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CURRENT EPIDEMIOLOGICAL ASPECTS OF TUBERCULOSIS AMONG CASES REPORTED IN ANÁPOLIS-GOIÁS BETWEEN 2011 AND 2016

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ABSTRACT

Objective: This study aimed at characterizing the clinical-epidemiological profile of tuberculosis cases reported in Anápolis-Goiás. Tuberculosis reported cases was retrieved from the notification of injury information system (NIIS) 2011 and 2016. **Method:** This is an epidemiological, descriptive and transversal study that was carried out in Anápolis-Goiás. Microsoft® Excel 2007 was used for data tabulation and statistical analysis performed by SPSS® (version 16.0) for Windows®. The significance level was 5% ($p < 0.05$) for all analyzes. **Result:** There were 268 cases of tuberculosis reported during the period of the study. 70.9% were male and 29.1% female patients. The most prevalent age group was from 41 to 60 years old (45.5%). The most prevalent clinical form of tuberculosis was pulmonary with 83.2% of the cases. 85.5% of patients were HIV negative and 14.5% positive. Bacilloscopy was performed in 77.2% of the cases with a positive result in 56.3%. The majority of cases were cured during the treatment (70.9%); 8.2% gave up treatment and 7.8% died. The notification system has contributed to the optimization of control programs, with positive results. **Conclusion:** However, a significant number of new cases, treatment abandonment and death rate persist, which highlight the need of population alerting. Therefore, it is necessary to reinforce preventive campaigns, since they can contribute to the clarification of risky behaviors in the population. In this context, the role of basic health care, which has direct contact with the community and is a great ally for the promotion of health, health education, can bring people knowledge preventing new cases.

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INTRODUCTION

Tuberculosis (TB) is an ancient infectious disease with historical reports in Greece and ancient Rome. TB was probably known by ancient Egyptians, as researchers found TB lesions in mummies 3,000 years before Christ (1). TB is possibly one of the oldest and known diseases of the world. However, the bacterium responsible for the disease, *Mycobacterium tuberculosis*, was isolated by the German scientist Robert Koch only in 1882; The TB bacillus, known as Koch's bacillus (BK), was named after him (2). During the 20th century, TB was recognized as a neglected disease and in the 21st century as a serious unsolved public health problem (3). According to the World Health Organization (WHO), Brazil is one of the 22 countries that concentrate 80% of the world burden of TB. Brazil occupies the 16th position in relation to the number of new cases and the 22nd position regarding the incidence coefficient (IC), prevalence and mortality. The mortality coefficient of TB has decreased over the years. However, 4,500 died from TB in 2011, even though

TB is curable and preventable (4). There were 63,189 new TB cases reported in Brazil in 2015 and an incidence rate of 30.9 cases/100,000 inhabitants. In addition, the cure rate was 72.5% and treatment abandonment of 11.0%, representing 0.9% of the estimated cases in the world and 33% in the American continent (5). TB primarily affects the lungs (pulmonary TB) but can also affect other organs, characterizing extrapulmonary forms of the disease. The infection is acquired by inhalation of the etiologic agent in the air. Airborne transmission of TB is efficient as infected individuals expectorate large amounts of mycobacteria by projecting them into the environment. The outer lipid cover of the pathogen resist dry condintion and survive for long periods in the air and dust (6). However, the probability of developing the disease is high in people infected with the human immunodeficiency virus (HIV). The presumptive diagnosis of pulmonary TB is made through data from the clinical history and radiological findings. The confirmation of the diagnosis is obtained through bacilloscopy and/or cell culture. The former identifies the acid-alcohol-resistant bacilli (AARB), which is a fast and cheap diagnostic method, chosen by the Brazilian public health services but presents a low sensitivity. The second form of diagnosis has high sensitivity but the culture of the bacillus is rather slow. Thus, the diagnosis is defined in 4 to 8 weeks (8) and may influence the control of TB because early diagnosis interrupts the disease transmission cycle. In Brazil, about 26.7% of patients are treated without the confirmation for pulmonary TB, based only on clinical and radiological results (9).

