Age transition of tuberculosis incidence and mortality in Brazil*

Transição etária da incidência e mortalidade por tuberculose no Brasil

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Keywords

Tuberculosis, epidemiology.# Aging health.# Health transition.# Demographic transition.# Tuberculosis mortality. BCG vaccine. Acquired immunodeficiency syndrome, epidemiology. Health service needs and demand. Health planning. Socioeconomic factors.

Abstract

Objective

Before the Aids pandemic, demographic transition and control programs prompted a shift in the age of incidence of tuberculosis from adults to older people in many countries. The objective of the study is to evaluate this transition in Brazil.

Methods

Tuberculosis incidence and mortality data from the Ministry of Health and population data from the Brazilian Bureau of Statistics were used to calculate age-specific incidence and mortality rates and medians.

Results

Among reported cases, the proportion of older people increased from 10.5% to 12% and the median age from 38 to 41 years between the period of 1986 and 1996. The smallest decrease in the incidence rate occurred in the 30–49 and 60+ age groups. The median age of death increased from 53 to 55 years between 1980 and 1996. The general decline in mortality rates from 1986 to 1991 became less evident in the 30+ age group during the period of 1991 to 1996. A direct correlation between age and mortality rates was observed. The largest proportion of bacteriologically unconfirmed cases occurred in older individuals.

Conclusions

The incidence of tuberculosis has begun to shift to the older population. This shift results from the decline in the annual risk of infection as well as the demographic transition. An increase in reactivation tuberculosis in older people is expected, since this population will grow from 5% to 14% of the Brazilian population over the next 50 years. A progressive reduction in HIV-related cases in adults will most likely occur. The difficulty in diagnosing tuberculosis in old age leads to increased mortality.

Descritores

Tuberculose, epidemiologia.# Saúde do idoso.# Transição epidemiológica.# Transição demográfica.# Tuberculose, mortalidade. Vacina BCG. Síndrome de imunodeficiência adquirida, epidemiologia. Necessidades e demanda de serviços de saúde. Planejamento em saúde. Fatores socioeconômicos.

Resumo

Objetivo

Antes da pandemia de Aids, a transição demográfica e os programas de controle estavam deslocando a incidência da tuberculose de adultos para idosos em diversos países. O objetivo do estudo é determinar se essa transição tem ocorrido no Brasil.

Métodos

Dados de incidência de tuberculose e de mortalidade decorrente dessa doença, derivados do Centro Nacional de Epidemiologia e Departamento de Informática do Sistema Único de Saúde (SUS), e os dados populacionais oriundos da Fundação Instituto Brasileiro de Geografia e Estatística foram empregados para calcular

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medianas e coeficientes de incidência e mortalidade por faixa etária.

Resultados

Entre 1986 e 1996, a proporção de casos em idosos subiu de 10,5% para 12%, e a mediana de idade de 38 para 41 anos. O menor declínio do coeficiente de incidência ocorreu nas faixas de 30-49 anos e 60 anos e mais . Entre 1980 e 1996, a mediana de idade dos óbitos subiu de 53 para 55 anos. O declínio generalizado dos coeficientes de mortalidade observado entre 1986 e 1991 tornou-se menos expressivo, nas faixas de 30 anos e mais, entre 1991 e 1996. Houve correlação direta entre idade e mortalidade. A maior proporção de casos sem confirmação bacteriológica ocorreu em idosos.

Conclusões

A incidência de tuberculose começa a ser deslocada para idosos. Por um lado, contribuem a eficácia da vacinação com BCG e redução do risco de infecção na comunidade. Por outro, o crescimento da população de adultos e idosos. O diagnóstico difícil nessa faixa etária determina elevada mortalidade. Nos próximos 50 anos deverá ocorrer redução progressiva dos casos associados à Aids em adultos, e expressivo aumento dos casos de reativação em idosos, cuja população saltará de 5% para 14% no Brasil. A proporção de idosos (5% para 14%) é estimativa dos demógrafos. Os casos associados a Aids e de reativação em idoso é uma conclusão baseada nas modificações incipientes reveladas por esta pesquisa.

