia.<sup>9,10</sup>

In The Gambia, tuberculosis control relies on passive detection and treatment of smear-positive cases through general and primary health care services.<sup>9</sup> All TB cases, including those diagnosed in non-governmental clinics or by private practitioners, are referred to the National TB Control Programme (NTCP), as TB drugs are not available in any pharmacies in the country. Suspect TB cases are referred to Leprosy/TB Inspectors (LTI), who are responsible for microscopic diagnosis and

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**Figure 1** Components of the time delay from the onset of symptoms to the start of treatment in patients with sputum smear-positive pulmonary TB. LTI = Leprosy/TB Inspector.

treatment of TB cases and are based in major health centres throughout the country. Since 1986, confirmed sputum smear-positive cases have been treated with a 6-month short course regimen (2RHZE/4RH\*), delivered three times weekly under strict supervision by the LTIs in the major health centres, by nurses in the peripheral health centres or by village health workers in remote areas. In 1997, 1504 new adult cases of TB were detected in the country, of whom 852 were smear-positive, corresponding to a case-detection ratio of 71/100 000.<sup>10</sup>

## METHODS

In 1997 we conducted a study among newly detected TB patients aged 15 years and over, investigating their health seeking behaviour and related expenditures before and during treatment. Those patients presenting to the LTIs in four health care facilities in the country over a 4-month period (January to April 1997) were invited to participate by the LTIs who obtained their consent for participation.

Those who agreed to participate were interviewed by an experienced MRC fieldworker, using a structured questionnaire in the language and location of their choice, within 2 weeks of diagnosis. Prior to the study, focus group discussions were held with TB patients to collect information on local terms used to describe the signs and symptoms of TB. These local terms (in various languages) were used in the structured interviews to identify the start of disease.

Information on the date of onset of first symptoms suggestive of TB was collected using a calendar based on local religious, political and agricultural events and validated prior to the study. During the interview, particular care was taken to collect information on the decision-making process concerning the choice of the person and the place for seeking care, and to identify the various health providers visited by the patient, the type of treatment given, its price and related expenditures. In the study, health providers were

broadly defined as any person consulted by the patient about his/her sickness who gave or prescribed something (whatever the form) for treatment. These included traditional healers, market drug sellers, pharmacists, village health workers (VHWs), friends and relatives as well as medical staff. The TB control programme ledgers were reviewed for each patient after they had completed, or were supposed to have completed treatment, to assess the outcome using the standard categories of the International Union Against Tuberculosis and Lung Disease (IUATLD) and the World Health Organization (WHO).<sup>1</sup> The four health centres chosen for the study detect about 80% of all TB patients diagnosed in the country. One is based in a large urban area, one in a semi-urban area and two in rural areas.

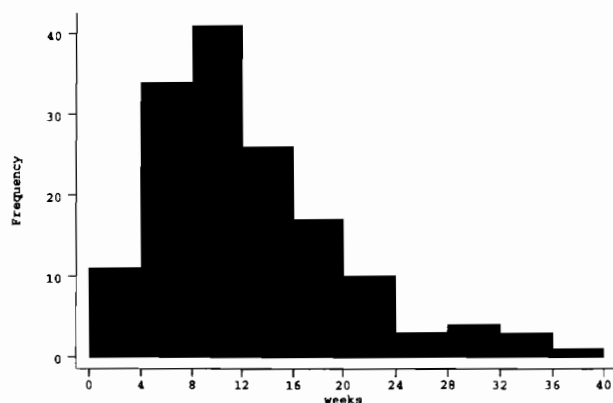
The total time from reported onset of symptoms to commencement of treatment is referred to as total delay to treatment. It was calculated using the date of initiation of treatment and the estimated date of onset of symptoms using the local calendar. Total delay to treatment is in turn divided into three periods (Figure 1): 1) patient delay—time from reported onset of symptoms to first visit to a health provider; 2) health provider delay—time from first visit to a health provider to first presenting or being referred to an LTI for diagnosis; 3) diagnosing facility delay—time from first presentation to an LTI until the start of specific anti-tuberculosis treatment.

