Deaths in adults with notified pulmonary tuberculosis 1983–5

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Abstract

For a study of fatality in pulmonary tuberculosis in England and Wales, a sample (n = 1222) of patients notified in 1983 as having tuberculosis confined to the lungs was selected and their mortality up to the time of finishing chemotherapy calculated. During that time 158 patients died, a case fatality of 12·9%. Stratification by age and radiographic extent of disease confirmed these as important predictors of death. Comparison with a referent population showed that the all cause mortality among people with pulmonary tuberculosis was 10 times greater than that of the age and sex matched general population. This ratio fell with increasing age and with extent of disease. Coefficients derived from a logistic regression analysis allowed probability of death during chemotherapy of patients with pulmonary tuberculosis to be estimated.

Over the past decade more than 3500 cases of pulmonary tuberculosis in England and Wales have been notified each year; in 1988 the figure was 3672 (Office of Censuses and Surveys, personal communication). Despite effective treatment the disease continues to have an appreciable mortality and in 1988, for example, it resulted in 382 deaths.

Published mortality statistics are unlikely to reflect case fatality accurately. Deaths certified with pulmonary tuberculosis as the underlying cause are classified in one of two different categories: International Classification of Diseases (ICD) code 011, "pulmonary tuberculosis," and ICD code 137, "late effects of tuberculosis." These codings do not reliably distinguish deaths in patients with recently notified disease from those whose disease is old and inactive. Furthermore, published mortality statistics do not provide information on the characteristics of patients that might be important in determining mortality, in particular racial origin and disease severity.

The purposes of this study were to determine the current case fatality rate in patients notified as having pulmonary tuberculosis in England and Wales, and to assess the factors that contributed to death.

A retrospective examination of the records of a random sample of patients with respiratory tuberculosis notified in Scotland in 1968[1] indicated a mortality of 11% in the two years after the start of chemotherapy. A case fatality rate before completion of chemotherapy of 12% was reported in a survey, similar to the present one, of adults with pulmonary tuberculosis notified in England and Wales in 1978–9.[2] Increasing age and radiographic extent of disease were found to be important prognostic factors; sex and racial origin were not independent risk factors. In a study of deaths from all forms of tuberculosis in Hong Kong in 1975–6[3] the death rate from tuberculosis was estimated to be 13·1/100 000 of the general population. Death rates rose with increasing age and were consistently higher in males than in females. More deaths in men than in women were associated with concurrent diseases, cigarette smoking, or living alone. In none of these surveys was comparison made with individuals of similar age and sex without tuberculosis.

Methods

PATIENTS

The present study is of adult patients notified with pulmonary tuberculosis in England and Wales in the first six months of 1983. We included only adults (aged 15 years or more) of white or Indian subcontinent* ethnic origin notified as having pulmonary disease alone, with no history of previous treatment for tuberculosis; those with evidence of initial resistance to antituberculosis drugs were excluded. We did not include 50 patients who were notified with pulmonary tuberculosis after postmortem examination, but in whom the disease had not been suspected in life. In this way 1643 subjects were initially selected for study.

Notifying physicians were asked to provide a chest radiograph taken in the period extending from six weeks before to four weeks after the start of treatment. Radiographs were not available for 90 (5·5%) subjects and these were excluded from further study. At independent assessment by a consultant radiologist 324 radiographs from the remaining subjects were judged not to show evidence of pulmonary tuberculosis; 302 (88%) of these showed only enlarged nodes or pulmonary effusions, and the remainder were either normal (32, 10%) or not assessable (6, 2%). These 324 subjects were excluded from analysis. Of the remaining 1229 subjects, seven were resident abroad at the time of notification and were also excluded, leaving 1222 cases for analysis; these represent 93% of those notified as having pulmonary tuberculosis who were found to have a pulmonary lesion at independent radiographic assessment.

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Table 1 Distribution of cases and case fatality by age, sex, and racial origin

	Male		Female		All	
Age (y)	*Cases*	*Deaths (%)*	*Cases*	*Deaths (%)*	*Cases*	*Deaths (%)*
White						
15–54	294	13 (4·4)	151	7 (4·6)	445	20 (4·5)
55–74	265	62 (23·4)	80	9 (11·3)	345	71 (20·6)
75+	99	42 (42·4)	38	15 (39·5)	137	57 (41·6)
All ages	658	117 (17·8)	269	31 (11·5)	927	148 (16·0)
Indian subcontinental origin						
15–54	105	1 (1·0)	140	2 (1·4)	245	3 (1·2)
55–74	21	3 (14·3)	25	1 (4·0)	46	4 (8·7)
75+	3	3 (100)	1	0 (0)	4	3 (75·0)
All ages	129	7 (5·5)	166	3 (1·8)	295	10 (3·4)

Basic demographic details and information on radiographic disease severity and outcome to the end of chemotherapy were collected for all the cases; information on social and economic circumstances was not available. The 90 subjects without radiographs were not significantly different from the remaining study subjects with respect to sex and racial distribution; their mean age (56·2 years), however, was greater than that of the other subjects (49·4 years).