INTRODUCTION

Despite the optimism of the 1960s and 1970s regarding the possibility of its control, tuberculosis (TB) remains one of the greatest public health challenges worldwide. Improvements in housing, sanitation conditions and TB control programs have reduced the risk of infection and mortality in many countries, but the human immunodeficiency virus (HIV) pandemic and the population aging process have modified some epidemiological characteristics of the disease.[5]

Infected by the tubercle bacilli in the early decades of the 20th century, older individuals (60+ years) are now susceptible to reactivation of latent foci due to age-related immune dysregulation. The interval between initial complaints and the diagnosis of TB is longer in older people[6] and leads to an aggravated outcome. Atypical symptomatology, difficulties in interpreting the tuberculin skin test, unusual radiological findings, and coexisting diseases or frequent alternative diagnoses often hinder the identification of TB before autopsy and contribute to the high mortality rates seen in this group.[6,10]

As TB transmission is reduced during the epidemic progression in a particular region, the age group at greatest risk shifts gradually to older individuals since there is a drop in the annual risk of infection but not in the frequency of reactivation disease.[1] Vaccination with the bacillus Calmette-Guérin (BCG) and the increase in treatment effi-cacy, reducing the chronicity of the disease and therefore its transmission in the community, also tend to shift the incidence of TB to older age groups.[4,11] In 1990, it was estimated that the majority of infected individuals in Europe were 50 years or older (80%) while in Africa 77% were less than 50 years old, although more than 90% of the older population was infected.[18] On one hand this is due to the lower proportion of young people in the European population and the lower prevalence of infection in this age group. On the other, this situation is a result of the higher proportion of young people in developing countries, with higher annual risk of infection, where only 15% of the population live beyond the age of 50.

Therefore, demographic factors (population growth and aging) have modified the impact of epidemiological factors (HIV epidemic, intervention programs).[5] In 1994, Dolin et al[5] estimated that by the end of the decade TB incidence rates would have fallen in all age groups in the Americas, although less markedly among adults and older people: 43% and 12%, respectively in the 0-14 and 15-34 age groups but only 6.2% and 5.5% in the 35-59 and 60+ age groups(excluding the US and Canada).

The objective of the present paper is to determine whether the age transition of TB is in fact taking place in Brazil, whether some disease categories (extrapulmonary, meningeal, miliary) have become especially frequent among older individuals and whether the available data suggest that diagnosis is more difficult and the mortality rates are higher in this group.

METHODS

Cases and definitions

Due to the lack of adequate nationwide TB data prior to 1985, data from 1986 to 1996 were used. The terms TB "cases" and "deaths" refer to reported cases and deaths. Data provided by the Ministério da Saúde, Fundação Nacional de Saúde[14] (Ministry of Health) through PNCT (National Tuberculosis Control Program) were used to analyze the incidence of TB cases and were grouped according to four categories: all forms, pulmonary, meningeal, and extrapulmonary (which include meningeal cases).

Mortality analysis was based on data provided by DATASUS (Statistics Department of the Ministry of Health),[13] which used the International Classification of Diseases, 9th revision for the period 1986 through 1995 and the 10th revision for 1996. The following categories were used so that the data from both classifications would be compatible: respiratory TB (which includes pulmonary, intrathoracic ganglia, larynx, bronchi and pleura) and non-respiratory TB (all other forms). Deaths from miliary TB (disseminated form), available until 1995, are also analyzed.

Population

Incidence rates reported by PNCT were recalculated since the official population data from Fundação IBGE (Brazilian Bureau of Statistics)* was not used. The IBGE data were also used with certain provisions due to the difference between the population estimates in the PNAD – Pesquisa Nacional por Amostra de Domicílios (National Household Sample Surveys) and the more complete 1980 and 1991 demographic census[7,8] and 1996 population count.[9,**] Incidence and mortality rates were not calculated for 1986, the year in which only the PNAD[9] was performed.