Time delays to treatment were compared between sub-groups of patients using multi-variate analysis and Kaplan-Meier survival analysis. Distribution of delays in the study population were compared using the non-parametric Wilcoxon rank test, with a significance level of 0.05. The influence of various factors on the delay to treatment was assessed using the Cox proportional hazard model. Analysis of the results was done in collaboration with the NTCP and the results were presented and discussed with the NTCP staff at their annual meeting.

## RESULTS

During the study enrolment period, 170 individuals were newly diagnosed with TB, of whom 152 (89%) agreed to participate. There were 110 males and 42

\* R = rifampicin; H = isoniazid; Z = pyrazinamide; E = ethionamide. The numbers indicate the duration of the phase of treatment in months.



**Figure 2** Reported duration of symptoms prior to treatment (total delay).

females (mean age 36 and 30,  $t$  test = 2.56,  $P$  = 0.01); 129 (85%) subjects were Gambians, 89 lived in urban areas and 40 in rural areas, and the 23 non-Gambians came from surrounding countries (Sénégal, Guinea Bissau, Guinée Conakry). The age and sex distribution of the TB patients and the distribution of smear results were similar in urban and rural areas, with a non-significant excess of young males in the urban area (data not shown).

The distribution of the reported duration of symptoms prior to treatment is shown in Figure 2. Among the 152 subjects, the median total delay to treatment was 8.6 weeks (inter-quartile range [IQR] 5–17) and the mean, 11.5 weeks (standard deviation 7.5) (Table 1). There was no effect of sex, but the median delay was shorter for patients aged under 25 years than for patients aged over 44 (8 weeks [IQR 3.5–11.5]) vs. 13 weeks [IQR 10–17],  $P=0.04$ ). For 26 (17%) subjects, the delay between onset of symptoms and treatment exceeded 16 weeks. These patients were more likely to be older, to live in a rural area (11/40 vs. 9/89,  $P$  = 0.02), not to have gone to school (16/116 vs. 10/36,  $P$  = 0.05) and to have a lower income ( $P$  = 0.05) than those experiencing a shorter delay (<16 weeks).

The median (IQR) total delay to treatment varied with the patient's area of residence: 8 weeks (4–12) for urban Gambian patients, 12 (8.5–17) for rural Gambians and 13.5 (4–17) for foreigners ( $P$  < 0.01). Restricting the analysis to Gambians only ( $n$  = 129), the main factors influencing delay were urban location and young age (Table 2). The median delay was

shorter in Gambian TB patients who had ever attended school (8 [4–12] weeks) than among those who had not (11 [5–17] weeks), but this effect disappeared after adjusting for age, sex and area of residence. Sex and income had no effect on the delay to treatment. A survival curve using duration of symptoms before treatment as time variable shows the effect of area of residence on delay to treatment for Gambian patients (Figure 3). The median total delay to treatment varied also with the subject's occupation: the shortest delays were reported by students (4 [3–8] weeks), traders (7 [4–11] weeks) and army or police officers (8 [4–10]), whereas the longest delays were reported by farmers (14 weeks [7–18]), unemployed persons (12 [7–17]) and housewives (10 [4–14]).

The symptoms described by the patients at onset were quite different from those expressed at the time of visit to the LTI. At onset of symptoms, 80 (53%) patients reported fever, 42 (28%) reported having a 'cold', 26 (17%) a headache, 15 (10%) general body pain and 35 (23%) had cough. These symptoms are rather non-specific and could suggest other diseases such as malaria or any viral syndrome at its start. At presentation to the LTI, the symptoms were much more specific: 149 (98%) patients had cough, 100 (66%) chest pain, 118 (78%) fever and 94 (62%) had lost weight.

