Original article

The impact of functional performance, HIV status, malnutrition, and clinical features on treatment outcomes of patients with pulmonary tuberculosis

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Abstract: We studied the influence of functional performance, clinical features, state of nutrition and HIV status at diagnosis on the outcome results of patients with pulmonary tuberculosis at a Yirga Alem Hospital in south Ethiopia. In prospective study, we investigated by functional, clinical, and nutritional methods 239 consecutive patients with pulmonary tuberculosis. Two handred out of 239 (83.7%) patients were unable to work (KPS= <70) at first presentation. HIV positive tuberculosis patients had lower KPS (mean (SD) 56.2 (21.9)) than HIV negative tuberculosis patients (66.1 (13.4)) (Mann-Whitney test, $p<0.013$). The poor functional performance was significantly correlated with malnutrition as measured by low body mass index, low arm circumference and low body weight. The 26 admitted patients had a mean KPS of 49 compared with 67 among the other patients (Mann-Whitney test, $p<0.001$).Five out of 26 (19.2%) hospitalized patients died compared with seven of 124 (5.6%) of patients treated at the outpatients' department (Fisher's exact test, $p=0.04$). Patients who died had a lower KPS than the other patients (Mann-Whitney test, $p=0.045$). Clinical features such as diarrhoea, skin disorders, neuropsychiatric impairment, and low Mantoux reactivity were significantly associated with a bad outcome of treatment. Our study concludes that some clinical features influence outcome of treatment with tuberculosis patients. However, the KPS is a better predictor to measure the need of health care than the outcome of treatment. [*Ethiop. J. Health Dev.* 2000;14(2):177-182]

Introduction

Some African countries have seen dramatic rises of tuberculosis (TB) case loads from HIV associated tuberculosis (1). The increase in cases of AIDS and HIV-related illness has placed an enormous burden on the already overstretched healthcare systems (2). Thus, studying the pattern of severity of the illness is important as it may help to predict medical care needs.

The association between severity of infection, malnutrition and functional status is complex. From rural Ethiopia we know that malnourished individuals are more likely to suffer from infections and have a reduced ability to work (3). Knowing the extent to which clinical variables, reduced functional performance, and malnutrition influence treatment needs and outcomes is important. However, the specific effect of disease-related clinical variables, extent of disease and level of functional performance in tuberculosis patients has been less well studied. Nor do we know if functional performance assessment is important to predict the treatment outcome in patients with pulmonary tuberculosis. To our knowledge, there is no study which looked at KPS with outcome of TB treatment.

The purpose of this study was to examine the influence of functional performance, HIV status, state of nutrition, and clinical features at the time of diagnosis on the treatment results of patients with pulmonary tuberculosis.

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Methods

We carried out the study at Yirga Alem Hospital in Sidama, one of the most densely populated areas in South Ethiopia. The rural population are mainly subsistence farmers. The hospital's primary catchment area is the Sidama Zone (province). Annually about 55, 000 out patients and 5, 000 admitted patients receive treatment of any form (4).

The tuberculosis control programme: The Yirga Alem Hospital Tuberculosis Control Programme has since 1992 been organized from the hospital through the existing networks of clinics and health stations in Dale, Shebedino, and Aletta Woredas (sub-provinces) with an estimated population of one million people (5). The Ministry of Health (MOH) and non-governmental organizations supporting health institutions cooperated on the tuberculosis programme. The tuberculosis cotrole programe in Sidama followed the National TB and Leprosy Control Programme (NTLCP) (6). A separate tuberculosis unit coordinated the work and a coordinator at the hospital regularly supervise all units within the control area.

All the key personnel were trained for this programme. The senior personnel (two physicians and one nurse) had completed national courses on tuberculosis control. The hospital's laboratory regularly did acid fast bacilli (AFB) staining and performed tuberculosis cultures. The drug supply was regular and there was no interruption in essential services such as supervision or laboratory functions. The project was supported by external funds.

Investigation of patients: From July to December 1995 we studied 239 consecutive patients with pulmonary tuberculosis (8). There were 166 (69.5%) men and 73 (30.5%) women. The median age was 25 while the range was(15-75 years. We have previously reported the main characteristics and clinical findings (7).Tuberculosis was considered proven when a Ziehl Neelsen stain of sputum showed AFB (8). We include only patients with smear positive sputum in the study. Standardized methods were used to measure anthropometric variables of patients (7,9).