Incidence and mortality rates as well as medians were calculated using Excel 7.0. The comparison between dichotomous variables from independent groups was performed using the Yates corrected χ^2 in the statistical program Epi Info 6, version 6.04b, 1997.

RESULTS

Between 1986 and 1996, there was a slight increase in the number of cases (from 84,990 to 85,859). Pulmonary TB represented the most com-

mon form in all age groups (89.6% in 1986 and 86.8% in 1996).

Reported cases

Between 1986 and 1991, there was a decline in the number of pulmonary, meningeal and extrapulmonary TB in the 0-29 age groups and an increase in the 30+ age groups (Table 1).

The trends changed from 1991 to 1996 (Table 1, Figure 1). In the 0-19 age group, the decline in TB cases was less marked while in the 20-29 age group the decline remained unchanged. In the 30+ age groups, the increase in the number of cases of pulmonary TB was less accentuated, with the exception of the 40-49 age group, in which there was still an increasing number of cases.
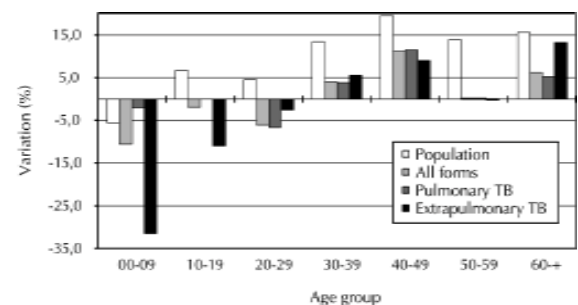

Figure 1 - Variation in population and reported TB cases by form and age group, Brazil, 1991-1996.

The unequal variation among age groups has resulted in a rightward shift in the incidence curve (Figure 2). The median age of new cases increased between 1986 and 1996: all forms of TB from 38.1 to 40.9; pulmonary TB from 38.6 to 41.1; meningeal TB from 16.7 to 36.4; and extrapulmonary TB from 35.1 to 39.6.
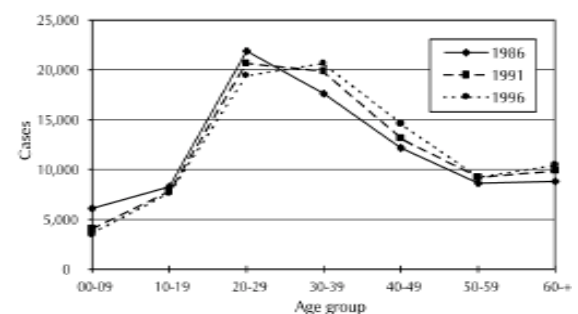
Figure 2 - Reported cases of TB by age group; Brazil, 1986, 1991 and 1996.

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*In 1996, the incidence rate of all forms of tuberculosis in the 60+ age group reported by PNCT (93.2/100,000) was 11% higher than the rate based on the number of cases reported by PNCT and the IBGE population estimates (84.3/100,000).[9]
**The 60+ population, overestimated in the 1995 PNAD, showed a "drop" of 2.5% when corrected by the data from the 1996 population count.[9]

Table 1- Reported tuberculosis cases in Brazil for 1986, 1991 and 1996, and incidence rates for 1991 and 1996, by age group and form.