Thirty-three patients (21.7%) reported ever having had blood in sputum prior to presenting to the LTIs, but there was no difference in delay between them and those without haemoptysis. Six subjects, however, described having blood in their sputum at onset of symptoms and in these, the median delay was significantly shorter (3 weeks [1.5–6] vs. 8 weeks [4–13], Wilcoxon test = 4.07,  $P$  = 0.04). One third (51/152) of the subjects reported contact with a known TB case, but this had no impact on delay to treatment.

The choice of first health care provider appeared to influence the median total delay to treatment (Table 3). Patients who first visited a hospital or a private doctor reported the shortest delay from first visit to treatment (median 7.5 weeks,  $n$  = 29), whilst those who first visited a VHW reported the longest delay (median 14.7 weeks,  $n$  = 4), although numbers are small. Patients who visited a traditional healer reported a median delay of 8.2 weeks ( $n$  = 15).

The majority of patients (86%) had consulted a health care provider within 2 weeks of their reported onset of signs and symptoms. In total, 104 (68.4%) patients reported ever visiting a government health centre, 27 (18%) a private doctor, 83 (54.6%) a pharmacist or a drug seller, 45 (29.6%) a traditional healer or herbalist, 16 (12.4%) a marabout (a religious authority) and six (4%) a VHW. Patients living in rural areas were more likely to see traditional healers and herbalists than those living in urban areas (odds ratio [OR] 4.8, 95% confidence interval [CI] 1.9–12.4). The median number of providers seen prior to

**Table 1** Distribution of the various time delays among 152 smear-positive pulmonary TB patients in The Gambia

Delay	Mean (weeks)	Median (weeks)	Inter-quartile range
Patient delay	0.7	0.3	0.14–1.0
Health provider delay	10.6	8.3	4.2–13.4
Diagnosing facility delay	0.2	0.2	0.1–0.3
Total delay to treatment	11.5	8.6	5–17

**Table 2** Risk factors for delay to treatment among Gambian TB patients ( $n=129$ ). Both unadjusted and adjusted hazard ratios as well as 95% confidence intervals are shown. Adjustment was on age, sex, area of residence and school

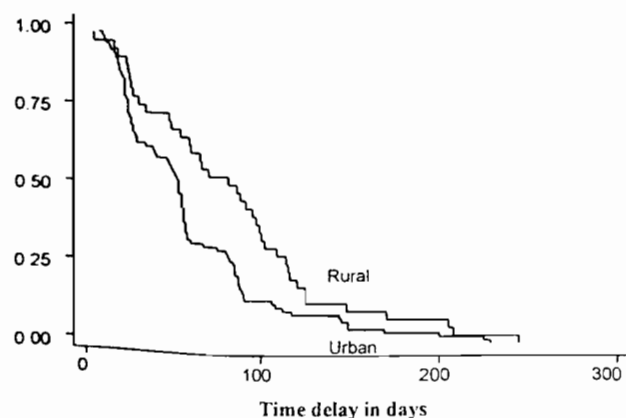
Variable	Unadjusted hazard ratio	95%CI	P	Adjusted hazard ratio	95%CI	P
Age (years)						
15-24	1			1		
25-34	0.61	0.38-0.98	0.04	0.54	0.32-0.91	0.02
35-54	0.69	0.42-1.14	0.15	0.61	0.36-1.05	0.07
>54	0.44	0.23-0.84	0.01	0.78	0.32-1.36	0.62
Sex						
F	1			1		
M	0.88	0.55-1.41	0.61	0.74	0.34-1.62	0.46
Residence						
Rural	1			1		
Urban	1.71	1.12-2.61	0.01	1.85	1.15-2.98	0.01
Income*						
1	1					
2	0.82	0.33-1.99	0.66			
3	0.95	0.57-1.58	0.85			
4	0.93	0.51-1.70	0.82			
School†						
No	1			1		
Yes	1.67	1.10-2.53	0.01	1.28	0.81-2.02	0.28
Contact						
No	1					
Yes	0.8	0.55-1.2	0.25			

\* Income group: 1) no income (housewife, student, unemployed); 2) irregular income (farmer); 3) regular income of 100-1000 Dalasis/month; 4) regular income >1000 Dalasis/month.