Patients were treated according to NTLCP protocol (6). The outcome of treatment in relation to various types of regimen was dealt with in a separate article (10). We assessed and categorized treatment outcomes as Cured (patient who is smear-negative at completion of treatment and on at least one previous occasion), Treatment Completed (patient who has completed treatment but without proof of cure), Treatment Failure (patient who remains or becomes smear-positive at five months or later during treatment), Died (patient who died for any reason during treatment), Treatment Interrupted or default (patient whose treatment was interrupted for two months or more), and Transferred Out (patient who has been transferred to another treatment unit and for whom the treatment outcome is not known) (8).

In July 1998, we reviewed the records of the same patients and information on initial documentation, diagnosis, treatment, followup procedures and treatment outcomes were recorded.

Functional performance status: Functional status assessments are frequently used to complement medical information to characterize the impact of disease on the patient (11). Loss of function is generally related to the cumulative physical, physiological, and psychological effects of the disease. The Karnofsky Performance Status Index (KPS) is a descriptive, ordinal scale by which the patient functional status is rated at 10-point intervals from zero to 100 (Table 1). Scoring is based on observable characteristics and patient interview. Patients' functional status was sub-categorized to three parts for some statistical analysis: mild (80-90, able to do usual activities of daily living with special care); moderate (50-70, able to live at home and care for most personal needs); severe

(=< 40, unable to care for self). We measured the KPS before we knew the result of the HIV test.

Ethical considerations: We obtained informed oral consent from each patient before the clinical examination and laboratory investigations. All the HIV positive patients received post test counselling.

Data analysis and statistical analysis: Data and statistical analysis were done with the SPSS for Windows Version 7.5 (SPSS 1997). Descriptions of the data and comparison between different groups were analysed using standard statistical procedures. All statistical tests for continuous (student's t-test) and categorical variables were two tailed. Differences between non-normally distributed groups were assessed using non-parametric Mann-Whitney test. We calculated the 95% confidence intervals (95% CI) for proportions as described by Gardner and Altman (12). P values <0.05 were considered statistically significant.

Result

Functional status, HIV infection, and malnutrition: The median KPS was 70while the range was 10-90 and similar for males and females. Of the patients 39 (16.3%) had a KPS between 80-90 (mild), 175 (73.2%) had a score of 50 to 70 (moderate) and 25 (10.5%) had KPS with a score of =<40 (severe).Two handred out of 239 (83.7%) of the patients were unable to work (KPS=<70) at first presentation. HIV positive tuberculosis patients had lower KPS (mean (SD) 56.2 (21.9)) than HIV- negative tuberculosis patients (66.1 (13.4)) (Mann-Whitney test, $p<0.013$).

One hundred eighty (77.9%) of the patients were malnourished (Body mass index or BMI <18.5). Of these, 44 (18.2%) were mildly, 39 (16.1%) moderatly and 104 (43%) were severely malnourished. Based on the mid upper arm circumference (MUAC) assessment 161/167 (96.4%) of men (MUAC=<24cm) and 91/75 (94.7%) of women (MUAC=<23) were malnourished. Poor functional performance was significantly correlated with reduced BMI ($r=0.49$; $p<0.001$), low MUAC ($r=0.56$; $p<0.001$), and low body weight ($r=0.45$; $p<0.001$), but not height ($r=0.12$; $p=0.07$).

Table 1: **The Karnofsky performance status index (K & S indese)**

General category	Index	Specific criteria
Able to carry on normal activity; no special care needed	100	Normal, no complaints, no evidence of disease
	90	Able to carry no normal activity; minor signs or symptoms of disease
	80	Normal activity with effort; some signs and symptoms of disease
Unable to work, able to live at home and care for must personal needs, varying amount of assistance needed	70	Cares for self; unable to carry on normal activiy or to do active work
	60	Requires occasional assistance but is able to care for most of needs
	50	Require considerable assistance and frequent medical care
Unable to care for self, requires institutional or hospital care or equivalent, disease may be rapidly progressing	40	Disabled; require special care and assistance
	30	Severely disabled; hospitalization is indicated although death is not imminent
	20	Very sick; hospitalization necessary'; active supportive treatment necessary
	10	Moribund; fatal processes progressing rapidly
	0	Death

Some factors associated with the outcome of treatment: After excluding the patients who transferred out, 100 (61.0%; 95% CI 53.0-68.4) were cured (22.6%) or completed the

treatment (38.4%), 3 (1.8%) remained smear-positive at five months or later during treatment, 12 (7.3%) died, and 49 (29.9%) interrupted their treatment.