Age group	Cases (in thousands)*			Variation %			Incidence rate**		Var. %
	1986	1991	1996	86-91	91-96	86-96	1991	1996	91-96
Tuberculosis - all forms									
00-09	6.1	4.0	3.6	-34.4	-10.6	-41.4	11.8	11.2	-5.2
10-19	8.3	7.8	7.7	-5.5	-1.9	-7.3	24.4	22.5	-8.1
20-29	21.9	20.7	19.4	-5.6	-6.1	-11.4	78.9	70.9	-10.1
30-39	17.7	19.9	20.6	12.6	4.0	17.1	96.8	88.8	-8.3
40-49	12.2	13.7	14.6	8.1	11.1	20.2	94.3	87.7	-7.0
50-59	8.6	9.2	9.2	6.9	0.1	7.0	97.9	86.1	-12.1
60-+	8.8	9.9	10.5	11.8	6.2	18.7	91.8	84.3	-8.2
Total	83.6	84.6	85.6	1.2	1.2	2.5	57.9	54.8	-5.4
Pulmonary tuberculosis									
00-09	4.6	2.9	2.8	-38.1	-2.0	-39.4	8.4	8.7	3.8
10-19	7.0	6.5	6.5	-7.5	0.0	-7.5	20.2	18.9	-6.3
20-29	19.0	17.9	16.7	-5.8	-6.7	-12.1	68.2	61.0	-10.7
30-39	15.3	17.0	17.6	11.1	3.8	15.3	82.7	75.7	-8.5
40-49	10.6	11.3	12.6	6.5	11.5	18.8	81.2	75.7	-6.7
50-59	7.6	8.1	8.1	6.1	0.1	6.3	86.0	75.6	-12.1
60-+	7.9	8.6	9.1	9.3	5.2	15.0	80.5	73.2	-9.0
Total	72.0	72.2	73.4	0.3	1.6	1.9	49.4	47.0	-4.9
Meningeal tuberculosis									
00-09	0.27	0.21	0.13	-25.7	-34.6	-51.4	0.6	0.4	-30.7
10-19	0.06	0.06	0.06	-3.2	-5.0	-8.1	0.2	0.2	-10.9
20-29	0.08	0.13	0.13	66.7	3.2	72.0	0.5	0.5	-1.2
30-39	0.07	0.1	0.16	34.2	67.3	124.7	0.5	0.7	47.6
40-49	0.05	0.08	0.1	86.7	15.5	115.6	0.6	0.6	-3.4
50-59	0.02	0.03	0.05	68.8	70.4	187.5	0.3	0.4	49.6
60-+	0.03	0.04	0.06	61.5	38.1	123.1	0.4	0.5	19.4
Total	0.57	0.64	0.68	11.9	6.9	19.5	0.44	0.44	0
Extrapulmonary tuberculosis									
00-09	1.5	1.2	0.8	-23.2	-31.5	-47.4	3.4	2.5	-27.4
10-19	1.3	1.4	1.2	5.2	-10.9	-6.3	4.3	3.6	-16.5
20-29	2.9	2.8	2.7	-4.2	-2.6	-6.7	10.7	10.0	-6.8
30-39	2.4	2.9	3.0	21.9	5.5	28.7	14.0	13.1	-6.9
40-49	1.5	1.8	2.0	19.1	9.0	29.8	13.1	12.0	-8.8
50-59	1.0	1.1	1.1	12.7	-0.2	12.4	11.9	10.5	-12.3
60-+	0.9	1.2	1.4	33.2	13.2	50.8	11.4	11.1	-2.1
Total	11.6	12.4	12.3	7.2	-0.9	6.3	8.5	7.9	-7.1

*Cases with ignored age are excluded.
**Cases/100.000.
Sources: Cases: Ministério da Saúde.[13] Population: Fundação IBGE,[7,8,9] 1980,1991,1996.

Similarly, the proportion of TB cases in older people increased from 10.5% in 1986 to 12.2% in 1996, when this group represented 7.9% of the population. The increase in the proportion of extrapulmonary cases in older people (from 7.9% to 11.2%) was even more significant for this period.

Incidence rates

The rise in TB cases between 1991 and 1996 was less marked than the population growth for the same period, causing a drop, with some exceptions, in the incidence rates of all analyzed forms (Table 1 and Figure 1). The highest incidence rates were seen in the 30+ age groups (between 92 and 97 per 100,000 in 1991 and between 84 and 89 per 100,000 in 1996). Among adults, the decline in the incidence rates varied from 7% and 12%, with the lowest decreases in the 40-49 (7.0%), 60+ (8.2%) and 30-39 (8.3%) age groups.