† School: koranic and/or secular school.

CI = confidence interval.

starting TB treatment was four (IQR 2-11), not taking into account the number of visits made to the same health provider. Female patients had seen a higher number of health providers than males (median 5 [2-11] vs. 4 [2-8], Wilcoxon  $t$ -test = 6.63,  $P=0.01$ ). Females were more likely to have visited government health centres than males (OR 4.71, 95%CI 1.62-14.2), while males were more likely to have gone to a hospital, a pharmacist or a private doctor (OR 2.12, 95%CI 0.95-4.81). There was no effect of age, area of residence, education, income or occupation on the



**Figure 3** Kaplan-Meier estimates of the proportion of patients not yet put on treatment, according to geographical area (urban/rural) in The Gambia.

number of providers seen. The majority of patients (73, 48.6%) were referred to an LTI by a government nurse or a doctor. NGOs and private nurses referred 50 (33.3%) patients, private doctors nine (6%), pharmacists two (1.3%), relatives or friends nine (6%), and seven (4.6%) self-referred, because they had heard that 'TB inspectors cure cough'.

Information on the outcome of treatment was available for 148 subjects: 112 (75%) were cured (proven smear negative after treatment), 19 (13%) defaulted, nine (6%) died and eight (5%) failed treatment. Cure was associated with sex (risk ratio [RR] for females = 1.42, 95%CI 1.19-1.72,  $P=0.001$ ), income ( $\chi^2=14.66$ , 3 df,  $P=0.002$ ) and area of residence (RR for urban residence = 1.29, 95%CI 0.98-1.69,  $P=0.04$ ). The duration of delay to treatment had no effect on cure rates. Although the death rate in the cohort was small, patients reporting a delay to treatment of more than 8 weeks were more likely to die than those reporting a delay of less than 8 weeks (RR = 5, 95%CI 1.1-24,  $P=0.02$ ). No association was found between delay to treatment and defaulting during treatment.

## DISCUSSION

The total delay to treatment observed in this study was shorter than the delays reported in other studies in adults in sub-Saharan Africa (12 weeks in Botswana,<sup>6</sup> 16 weeks in Ghana,<sup>7</sup> 16-20 weeks in

**Table 3** Choice of first provider by area of residence and influence on total delay to treatment among pulmonary TB patients in The Gambia

Type of health provider	Rural <i>n</i>	Median delay (inter-quartile range)	Urban <i>n</i>	Median delay (inter-quartile range)
Health centre	13	12.1 (5.8–21.1)	29	7.8 (3.5–10.8)
Traditional healer	6	10.0 (8.2–11.8)	7	8.2 (8–8.5)
Drug seller	9	12.2 (5.7–16.5)	20	8.2 (4.1–12.5)
Private doctor	2	13.0 (9.0–17.0)	10	4 (2.8–4.5)
Hospital	2	14.7 (5.7–23.3)	17	8 (4.1–10.8)
Friends	5	16.5 (12.7–16.8)	5	6.4 (3.2–8.2)
Village health worker	3	16.8 (12.5–29.5)	1	12.7
All	40	12.3 (7.4–16.8)	89	8 (4–11.8)

Kenya<sup>11</sup>). This could be related to the method of estimating the time from onset of symptoms to initiation of treatment, but could also reveal a true difference in delay to diagnosis and treatment. To estimate the date of onset of symptoms, we used a local calendar listing the main national, religious and agricultural events chronologically over the year. Despite prior validation of this local calendar and careful interview of the patients, the estimation of the date of onset of symptoms is liable to error, due to recall bias and individual variations in the perception of disease. In addition, what has been defined as the 'onset of symptoms' by the patient could in fact be related to another disease that either coincided with the beginning of TB or had favoured it.<sup>12</sup> Indeed, patients frequently reported symptoms suggesting malaria or a viral infection at onset of disease. The estimate of the delay to treatment therefore lies within a wide range, whose limits are defined by the occurrence of main events over the year (the local calendar) and the individuals' perception of disease.

