

Epidemiology of Tuberculosis in a Cohort of Children in the Colombian Pacific Coast 2009-2013

Epidemiología de la Tuberculosis en una Cohorte de Niños en la Costa Pacífica Colombiana entre 2009 y 2013

Johanna Cándelo Montenegro¹, Jennifer Rojas Forero², Liliana Forero³,
Robinson Pacheco López⁴

¹ Centro de Fisioterapia y Rehabilitación Pacifico, Buenaventura, Colombia.

² Unidad Pediátrica Clínica Farallones, Cali, Colombia.

³ Secretaría Departamental de Salud del Valle del Cauca, Cali, Colombia.

⁴ Universidad Libre, Maestría en Epidemiología, Grupo de Investigación en Epidemiología y Servicios (GRIEPIS), Cali, Colombia.

Correspondence to: Jennifer Rojas Forero
Current Address: 607,492 Springbank Drive, London, ON, Canada. N6J1H1.
jenniferrojas.f86@gmail.com.

Received: July 15, 2018

Accepted: September 27, 2018

Keywords: Tuberculosis, Pulmonary tuberculosis, child, cohort, Colombia.

Palabras clave: Tuberculosis, tuberculosis pulmonar, niños, cohorte, Colombia.

Cite this as: Candeló MJ, Rojas-Forero J, Forero L, Pacheco LR. Epidemiology of Tuberculosis in a Cohort of Children in the Colombia Pacific Coast 2009-2013. *ijEPH*. 2018; 1(1): e0003. doi: [10.18041/2665-427X/ijeph.1.3871](https://doi.org/10.18041/2665-427X/ijeph.1.3871).

Abstract

Introduction: The diagnosis of pulmonary tuberculosis in children is a challenge in all tuberculosis programs. The adverse social and economic conditions of the Colombian Pacific Coast make it a complex area for the management of the disease, especially in children.

Objective: To describe the demographic and clinical characteristics, and the outcomes in the pediatric population with pulmonary tuberculosis in Buenaventura, Colombia.

Methods: We conducted a descriptive observational study of a historical cohort (2009-2013) of children enrolled in the tuberculosis control program of Buenaventura. Results: A total of 163 cases were found and analyzed. There was no significant difference in sex distribution. The most frequent age group was 1-5 years (51%) and 55% belonged to the subsidized health system. The clinical TB diagnosis prevailed (55%), while the laboratory diagnosis was significant in patients older than 7 years. 92% entered the program as new cases, and 40% had their treatment finished at discharge. Adherence to treatment compliance was less than 50% in both phases of treatment. The incidence of childhood pulmonary tuberculosis during the study period ranged between 2 and 4 x 100,000 inhabitants. There were inconsistencies in the information between the Tuberculosis program of the Municipality and the National Surveillance System of Colombia.

Conclusion: The social and political difficulties in depressed areas of Buenaventura, a remote town in the Pacific Coast of Colombia, have a negative impact on the control of TB, despite strategies of childhood pulmonary tuberculosis based on timely diagnosis and treatment; effective follow-up of cases; study of contacts; and efficient, timely notification.

Resumen

Introducción: El diagnóstico de la tuberculosis pulmonar infantil es un reto en los programas de control. Las condiciones sociales y económicas adversas presentes en la Costa Pacífica Colombiana la convierten en un área compleja para el manejo de la enfermedad, especialmente en los niños.

Objetivo: Describir las características demográficas y clínicas, y su desenlace en la población pediátrica que presentan tuberculosis pulmonar, en Buenaventura, Colombia.

Métodos: Se realizó un estudio descriptivo observacional en una cohorte histórica de niños (2009-2013) incluidos en el programa de control de tuberculosis.

Resultados: Un total de 163 casos se incluyeron en el análisis. No encontramos diferencias significativas en la distribución por sexo. La edad más frecuentemente afectada estuvo entre 1-5 años (51%) y el 55% pertenecía al régimen de salud subsidiado. El diagnóstico clínico fue el más prevalente (55%), mientras que el diagnóstico por laboratorio fue significativo en niños >7 años. El 92% de los casos fueron casos nuevos, y el 40% finalizaron su tratamiento al darles de alta. La adherencia al tratamiento fue >50% en ambas fases del tratamiento. La incidencia de la tuberculosis infantil estuvo en un rango entre 2-4 por 100,000 niños. Se encontraron inconsistencias entre el programa de tuberculosis municipal y el sistema de vigilancia de Colombia.