The treatment of TB is long, at least six months, daily and without interruption. It is based on the combination of four drugs: rifampicin, isoniazid, pyrazinamide and etambutol. Dropout rate is high due to several side effects and the loss of symptoms as early as the first days of treatment. Discontinuation of treatment may lead to the spread of TB and increase the risk of resistance to prescription drugs. Treatment for multidrug-resistant TB is longer and requires more expensive and toxic drugs (10). These facts represent a paradox, the diagnosis of transmissible cases is easiery and inexpensive. In addition, the current treatment available in the public health system of Brazil is effective in such cases (95% successful rate, provided the drugs are taken daily for six months without interruptions) (11). Tuberculosis is a notifiable disease in Brazil. In order to minimize the problems related to compulsory notification, the Ministry of Health created the notification of injury information system (NIIS). It was developed in the beginning of the 1990s, aiming at collecting and processing data on notification throughout the national territory. It provides information regarding morbidity profile of diseases, which contributes to decision making at the municipal, state and federal levels on disease management (12). Anti-tuberculosis drugs are free, guaranteed by the National Tuberculosis Control Program (NTCP). Those drugs are not commercially available; the public health system deliver to the patient only through a notification form provided by a healthcare professional (11). The development of better tools and strategies to control and eliminate TB, multidisciplinary approaches are necessary. Epidemiological studies, comparative genomics, study on the evolution and interaction of host-pathogen interatcion can help the improvement of the status of the disease (13). The present study aimed at characterizing the clinical-epidemiological profile of TB cases reported by NIIS in Anápolis-Goiás from January 2011 to December 2016.

MATERIAL AND METHODS

This study was conducted by the Department of Epidemiological Surveillance of the Municipal Health of Anápolis - Goiás, Brazil, which is linked to the University Center of Anápolis - UniEVANGÉLICA. It was approved by the Research Ethics Committee (CEP) with human beings (CEP/UniEvangélica: 75083-515). This is an epidemiological, observational, descriptive and cross-sectional stud. The source of information is from the Tuberculosis Notification/Investigation Data on the NIIS database from 2011 to 2016. The socio-demographic characteristics evaluated were gender, age, ethnicity, level of education and area of residence. The clinical and epidemiological variables comprised clinical form (pulmonary, pleural, ganglionar, miliary, among others), type of registration into the system (new case, re-entry after abandonment, transfer, recidivism, post-abandonment, death, unknown causes), termination of treatment (cure, abandonment, transfer, death from TB, death from other causes), HIV infection and sputum smear microscopy. Microsoft® Excel 2007 was used for data tabulation and statistical analysis performed by SPSS® (version 16.0) for Windows®. The chi-square test ($\chi 2$) and Fisher's exact test were used to perform the descriptive statistical analysis. The significance level was 5% ($p < 0.05$) for all the analysis.

RESULTS

According to the data obtained from TB notification forms registered in NIIS of the Department of Epidemiological Surveillance of the Municipal Health of Anápolis, assistance was offered to 268 patients from January 2011 to December 2016. Among patients, 70.9% (190/268) were males and 29.1% (78/268) females and the male/female ratio was 2.43:1. There was no statistically significant difference in gendre distribution (p=0.098). The age of patients ranged from 10 to 80 years. The most prevalent age group was 41 to 60 years old represeting 45.5% (122/268) of patients. There was no statistically significant difference (p=0.857) related to age (Table 1). Regarding ethnicity, brown skin patients were prevalent accounting for 47.8% (128/268) of cases and followed by Caucasians accounting for 36.6% (98/268) of cases. A statistically significant difference (p=0.0005) was found for the ethnicity. Interestingly, Brazil presents significant ethnic diversity. Considering the level of education, 28.4% (76/268) of cases were between the 1st and 5th year of primary school and 26.5% (71/268) between the 6th and 9th year of secondary school; thus, 54.9% (147/268) of patients had elementary education. There was statistically significant difference (p=0. 0002) between groups. 98.9% (265/268) of patients were in the urban area and there was no statistically significant difference (p = 0.170) regarding residence. Socio-demographic features of TB cases are described in Table 1. Table 2 compared the patients distributed according to the clinical forms of TB reported in NIIS. It was observed that 83.2% (223/268) of patients were affected by the pulmonary form of TB followed by the pleural form with 4.5% (12/268). The the ganglionar form of TB affected 4.1% (11/268) of patients, 1.1% (3/268) of the patients had miliary TB and 7.1% (19/268) developed other forms of tuberculosis, such as genitourinary, bone, ocular and laryngeal. Thus, 16.8% (45/268) of the developed extrapulmonary forms of the disease. Pulmonary TB was the most prevalent form of the disease during the period of the study. Table 3 shows patient

distribution according to type of entry into the NIIS system during the period of the study. New cases of TB corresponded to 85.8% (230/268) of patients; 8.3% (22/268) of patients were in the category transference; 3.3% (9/268) with TB recurrence; 1.5% (4/268) re-admitted after abandonment of treatment and 1.1% (3/268) were TB cases diagnosed after death. According to table 4, we found no statistical significance regarding the termination of treatment and gender. The majority of the cases were cured after the treatment, accounting for 70.9% (190/268) of the patients and 7.8% (21/268) of patients died from TB