Together, the health provider delay and the diagnosing facility delay form the 'health services delay', also referred to by other authors as 'doctor's delay'.<sup>13</sup> We prefer the use of 'health provider delay', which takes into account the wide variety of health providers seen by patients in The Gambia. In this study, the health provider delay represented the main part of the total delay to treatment, whereas patient delay and diagnosing facility delay accounted on average for less than 10% of the total delay. The majority of patients reported visiting a health provider within 2 weeks of the onset of signs and symptoms. This short patient delay probably reflects good awareness of health problems in the population and easy access to health care. The Gambia is a small, densely populated country with good access to health care facilities. Over 85% of the population lives within 3 km of a primary health care or outreach health post and over 97% of the population lives within 5 km. The short diagnosis facility delay observed in the study probably reflects the fact that patients were recruited into the study when they were diagnosed by an LTI as sputum smear-positive pulmonary TB case, and the stan-

dard practice in the Gambia is to start treatment as soon as a positive diagnosis is made.

The median time observed between the first visit to a health provider and referral to an LTI was, however, much longer than the period from onset of symptoms to first visit to a health provider. This is similar to observations in Botswana<sup>6</sup> and in Ghana,<sup>7</sup> where doctor's delay largely exceeded patient's delay, but opposite to what was observed in Korea.<sup>13</sup> The results presented here are, however, not directly comparable to other studies, as we used a broader definition of health provider and included alternative providers who play an important role in The Gambia. Whilst the interviews showed that traditional healers and herbalists were not frequently visited at the onset of symptoms (only 15% of the patients reported visiting them as the first provider), they were used by a number of patients (51/152 = 39%) during the course of their illness, in parallel with other providers. The long health provider delay almost certainly reflects insufficient knowledge of the signs and symptoms of TB among the different types of health providers and the general population. This is substantiated by the fact that 49% of TB suspects were referred to the LTIs by government health services, although altogether 68% of patients reported ever visiting a health centre.

We observed a striking difference in health seeking behaviour patterns between urban and rural areas and young and old individuals. As in Botswana,<sup>6</sup> Ghana,<sup>7</sup> Kenya<sup>12</sup> and Korea,<sup>13</sup> rural residence was a risk factor for late diagnosis. This can be explained by several factors, including poorer access to health care in rural areas, lack of training of village health workers, lack of supervision of health staff at peripheral level and differences in education levels between rural and urban areas.<sup>14</sup> However, despite a male excess among TB patients, we found no difference in time to diagnosis between men and women, a finding similar to Botswana.<sup>6</sup> This is different from Ghana,<sup>7</sup> where women reported a longer delay to treatment than men. A possible explanation is that in The Gambia women regularly attend health centres for antenatal care and child immunisations, and hence may report more easily to health centres when necessary.<sup>7</sup>

The fact that patients reporting a delay to treatment of more than 8 weeks were more likely to die than those reporting a delay of less than 8 weeks might reflect a difference in severity of disease, but also the deterioration of the physical condition of the patients in the absence of effective treatment. This reinforces the importance of detecting TB as early as possible, both for the patient's own health and for the decrease in transmission of infection in the community.