Reported mortality

The number of TB deaths in 1996 (5,708) was 23% lower than in 1980 (7,022). The deaths from TB had

a unimodal distribution centered on the 40-49 age group (Table 2). The decline seen in almost all age groups in the 1980-1986 period was replaced in 1991-1996 period by an increase in the number of deaths in the 30+ age groups.

Mortality rates

Between 1980 and 1991, the mortality rates of TB declined more than 35% in all age groups except for the 80+ (Table 2 and Figure 3). In the 1991 to 1996 period, the decrease was less significant in the 30+ age groups (<10%, except for 80+). The median age of death increased between 1980 and 1996 from 53 to 55 years (respiratory TB) and from 30 to 47 years (non-respiratory TB). With the exception of the 0-9 age group, there was a direct correlation between age and mortality rate in all studied periods (Figure 3).

Miliary TB mortality

Nearly 20% of all deaths from miliary TB reported between 1980 (290 deaths) and 1995 (244 deaths)

Table 2 - Deaths from tuberculosis and mortality rates by age group; Brazil, 1980, 1986, 1991 and 1996.

Age group	Deaths*			Variation %			Mortality rates**			Variation %		
	80	86	91	96	80-86	91-96	80-96	80	91	96	80-91	91-96	80-96
00-09	556	244	151	99	-56.1	-34.4	-82.2	1.8	0.4	0.3	-74.9	-31.0	-82.7
10-19	228	175	132	113	-23.2	-14.4	-50.4	0.8	0.4	0.3	-49.7	-19.7	-59.6
20-29	709	500	542	455	-29.5	-16.1	-35.8	3.4	2.1	1.7	-38.9	-19.7	-50.9
30-39	1,019	855	960	976	-16.1	1.7	-4.2	7.2	4.7	4.2	-35.0	-10.3	-41.7
40-49	1,341	956	1,031	1,229	-28.7	19.2	-8.4	13.0	7.4	7.4	-43.0	-0.3	-43.1
50-59	1,246	969	965	989	-22.2	2.5	-20.6	17.2	10.3	9.2	-40.2	-10.0	-46.2
60-69	1,006	769	711	813	-23.6	14.3	-19.2	22.2	11.1	11.3	-50.2	1.5	-49.4
70-79	626	689	524	590	10.1	12.6	-5.8	29.2	16.5	15.9	-43.6	-3.8	-45.8
80-+	189	164	320	321	-13.2	0.3	69.8	31.8	28.3	22.1	-10.8	-22.1	-30.5
Total	7,022	5,321	5,336	5,708	-24.2	6.8	-18.7	5.8	3.6	3.6	-37.9	0	-37.9

* In 1980 and 1996 there were respectively 102 and 123 deaths of unknown age.
** Deaths/100,000
Sources: Cases: Ministério da Saúde.[13] Population: Fundação IBGE,[7,8,9] 1980,1991,1996
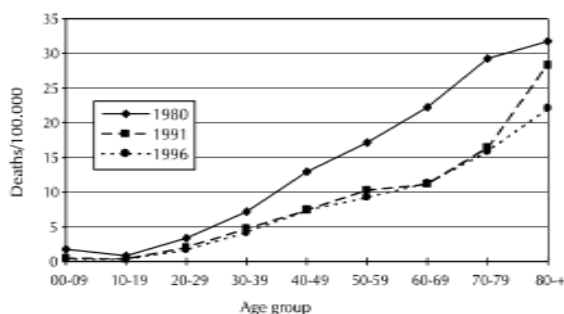

Figure 3 - Tuberculosis mortality rates by age group, Brazil, 1980, 1991 and 1996.

occurred in older individuals. The mortality rates of the 60-69, 70-79 and 80+ age groups (about 0.5/ 100,000 in 1991) have been the highest among all age groups since 1980.