Table 1. Socio-demographic characteristics of the reported cases of tuberculosis in Anápolis-GO from 2011 to 2016

Period	2011	2012	2013	2014	2015	2016	Total	*P*
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	
GENDER								0.098[a]
Male	29 (60.4)	32 (74.4)	33 (66.0)	19 (61.3)	29 (76.3)	48 (82.8)	190 (70.9)	
Female	19 (39.6)	11 (25.6)	17 (34.0)	12 (38.7)	9 (23.7)	10 (17.2)	78 (29.1)	
AGE								
10-19	1 (2.1)	1 (2.3)	4 (8.0)	1 (3.2)	1 (2.6)	2 (3.4)	10 (3.7)	0.857[a]
20-40	18 (37.5)	16 (37.2)	21 (42.0)	10 (32.2)	16 (42.1)	28 (48.3)	109 (40.7)	
41-60	24 (50.0)	21 (48.9)	22 (44.0)	18 (58.1)	16 (42.1)	21 (36.2)	122 (45.5)	
61-80	5 (10.4)	5 (11.6)	3 (6.0)	2 (6.5)	5 (13.2)	7 (12.1)	27 (10.1)	
ETHNICITY								
Caucasian	24 (50.0)	14 (32.6)	13 (26.0)	12 (38.7)	13 (34.2)	22 (37.9)	98 (36.6)	0.0005[b]
Black	2 (4.2)	2 (4.7)	5 (10.0)	8 (25.8)	3 (7.9)	9 (15.5)	29 (10.8)	
Yellow	0 (0)	3 (6.9)	2 (4.0)	0 (0)	0 (0)	0 (0)	5 (1.9)	
Brown	22 (45.8)	22 (51.2)	24 (48.0)	11 (35.5)	22 (57.9)	27 (46.6)	128 (47.8)	
Indigenous	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
Unclassified	0 (0)	2 (4.6)	6 (12.0)	0 (0)	0 (0)	0 (0)	8 (2.9)	
EDUCATION								
Illiterate	6 (12.5)	5 (11.6)	2 (4.0)	2 (6.5)	0 (0)	3 (5.2)	18 (6.7)	0.0002[b]
1st a 5th grades	11 (22.9)	10 (23.3)	13 (26.0)	13 (41.9)	17 (44.7)	12 (20.7)	76 (28.4)	
6th a 9th grades	16 (33.3)	7 (16.3)	11 (22.'0)	8 (25.8)	8 (21.1)	21 (36.2)	71 (26.5)	
High School	8 (16.7)	6 (13.9)	10 (20.0)	5 (16.1)	13 (34.2)	18 (31.0)	60 (22.4)	
Higher education	2 (4.2)	2 (4.7)	4 (8.0)	3 (9.7)	0 (0)	4 (6.9)	15 (5.6)	
Unclassified	5 (10.4)	13 (30.2)	10 (20)	0 (0)	0 (0)	0 (0)	28 (10.4)	
RESIDENCE								
Rural	0 (0)	2 (4.7)	0 (0)	0 (0)	1 (2.6)	0 (0)	3 (1.1)	0.170[b]
Urban	48 (100)	41 (95.3)	50 (100)	31 (100)	37 (97.4)	58 (100)	265 (98.9)	

[a]Probability of significance (p-value) refers to the chi square test; [b]Probability of significance (p-value) refers to the Fisher's exact test.

Table 2. Distribution of reported cases of tuberculosis according to TB clinical forms in Anápolis - GO from 2011 to 2016

Clinical Forms	2011	2012	2013	2014	2015	2016	Total
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Pulmonary	41 (85.4)	36 (83.8)	41 (82.0)	27 (87.0)	31 (81.6)	47 (81.0)	223 (83.2)
Pleural	2 (4.2)	4 (9.3)	2 (4.0)	2 (6.5)	1 (2.6)	1 (1.7)	12 (4.5)
Ganglionar	4 (8.3)	1 (2.3)	2 (4.0)	0 (0)	3 (7.9)	1 (1.7)	11 (4.1)
Miliary	0 (0)	1 (2.3)	1 (2.0)	0 (0)	0 (0)	1 (1.7)	3 (1.1)
Other	1 (2.1)	1 (2.3)	4 (8.0)	2 (6.5)	3 (7.9)	8 (13.8)	19 (7.1)

Table 3. Distribution of TB cases according to the type of entry into the NIIS system and year of registration. Anápolis - GO. 2011 a 2016