Studies like the one presented in this paper can be conducted by national TB control programmes and generate useful information to improve the quality of services and strengthen the objectives of disease control. This study, conducted in collaboration with the NTCP in the Gambia, highlights the importance of improving referral systems and access to diagnostic facilities for TB, at the same time as improving access to treatment if one wants to reduce transmission of TB in the community. It shows also the importance of increasing awareness of the signs and symptoms of TB in the general population and working closely with health providers at all levels, including pharmacists, drug sellers, traditional healers and herbalists. The research results were presented to the TB control staff during a workshop and a series of recommendations based on these results have been made. These recommendations include the provision of on-the-job training to health providers working within and outside the government health services, and the promotion of a concerted effort to increase awareness of the signs and symptoms of TB in the general population to encourage self-referral to the health services and thereby increase passive case detection.

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#### RÉSUMÉ

**CADRE :** Centres de santé en zones rurales et urbaines en Gambie, Afrique de l'Ouest.

**OBJECTIFS :** Estimer le retard au diagnostic et la mise en route du traitement et identifier les facteurs de ce retard chez les patients tuberculeux.

**SCHÉMA :** Interviews structurés de patients tuberculeux âgés de plus de 15 ans nouvellement diagnostiqués par le Programme de lutte antituberculeuse dans quatre centres de santé.

**RÉSULTATS :** On a interviewé 152 patients tuberculeux. La durée médiane allant du début des symptômes au commencement du traitement était de 8,6 semaines (5-17). Le retard à la mise en route du traitement était

indépendant du sexe mais plus court chez les jeunes patients tuberculeux. Le retard médian était plus long en zone rurale qu'en zone urbaine (12 semaines [8,5-17] vs. 8 [4-12],  $P < 0,01$ ) et chez ceux qui n'étaient pas scolarisés. Ce dernier effet disparaissait toutefois après ajustement pour l'âge et le lieu de résidence. Le retard au diagnostic était plus court chez les patients qui ont signalé une hémoptysie parmi leurs symptômes initiaux. On n'a pas noté de relation entre la durée du retard au traitement et le taux de guérison, mais un retard prolongé augmentait le risque de décès.

**CONCLUSION :** La mise en route aussi précoce que possible du traitement chez les patients TB a un impact

majeur sur la réduction de la transmission de la tuberculose dans la communauté. Deux aspects essentiels en sont la connaissance des signes et symptômes de la maladie

par le personnel médical, para-médical et la communauté, et l'assurance d'un accès facile des patients aux structures de diagnostic et au traitement.

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**RESUMEN**

**MARCO DE REFERENCIA:** Centros de salud rurales y urbanos en Gambia, África Occidental.

**OBJETIVO:** Estimar el lapso entre el comienzo de los síntomas y la iniciación del tratamiento e identificar los factores de riesgo que influenciaron esta demora en los pacientes con tuberculosis (TB).

**MÉTODO:** Entrevistas estructuradas de nuevos pacientes con TB de más de 15 años de edad que consultan en cuatro centros de salud.

**RESULTADOS:** Se entrevistaron 152 pacientes con TB. La mediana de la demora desde el comienzo de los síntomas hasta el inicio del tratamiento fue de 8,6 semanas (5-17). La demora para el tratamiento fue independiente del sexo, pero fue más corta en los pacientes más jóvenes. La mediana de la demora fue más larga en las

áreas rurales que en las urbanas (12 semanas [8,5-17] vs. 8 [4-12],  $P < 0,01$ ) y en quienes no concurrían en la escuela, pero este efecto desapareció con el ajuste por edad y área de residencia. Los pacientes que presentaban hemoptisis como uno de los síntomas iniciales tenían demoras más cortas para el tratamiento. No existió relación entre la demora para el tratamiento y la tasa de curación, pero las demoras más prolongadas aumentaron el riesgo de muerte.

**CONCLUSIÓN:** El comienzo del tratamiento de la TB lo más temprano posible desempeña un papel importante para reducir la transmisión en la comunidad. La clave para ello es el mayor conocimiento de los signos y los síntomas de la TB y asegurar el acceso a los centros de diagnóstico y tratamiento.

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