Table 2 shows the association between treatment outcome and KPS values at the start of treatment. Patients who died had a lower KPS than the other patients (Mann-Whitney test, p=0.045). 3 of 14 (21%) patients with severe functional impairment died compared with 9/136 (6.6%) with better KPS score (Fisher's exact test, p=0.08). 4/23 (17.4%) patients with HIV infection died compared with 8/127 (6.3%) among the HIV negative patients (Fisher's exact test, p=0.09, which was not significant).

Table 2: **Treatment outcome for the different types of patient categories and KPS values at the start of treatment**

Treatment outcome	Count	Mean	Median	Percentile	
				25	75
Cured	37	65	70	60	70
Treatment completed	63	66	70	60	70
Died	12	52	60	27,5	67,5
Bact pos	2	70	70	70	70
Defaulted	49	62	70	57,5	70
Transferred out	76	65	70	60	70

KPS = Karnofsky Performance Status Index

Twenty six patients who were admitted and had a mean KPS of 49 compared with KPS value of 67 among the other patients treated at the outpatients' department patients (Mann-Whitney test, p<0.001). Among the hospitalized patients, 5/26 (19.2%) died compared with 7/124 (5.6%) of patients treated at the outpatients' department (Fisher's exact test, p=0.04). 14.6% of the malnourished patients died compared with 6.5% among the well-nourished group (Fisher's exact test, p=0.31).

Common clinical findings such as cough, fever, night sweat, and chest pain were not associated with increased risk of death (data not shown). However, patients with clinical features such as diarrhoea, skin disorders, neuropsychiatric impairment and low Mantoux reactivity had higher death rates (Table 3).

Table 3: **The association of clinical factors and outcome of treatment**

Variable		Cured and treatment completed	Treatment failure	Defaulted	Died	Total	OR death	95%CI
Diarrhoea								
	Yes	12	0	8	5	22	5.63	1.61-19-72
	No	88	2	44	7	141		
Neuropsychiatric impairment		19	0	13	6	38	3.72	
	Yes	81	2	36	6	125		1.12-12.31
	No							
Skin lesion (generalized)		19	0	15	7	41	4.92	
	Yes	81	2	34	5	122		1.44-16.15
	No							
Generalized pruritus		12	0	13	5	30	3.60	
	Yes	80	2	36	7	133		1.06-12.26
	No							
Low Mantoux reactivity		15	0	12	5	32	3.64	
	Yes	83	2	33	6	124		1.03-12.82
	No							

95%CI : confidence interval

Discussion

Many Ethiopian patients with tuberculosis have low functional status when first seen at a tuberculosis treatment unit. Low functional status is associated with HIV infection and malnutrition. Although patients with a low functional status had higher mortality rates, the functional status may be a better predictor to measure the burden of disease, e.g. need of hospitalisation, than to predict the outcome of the disease.

One of the limitations of the KPS method is that it excludes some aspects of health-related quality of life measures such as the cognitive state of patients. The value of the KPS measure as a predictor for the outcome of treatment of tuberculosis has also been inconclusive in our study as also observed for non-cancer patients (13-15). However, it appears to be important in tuberculosis patients to measure the burden of health care needs (16) as our patients who were admitted had significantly low KPS compared to the other patients treated at the outpatients' department patients.

We have identified that HIV infection and malnutrition are significantly associated with poor functional status (KPS). Our study also concludes that certain clinical features such as diarrhea, neuropsychiatric impairment, skin disorders (generalized), and lower reactivity of Mantoux will influence outcomes of treatment with tuberculosis patients. These are clinical features often associated with HIV infection or severe malnutrition (7). Our study confirms previous reports that tuberculosis patients have a favourable prognosis provided they receive proper treatment (17). However, many of these patients are at the late stage of HIV infection and have severe malnutrition (7) and are in need of special care and attention. Such patients may place a heavy burden on already limited resources in the hospital wards.

The increase in cases of tuberculosis and AIDS has placed on an enormous burden on an already overstretched healthcare system at hospitals such as in Yirga Alem. Many of these patients may therefore need more resources. In another study from Yirga Alem we have shown that patients with pulmonary tuberculosis present late to treatment (18). Patients who present late may be more infective and have more severe disease. Also, low level of education is associated with longer duration of symptoms and more severe disease (18). Therefore, health workers need practical advice on how to start interventions early to reduce the long duration of symptoms. Health education both to patients, their families, to schools and to community leaders may thus be appropriate.

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