Conclusiones: Las dificultades políticas y sociales en esta área deprimidas de Buenaventura, tienen un impacto negativo en el control de la tuberculosis, a pesar de las estrategias de diagnóstico, tratamiento y seguimiento oportuno, estudios de contactos y la notificación oportuna, implementadas para el control de la tuberculosis infantil.

Key Study Facts

Objective	To describe the demographic and clinical characteristics, and the outcomes in the pediatric population with pulmonary tuberculosis in Buenaventura, Colombia. Methods: We conducted a descriptive observational study of a historical cohort (2009-2013) of children enrolled in the tuberculosis control program of Buenaventura.
Study design	Descriptive observational study of a historical cohort
Source of data	Historical cohort (2009-2013) of children enrolled in the tuberculosis control program of Buenaventura
Population/Sample	163 cases
Statistical analysis	Descriptive statistics, Incidence, Chi square to compare proportions Key variables:
Main finding	The incidence of childhood pulmonary tuberculosis during the study period ranged between 2 and 4 x 100,000 inhabitants. The most frequent age group was 1-5 years (51%)



Introduction

Tuberculosis (TB) is a chronic bacterial infection of worldwide distribution, caused by the *Mycobacterium tuberculosis* complex (1). 90% of infected people are asymptomatic (2,3), with pulmonary localization being the most frequent clinical form (4). Although the disease affects especially men of productive age in low-income countries, it is increasingly common in children. According to the World Health Organization (WHO), about one million cases of childhood TB are reported annually, equivalent to 11%, with an estimated mortality of 136,000 cases, of which 40% are HIV positive (5).

According to the Pan American Health Organization (PAHO), TB is the second cause of death by an infectious agent, after HIV-AIDS (5). In Colombia in recent years, the incidence of TB has ranged between 24 and 26 cases per each 100,000 inhabitants (6). Buenaventura reported an incidence of 90 cases per 100,000 inhabitants in 2011, the highest incidence in the country (7). For the year 2010, there were reported 719 cases of childhood TB (6.3%), for an incidence of 5.47 cases per 100,000 children aged under 15 years (8); and in 2016, there were reported 584 cases of childhood TB (18%).

The diagnosis of pulmonary TB in children is complex, due to the diversity of non-specific symptoms and the difficulty in obtaining sputum samples in a spontaneous manner that allow the observation and isolation of the microorganism, so the diagnosis is based on the joint evaluation of epidemiological, clinical, radiological, immunological and microbiological criteria, which raises costs and delays diagnosis (9).

The exposure, infection and development of the disease in children is determined by close contact with baciliferous adults (parents or caregivers) (10); for this reason, accuracy and timeliness in diagnosis and treatment, as well as an effective contact study, are essential to cut the chain of transmission and achieve the objectives of TB prevention and control programs. However, the adverse social, political and security conditions of depressed areas of Buenaventura are the main obstacle that hinder the actions of diagnosis, treatment, follow-up and notification for the TB control program of the municipality (11).

The objective of this research was to describe demographic and clinical characteristics and treatment outcomes of the infant population diagnosed with pulmonary tuberculosis enrolled between 2009 and 2013 in the municipal TB control program of Buenaventura - Colombia.

Methods

Study design

It was carried out an observational, descriptive study of a historical cohort of children aged between 1 and 15 years, with diagnosis of Pulmonary Tuberculosis.

Study area

Buenaventura is the most important seaport of the Colombian Pacific, with an area of 6,078 km² of tropical rainforest and an

estimated population in 2016 of 374,000 inhabitants (12); it is estimated that 40% of the population live in conditions of poverty and overcrowding, and another 40% live in extreme poverty. Deficiencies in infrastructure limit the population's access to employment, public services, education and health (5,13).

Source of information

The collection of the information was supported by the municipal tuberculosis control program of Buenaventura, the health care institutions and the Tuberculosis Program of the Valle del Cauca Province. The sources of consultation were: a) Records of patients diagnosed with pulmonary TB, provided by the municipal TB control program. b) Tuberculosis individual follow-up cards, from which there were extracted demographic information, follow-up and programmatic outcomes. c) Clinical Histories, from which the clinical information of the patients was verified and supplemented. d) Notification sheets of the National Public Health Surveillance System (SIVIGILA), provided by the TB control program, with which there was validated all the demographic, clinical, and programmatic information of the records included in the study.

Management and analysis of information

The information was consolidated in an electronic database in Microsoft Excel and analyzed in the IBM SPSS Statistic 20.0 program. To evaluate the quality of the data and control possible biases of information, 100% of the recorded information was verified against the source documents.