Diagnostic characteristics

In 1996,* among pulmonary cases, the highest proportion of bacteriologically unconfirmed notifications was seen among older people, a statistically significant difference compared to the average for other adults (43.7% vs. 35.6%; χ^2 =226.2; p=0.00). On one hand, this trend is due to the higher frequency of case reports in older individuals who did not even have a sputum smear (18.8% vs. 17.1% of other adults; χ^2 =13.2; p=0.00). On the other, it is due to the lower proportion of positive smears among those performed in older people (68.0% vs. 76.8% of other adults; χ^2 = 294.3; p=0.00).

Among cases reported without positive smears, cultures were performed on a minority of the cases, although more frequently in older individuals (14.6% vs. 12.5% of other adults; χ^2 =7.2; p=0.01). Among these cases without positive smears, nearly one-third of the cultures were positive in older peo-

ple and adults (29.4% vs. 30.9% of other adults; χ^2=0.16; p=0.7).

DISCUSSION

Demographic transition has influenced the TB age transition

In the period between 1986 and 1996, there was a rightward shift in the age-specific incidence of TB. There was an increase in the median age of cases of all TB forms and in the proportion of cases among older individuals and adults aged 30 or more. As predicted by Dolin et al[5], these trends have possibly been determined by demographic (population growth and aging) as well as epidemiological factors (TB control programs, HIV infection).**

The current phase of demographic transition in Brazil[2] is characterized by the passage through adulthood of the large cohorts born between 1940 and 1965; the population aged 30-59 grew from 43.9 million in 1991 to 50.7 million in 1996, or 13.4%. This is one of the reasons for the increase in the absolute number of cases in the 30+ age groups. Meanwhile, the fall in fertility rates that started in the middle of the 1960s has kept the absolute number of young people constant; the population aged 0-29 grew from 92.2 million to 93.6 million, or 1.5% in the above mentioned period. This situation may have contributed to the stability in the number of TB cases in these age groups.

TB control programs, reducing the annual risk of infection, are also contributing to the decrease in incidence seen in the under 30 age groups and that has probably been helped by the lack of growth in these groups. As seen in the present study, steeper declines

*The 0-9 and 10-19 age groups are excluded from this section.
**It is possible that variations in the notification registry quality as well as socioeconomic changes, such as nutritional and housing conditions, during the analysis period influenced the observed trends.

in incidence rates are unlikely to occur in the 0-19 age group as lower values are reached. The incidence rates in the 30+ age groups almost surpassed 80 per 100,000 in 1991 while in the 0-19 age group they were below 25 per 100,000,* close to the level of developed countries.[18]

HIV-related tuberculosis cases will probably decrease

Tuberculosis is one of the most common opportunistic infections in HIV-infected patients, which has contributed to the resurgence of the disease in many countries.[17] In Brazil, between 1988 and 1996, pulmonary TB was associated with Aids in 10% of patients at the time of diagnosis.[15]

The probability that an HIV-infected patient will develop TB depends on certain factors: 1) the annual risk of infection, which is decreasing in Brazil; 2) the chance of being host to latent infections, associated with the historic prevalence in the cohort; and 3) the integrity of the immune system.

Between 1980 and 1996, the distribution of Aids cases was unimodal centered on the 20-49 age group (87% of cases).[16] An interaction between the high prevalence of immune deficiency (HIV infection, alcoholism) and the high proportion of individuals with latent infections was probably responsible for the increase in the rates of TB reactivation and contributed to the slow decline in the incidence rates seen in the 30-49 age group.

Several factors will probably reduce the incidence of HIV-related TB in Brazil over the next few years. HIV transmission has been reduced, treatment efficacy is improving and the availability of anti-retroviral therapy and TB prophylaxis for HIV-infected individuals has increased.[15] Furthermore, in the next decades, cohorts with higher proportions of individuals immunized with BCG will reach adulthood and, if infected with HIV, will not be harboring dormant bacilli. In virtue of the progressive reduction in TB transmission in the community, the risk of primary infection will also be progressively lowered.