Type of entry	2011	2012	2013	2014	2015	2016	Total
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
New case	43 (89.6)	37 (86.1)	42 (84)	27 (87.2)	34 (89.5)	47 (81.1)	230 (85.8)
Re-entry	0 (0)	0 (0)	0 (0)	2 (6.4)	2 (5.3)	0 (0)	4 (1.5)
Unknown	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Transference	4 (8.3)	6 (13.9)	4 (8)	0 (0)	1 (2.6)	7 (12.1)	22 (8.3)
Recidivism	1 (2.1)	0 (0)	4 (8)	2 (6.4)	0 (0)	2 (3.4)	9 (3.3)
Post-death diagnosis	0 (0)	0 (0)	0 (0)	0 (0)	1 (2.6)	2 (3.4)	3 (1.1)

Table 4. Distribution TB cases according to gender and TB treatment termination in Anápolis - GO from 2011 to 2016

Treatment termination		Cure	Dropout	Transference	Death by TB	Death by other cause	*P*
		n (%)	n (%)	n (%)	n (%)	n (%)	
2011	Male	20 (41.7)	3 (6.3)	1 (2.1)	1 (2.1)	4 (8.3)	0.769
	Female	13 (27.1)	2 (4.1)	2 (4.1)	1 (2.1)	1 (2.1)	
2012	Male	21 (48.8)	6 (13.9)	2 (4.7)	1 (2.3)	2 (4.7)	0.279
	Female	11 (25.6)	0 (0)	0 (0)	0 (0)	0 (0)	
2013	Male	24 (48.0)	4 (8.0)	3 (6.0)	0 (0)	2 (4.0)	0.769
	Female	13 (26.0)	2 (4.0)	2 (4.0)	0 (0)	0 (0)	
2014	Male	16 (51.6)	1 (3.2)	1 (3.2)	1 (3.2)	0 (0)	0.552
	Female	12 (38.7)	0 (0)	0 (0)	0 (0)	0 (0)	
2015	Male	16 (42.1)	4 (10.5)	1 (2.6)	7 (18.5)	1 (2.6)	0.485
	Female	7 (18.5)	0 (0)	1 (2.6)	1 (2.6)	0 (0)	
2016	Male	28 (58.3)	0 (0)	6 (12.5)	9 (18.8)	5 (10.4)	0.249
	Female	9 (90.0)	0 (0)	0 (0)	0 (0)	1 (10.0)	
	Total	190 (70.9)	22 (8.2)	19 (7.1)	21 (7.8)	16 (6.0)	

The Probability of significance (p-value) refers to the Fisher's exact test.

Table 5: Distribution of HIV infection-related TB cases according to gender

HIV		Positive	Negative	*p*
		n (%)	n (%)	
2011	Male	5 (10.4)	24 (50)	0.518
	Female	2 (4.2)	17 (35.4)	
2012	Male	7 (16.3)	25 (58.1)	0.347
	Female	1 (2.3)	10 (23.3)	
2013	Male	4 (8)	29 (58)	0.486
	Female	1 (2)	16 (32)	
2014	Male	0 (0)	19 (61.3)	0.0003*
	Female	0 (0)	12 (38.7)	
2015	Male	7 (18.4)	22 (57.9)	0.905
	Female	2 (5.3)	7 (18.4)	
2016	Male	8 (13.8)	38 (65.5)	0.949
	Female	2 (3.4)	10 (17.3)	
	Total	39 (14.5)	229 (85.5)	

Table 6. Distribution TB cases according to smear microscopy results

Bacilloscopy	2011	2012	2013	2014	2015	2016	Total
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Positive	21 (43.8)	26 (61)	28 (56)	20 (64.5)	24 (63.2)	32 (55.2)	151 (56.3)
Negative	16 (33.3)	6 (13.4)	11 (22)	3 (9.7)	7 (18.4)	13 (22.4)	56 (20.9)
Not performed	11 (22.9)	11 (25.6)	11 (22)	8 (25.8)	7 (18.4)	13 (22.4)	61 (22.8)

during the period of the study. Table 5 refers HIV infection-related TB according to the gender. Among thoser, 85.5% (229/268) of the patients were HIV negative and 14.5% (39/268) were HIV positive. The Probability of significance (p-value) refers to the Fisher's exact test. *Statistically significant. Smear microscopy, an important diagnostic tool for tuberculosis, was performed in 77.2% (207/268) of the cases, with a positive result in 56.3% (151/268), 20.9% (56/268) with a negative result and for 22.8% (61/268) of the patients the exam was not performed (Table 6).