The distribution of the data was evaluated for all the numerical variables through the Kolmogorov–Smirnov test and they were summarized with measures of central tendency and dispersion, as appropriate. The qualitative variables were presented as proportions in frequency tables. The dependence of the variables was determined through Chi-square test or Fisher's exact test, as appropriate, and a value of $p < 0.05$ was assumed as significant. Possible determining factors were explored at the beginning of management and treatment through the Kaplan–Meier method.

Ethical Implications

This study was approved as a risk-free investigation by the research ethics committee of the Universidad Libre, Cali Section, according to the minutes 02-1 April 2015. All the researchers state that they have no conflicts of interest.

Results

Between January 2009 and December 2013, there were registered 238 children aged 1 to 15 years with a diagnosis of Tuberculosis Pulmonary in the municipal Tuberculosis control program in Buenaventura. After evaluating the selection criteria, the information of 163 patient records was analyzed (Figure 1).

According to the demographic characteristics, there were no differences by sex; however, when stratifying for age, it was found that the age group of 6-10 years had an increase in the number of cases in males in a ratio of 1.6:1; situation that is reversed in the age group of 11-15 years, in which females have a higher percentage of TB in a 1.5:1 ratio. Taking into account the

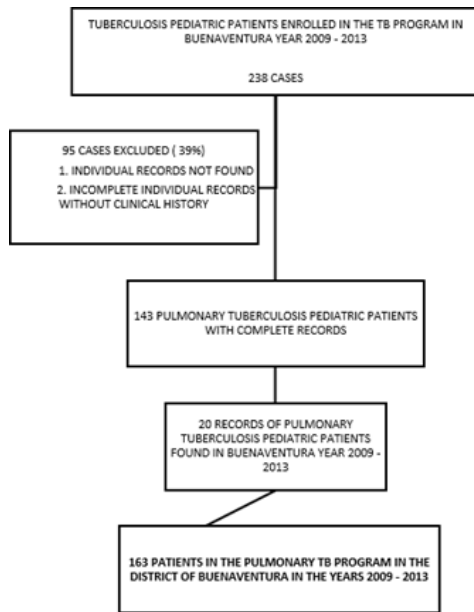


Figure 1: Flow chart for the study population. Buenaventura, Colombia. 2009 – 2013

Source of information: TB Control Program Database and individual tracking cards.

previous classification, the age group of 1 to 5 years contributed 51% of cases of childhood TB, and the remaining 49% was evenly distributed between the two other groups (Table 1). When comparing the variable sex with age group, these were independent, according to the chi-square test: 3.83 (p-value: 0.15).

Regarding the health system, only 14% of the population belonged to the contributory or special regime; 55% of the population belonged to the subsidized regime; while 31% did not have any type of insurance. Analyzing the geographical distribution, the largest numbers of cases were concentrated in communes 3, 11 and 12; and the rural area; corresponding to 61% of the location of cases.

Diagnostic Method

The predominant diagnostic method was the clinical one, with 55%; followed by diagnosis by epidemiological link, with 27%; and only 18% of the patients could be confirmed by laboratory. When analyzing the interrelation between the diagnostic methods, the clinical diagnosis and the epidemiological link were found in 49 cases, the clinical and laboratory diagnosis in 23 cases, epidemiological link and laboratory in 2 cases, while the three methods converged in 28 TB cases (Figure 2). However, the diagnosis by laboratory was significant only in children older than 7 years (p: 0.0002).

Ninety two percent of patients were admitted to the program as new cases; the remaining 8% were classified as readmissions or previously treated cases. According to the category of discharge, 25% of the patients completed the treatment as Cured and 40% of the patients finished the anti-tuberculosis treatment without bacteriological control test. It was evidenced that 32% abandoned

Table 1. Demographic characteristics of the study population. Buenaventura, Colombia 2009 - 2013

Characteristic	%
Sex (total of population)	
Male	50.0
Female	50.0
Age (years)	
1-5	51.0
6-10	24.5
11-15	24.5
Health system	
Subsidized	55.0
None	31.0
Contributive	12.0
Special	2.0
Commune	
12	23.0
Rural	18.0
3	10.0
11	10.0
Other Communes	39.0