The proportion of cases in older people will probably increase

The decrease in the incidence of TB was equally slow among older and adult individuals, despite the fact that the former represented only 1.8% of Aids cases for the 1980 to 1996 period.[15] It is likely that in this group an interaction between age-associated immune dysregulation and the high proportion of individuals with latent infections is contributing to the high frequency of reactivation. Since the proportion of people aged 65 years and older in Brazil will increase from 5.1% to 14.2% in the next five decades,[2] it is probable that the age-specific TB incidence curve will shift even further to the right. This possibility seems even more plausible when one considers that adults reaching 65 years in the next decades are part of cohorts born in the 1940s and 1950s and thus were exposed to a high annual risk of infection during their childhood. In the future, nosocomial transmission in nursing homes may also contribute to higher incidence rates of TB.[3,6]

Miliary TB is associated with cell-mediated immunity disorders and in many countries it is already more common in older rather than younger people.[6] In Brazil, 20% of miliary TB deaths in 1995 were in older individuals who represented less than 8% of the population. It is possible that as HIV-related TB cases decreases, the proportion of miliary TB cases in older people will rise. Likewise, one would expect an increase in the mortality rates – already the highest among all age groups – proportional to the increase of the very old group (85+) over the next few decades.

Diagnosis is more difficult among older people

Several factors – from age-related immune dysregulation and decreased mucociliary transport to lack of cooperation among frail older people – contribute to the difficulties in diagnosing TB in this group.[6,2]

In the analysis period, little more than half the reported cases of TB in older patients were confirmed by sputum smear or culture. This trend may be the result of the difficulty in obtaining specimens for examination, the higher rates of negative results or the careless and unthoughtful assumption that pulmonary disease in an elderly patient is TB. The need for bacteriological confirmation is stressed by the fact that symptoms such as fever, night sweats, cough, sputum production, and hemoptysis are less frequent in older patients with TB,[12,16] although they may actually be caused by other diseases like heart failure, pulmonary embolism, endocarditis, cancer and pneumonia, which are all common in this age group.[10]

Among cases reported with negative sputum smears between 1986 and 1996, in less than 15% cultures were performed. This could have been related to the difficulty in obtaining specimens for examination or negligence on the part of health professionals. Of these 15%, the

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*These low levels may be partially explained by difficulties in diagnosing TB in this age group.

culture confirmed the diagnosis in an additional one-third of cases, a rate similar to adults, reinforcing its importance. In a prospective study that followed up 1,200 institutionalized older subjects for 26 months, all the 19 diagnosed TB cases confirmed by culture had negative sputum smears.[16]

Mortality is higher in older people

The difficulty in diagnosing, delayed initiation of treatment and frequency of other diseases increase the mortality of TB in older individuals. But, on the other hand, an incorrect diagnosis of TB unnecessarily exposes patients to the risks of medication and delays the treatment of the actual disease, which artificially increases the mortality rate among the reported cases.

The correlation between age and TB mortality in Brazil stresses the importance of early and accurate diagnosis in older patients since treatment efficacy is the same as in younger individuals.[6] The lower decline in the mortality rates in the 1991 to 1996 period, however, suggests that health care quality worsened in that period. It is worth noting the high mortality rate (22 deaths per 100,000, the smallest decrease since 1986) in those aged 80 years and older, exactly the group that will experience the highest population growth in the next decades.[2]

The precarious nature of living conditions in Brazil has created a population of older people who suffer from numerous chronic disorders and have difficulty in accessing the health system. When coupled with disadvantages in the economic and social spheres, this group's health becomes severely compromised.[2] While TB cases in children and HIV-infected individuals will probably decline over the next decades, the proportion of cases among older people will grow significantly. After some interference resulted from the HIV pandemic, the TB epidemic will reach its final stage when the decline in morbidity will be associated with an increase in the proportion of cases in older patients.[1] Only the reordering of public health policies will enable to reduce morbidity and mortality in this age group.

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