In view of the difficulty in distinguishing, on the basis of death certificates, deaths due to active tuberculosis from those in which tuberculosis was only contributory,[4] the analyses refer to deaths from all causes.

FOLLOW UP

Two years after notification the physician responsible for each patient in the study group was contacted and asked to provide details of the patient's treatment and condition at the time of finishing chemotherapy. Severity of disease at the time of starting treatment was assessed on the basis of the pretreatment radiographic extent of disease. Cases were divided into three categories of increasing severity according to the number of lung zones or equivalent area affected (1—less than one; 2—one but less than three; 3—three or more).

Case fatality rates were calculated for the whole study group and analysed by age, sex, racial origin, and radiographic extent of disease. The observed deaths before completion of chemotherapy were compared with the expected number based on age and sex specific all cause mortality rates for 1983 for the total population of England and Wales.[5] Expected numbers were calculated by applying national rates to each individual's period of risk (that is, duration of chemotherapy).

A stepwise logistic regression analysis, with the probability of death during chemotherapy as the outcome variable, was used to determine which factors most strongly predicted death during chemotherapy. Age, category of radiographic severity, sex, and racial origin were taken as independent variables. The regression coefficients derived from this model were used to estimate probabilities of death in patients with pulmonary tuberculosis.

Results

DISTRIBUTION OF CASES AND CASE FATALITY RATES

The age and sex distributions of the patients, by racial origin, are shown in table 1; 927 (76%) of the patients were white. Of these 482 (52%) were aged 55 years or more, compared with

Table 2 Case fatality by age, sex, and severity of disease

	Total radiographic extent of disease*					
	<1		*1–2*		*>3*	
Age (y)	*Cases*	*Deaths (%)*	*Cases*	*Deaths (%)*	*Cases*	*Deaths (%)*
MALE						
15–54	177	2 (1·1)	169	6 (3·6)	53	6 (11·3)
55–74	86	16 (18·6)	145	31 (21·4)	55	18 (32·7)
75+	25	5 (20·0)	51	26 (51·0)	26	14 (53·8)
All ages	288	23 (8·0)	365	63 (17·3)	134	38 (28·3)
FEMALE						
15–54	147	3 (2·0)	123	3 (2·4)	21	3 (14·3)
55–74	46	0 (0)	41	5 (12·2)	18	5 (27·8)
75+	10	2 (20·0)	22	8 (36·4)	7	5 (71·4)
All ages	203	5 (2·5)	186	16 (8·6)	46	13 (28·2)
ALL						
15–54	324	5 (1·5)	292	9 (3·1)	74	9 (12·2)
55–74	132	16 (12·1)	186	36 (19·4)	73	23 (31·5)
75+	35	7 (20·0)	73	33 (46·6)	33	19 (57·6)
All ages	491	28 (5·7)	551	79 (14·3)	180	51 (28·3)

*Number of lung zones or equivalent area.

Table 3 Standardised mortality ratios by radiographic extent of disease

	*Total radiographic extent of disease**								
	<1			*1–2*			*>3*		
Age (y)	*O†*	*E†*	*O/E*	*O†*	*E†*	*O/E*	*O†*	*E†*	*O/E*
MALE									
15–54	2	0·27	7·4	6	0·26	23·1	6	0·09	66·7
55–74	16	1·72	9·3	31	3·10	10·0	18	1·13	15·9
75+	5	2·19	2·3	26	2·45	10·6	14	1·27	11·0
All ages	23	4·18	5·5	63	5·80	10·9	38	2·49	15·3
FEMALE									
15–54	3	0·13	23·1	3	0·12	25·0	3	0·02	150·0
55–74	0	0·47	0	5	0·51	9·8	5	0·17	29·4
75+	2	0·44	4·5	8	1·06	7·5	5	0·28	17·9
All ages	5	1·04	4·8	16	1·69	9·5	13	0·47	27·7

*Number of lung zones or equivalent area.
†—number of observed deaths; E—number of expected deaths.

only 50 (17%) cases of Indian subcontinent ethnic origin. Seven hundred and eighty seven (64%) of all the patients were men and 658 (54%) were white men.