DISCUSSION

The population under study is predominantly male and the highest incidence of bacilli were observed in the age group of 41 to 60 years followed by the age group of 20 to 40 years. These findings are similar to those found at national level (14, 15). According to Vendramini et al. (16), there has been an increase in the incidence of TB in the population aging from 39 to 49 years and for those older than 60. Therefore, the median age is around 41 years old, affecting the age group with greater productive capacity. These data have important social complications, because the population within this group should be inserted in the labor market and provide financial support for their families (17). The predominance of TB in 10.1% of patients over sixty years old emphasizes that the disease deserves attention regarding this age group. Life expectancy has increased, causing an increase in the number of elderly individuals and consequently the incidence of diseases. Health professionals should be aware of the TB susceptibility in elderly people in order to reduce death rate (18). In relation to the educational attainment of the population, the majority of the patients attended only elementary school. The prevalence of the disease is related to the low level of education, which is a TB risk factor and contribute to the poor patient adherence in TB treatment (19, 20). The low level of education reflects a set of precarious socioeconomic conditions, which increase the vulnerability to TB and is responsible for the higher incidence of the disease. Regarding ethnicity, there was a predominance of brown skin patients, which reproduces the historical process of colonization of Brazil, miscegenation, migratory movements, dynamics of territorial occupation and spatial organization (21, 22). The prevalence of the pulmonary form corroborates general epidemiological studies (23-26). The higher incidence of pulmonary TB refers to the fact that the lungs are have higher levels of oxygen, facilitating the installation of the obligately aerobic bacteria. It is important to emphasize that the pulmonary TB deserves greater attention because it is the transmissible form of the disease. Since the pulmonary form is easy to diagnose and can be performed at low cost, it is expected that it can be promoted by the primary health care (27). HIV is one of the most important risk factors of tuberculosis (27). In the present study, 85.5% of the patients were HIV negative and 14.5% were HIV positive. These data highlight the importance of the TB treatment since HIV brings serious implications for the control of the TB transmission (29). The likelihood of an immunocompetent individual infected by the TB bacillus develop the disease is about 10% throughout their life, whereas in the HIV seropositive patients without treatment, this possibility rises to 10% per year and increase the number of deaths in coinfected patients (30).

The presumptive diagnosis of tuberculosis is performed through data from the clinical history and radiological findings. The gold standard diagnostic confirmation is obtained by bacilloscopy and/or cell culture. However, late diagnosis may favor the transmission and severity of the disease (31). Bacilloscopy was performed in 77.2% of the patients with a positive result in 56.3%, negative result in 20.9% and 22.8% of the cases did not undergo such examination. Smear microscopy is one of the diagnostic methods used in public health that is effective considering speed and cost. However, it has limitations because TB confirmation requires a significant count of bacilli (5,000 cm^3), leading to a high false negative rate. Negative results may be due to the initial stage of the disease because the bacillus presents a slow growth and the immunity system may keep be keeping the TB infection under control (32). The vast majority of the patients (85.8%) registered in the NIIS system were new cases of tuberculosis. The cure rate was 70.9% but the

Anápolis TB control program has not reached its goal. According to the criteria recommended by WHO for tuberculosis, an efficient control program is expected to ensure that at least 85% of the diagnosed cases of the disease are cured. The effectiveness of the health care service was also evaluated by the dropout rate of 8.2%, which was lower than the 10% tolerated by the Ministry of Health (26). Discontinuation of treatment involves a number of factors, such as side effects and health care issues (33). The rate of death caused by tB was 7.8%. It is important to note that TB can be prevented and is curable in almost 100% of cases, provided that the appropriate treatment regimen is followed. Nowadays, death of a patient affected by TB should be an exceptional event. Therefore, there should be a greater commitment of health professionals in order to guide and maintain antituberculosis therapy. Activities related to prevention and the enlightment of the population regarding treatment may improve TB cure rate. The Ministry of Health, through the General Coordination of the National Tuberculosis Control Program, created a national plan with the objective of reducing TB incidence and mortality rate in order to eliminate the disease from the contry. The main goal is to reach less than 10 cases and less than 1 death per 100 thousand inhabitants by the year 2035 (34). During the period of the study, the TB control Program in Anápolis was not within the Ministry of Health's goal. Therefore, we believe that campaigns of awareness, TB patient screening and early treatment should be well structured and maintained in order to fight against this chronic infectious and contagious disease. In conclusion, mass preventive campaigns could contribute to the clarification of risk behaviors of the population, stressing out the importance of an individualized approach. Further integration between population and primary health care must also be encouraged, a crucial step for health education in order to eradicate TB.

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