Of the 1222 patients, 158 (12·9%) were reported to have died before completion of chemotherapy; death certificates were obtained for 132 (88%). In 69 (50%) of these 132 cases tuberculosis was mentioned in part 1 of the death certificate and in 43 (31%) in part 2. Sixty five (5%) patients defaulted or emigrated before completion of chemotherapy and their outcome is unknown. Case fatality rates by age, sex, and racial origin are displayed in table 1; in both sexes rates rose with increasing age. Of the 158 deaths, 124 (78%) occurred in male patients, almost of all them white; male case fatality within each age group was consistently higher than female. The overall number of deaths in patients of Indian subcontinent origin was small (6% of all deaths), and a smaller proportion died than of white patients, but the trends of increasing case fatality with age and of higher rates in men than women cases were also present.

To assess the effect of disease severity, case fatality rates by radiographic extent of disease were calculated (see table 2). In all age and sex groups fatality rates rose with increasing extent of disease. Rates were particularly high (over 50%) in elderly patients with disease affecting an equivalent of three lung zones or more. With a few exceptions (where the numbers were small) male rates were higher than female in each category and in each age group.

Table 4 Probability of death during chemotherapy for patients with previously untreated pulmonary tuberculosis: hypothetical values derived from logistic regression analysis

Age (y)	*Total radiological extent of disease**	*Probability of death during chemotherapy (%)*	*95% confidence limits*
25	<1	0·7	0·4–1·3
25	2–3	1·5	0·8–2·6
55	<1	5·9	4·1–8·2
55	2–3	12·0	9·3–15·3
75	<1	21·4	15·9–28·3
75	2–3	37·4	30·7–44·5

*Number of lung zones or equivalent area.

STANDARDISED RATES

The numbers of observed deaths in the group studied were compared with the number of deaths expected from the all causes age and sex standardised national mortality rates. Overall, observed deaths were 10 times higher than those expected. Ratios of observed to expected deaths are displayed by age and severity in table 3. Ratios rose consistently with increasing extent of disease. In both sexes and within each category of severity the ratios fell with increasing age.

TIME OF DEATH

Twenty one patients died before starting chemotherapy; 66 (48%) of the remaining 137 deaths occurred within four weeks of the start of treatment (data not tabulated). In the first two months after the start of chemotherapy the weekly death rates for patients over 65 years of age were at least five times as high as those for younger patients, but after the 10th week the rates were much lower and alike in the two groups. Similarly, when patients with more than one lung zone affected were compared with those with less extensive disease, the weekly death rates in the first two months of treatment were very much higher in those with more widespread disease.

LOGISTIC REGRESSION ANALYSIS

Logistic regression analysis of four clinical variables confirmed increasing age and radiographic evidence of extensive disease ($p < 0·01$ for each) and to a lesser extent male sex ($p = 0·06$) as important independent risk factors for death during chemotherapy. Racial origin was not an independent risk factor of significance ($p = 0·09$). The regression coefficients derived from this analysis were used to model the probability of death during chemotherapy for hypothetical patients of various ages and with different severities of disease. These probabilities are shown in table 4.

Discussion

The case fatality rate (all causes) of 12·9% reported here is similar to that calculated for patients with tuberculosis in England and Wales in 1978–9[2] and in Scotland in 1968.[1] The independent relationships between mortality and both age and extensive disease were again evident. The combined effects of these factors are seen in the (hypothetical) probabilities of death during chemotherapy shown in table 4. The relation to male sex, which is slightly weaker, may be attributable to a higher prevalence of coexistent disease, alcoholism, or poorer social circumstances in the men.

This study is of notified cases only; the degree of undernotification of pulmonary tuberculosis in England and Wales is unknown. A group of notified cases was excluded because at independent assessment there was no radiographic evidence of pulmonary disease; most of these patients had non-pulmonary tuberculosis. Disease severity was measured by extent of disease on the chest radiograph at the start of treat-

ment. For this reason a small percentage (6%) of notified cases was excluded from analysis because suitable radiographs were not available. The age distributions showed that these patients were slightly older than the remaining subjects and their exclusion means that the reported case fatality may be an underestimate, though the effect is likely to be slight. The loss to follow up a small number of subjects may also have produced a small bias.

This study, which compared the mortality of patients with pulmonary tuberculosis with that of the general population, shows a considerably greater all cause mortality than expected. As the socioeconomic distribution of people with tuberculosis is likely to be different from that of the general population and as mortality rates were not adjusted for socioeconomic group, the excess mortality reported here may be an overstimate. The higher standardised mortality ratio in young patients, particularly women and those with extensive disease, reflects the fewer conflicting causes of death in young people.

No attempt was made to study the effects of different treatment regimens but the preponderance of deaths occurring soon after the start of chemotherapy is consistent with observations in earlier case series.[6 7] These findings reinforce the importance of early diagnosis and of careful monitoring of patients with pulmonary tuberculosis, particularly the elderly and those with extensive disease, and especially in the first weeks of chemotherapy.

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