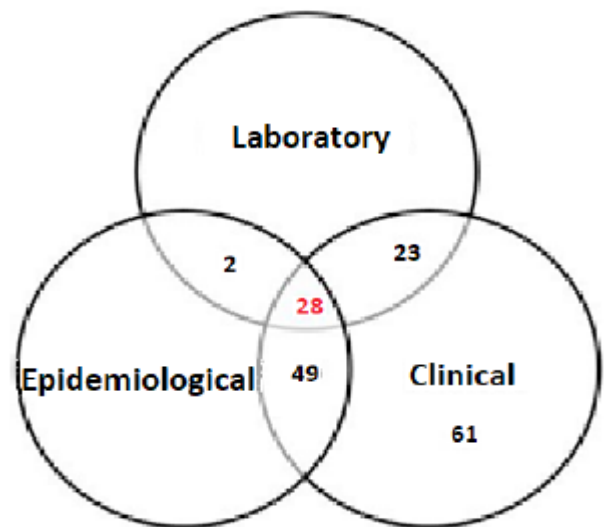


Figure 2. Diagnostic relationship of pediatric pulmonary TB according to the method. Buenaventura, Colombia 2009 – 2013

Source of information: Records of patients diagnosed with pulmonary TB, provided by the municipal TB control program and individual follow-up cards.

Table 2. Relationship between the admission and discharge conditions of the pediatric pulmonary TB cases in the program. Buenaventura, Colombia 2009 – 2013

Admission condition	Discharge condition				Total n (%)
	Abandoned n (%)	Cured n (%)	Finished n (%)	Died n (%)	
New	48 (29)	36 (22)	62 (38)	4 (2)	150 (92)
Relapse	0 (0)	1 (1)	0 (0)	0 (0)	1 (1)
Re-admission	4 (2)	4 (2)	3 (2)	1 (1)	12 (7)
Total	52 (32)	41 (25)	65 (40)	5 (3)	163 (100)

Source: Information provided by the individual monitoring cards, medical records and compulsory notification cards of the National Public Health Surveillance System (SIVIGILA).

the TB program. Only one case of mortality occurred during anti-tuberculosis treatment (Table 2). Evaluating the relationship of variables, it was established dependence between the abandonment of the TB control program and the fact of coming from the rural area ($p: 0.0007$).

When assessing whether the health affiliation regime influenced the timely initiation of anti-tuberculosis treatment and continued adherence to anti-tuberculosis treatment, no significant differences were found in the Kaplan Meier analysis (log Rank $p: 0.62$ and p -value: 0.60). There was also no dependence on the origin of the patients (the place they came from), whether rural or urban. (log Rank $p: 0.47$ and 0.21).

For this period, the Ministry of Social Protection, recommended 48 doses for the first phase; in this study, compliance with the standard was presented in 23%. Regarding the second phase, 36 doses were established, but in this population none of the patients received the recommended dose number. The highest percentage of patients received 54 doses (36%).

During the study period, the incidence of childhood TB in Buenaventura reported by the TB control program and the National Public Health Surveillance System (SIVIGILA) presented diversity with respect to the report for the years 2009 to 2011.

During the years 2012 and 2013, the incidence reported by the two systems coincided (Figure 3).

Discussion

Tuberculosis in children is difficult to diagnose; its management and follow-up are challenging for TB control programs. This is the first study that describes the demographic, diagnostic and programmatic outcomes of pulmonary tuberculosis in a cohort of children enrolled in the Buenaventura TB control program, between 2009 and 2013.

The characteristics of the population according to the sex distribution did not show significant differences, reflecting the population distribution of Buenaventura, where there were no changes in the gender registered by the 2005 census with a projection to the year 2011 (14); also resembling a study conducted in Cuba from 2009-2011 (15).

According to age, a greater percentage of cases occurred between 1-5 years, which probably does not imply a higher incidence, but rather corresponds to a better screening strategy and epidemiological surveillance, based on the strengthening of the IMCI strategy (16) and the support of the NGO Médicos sin Fronteras (Médecins Sans Frontières, France) in the generation

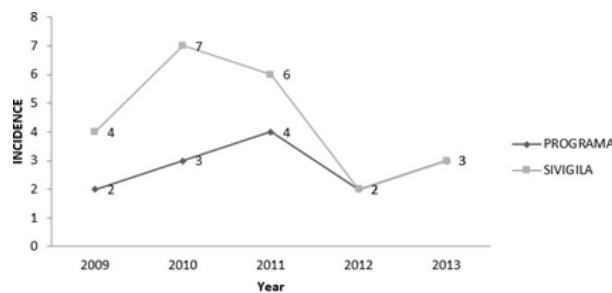


Figure 3. Behavior of the incidence of pediatric pulmonary TB according to the tuberculosis program and the National System of Public Health Surveillance (SIVIGILA). Buenaventura, Colombia 2009 – 2013.

Source: Information taken from the Buenaventura TB program and the National Public Health Surveillance System (SIVIGILA)

and capture of patients and home visits, identifying all children under 5 years of age living in the home of an adult with pulmonary tuberculosis, and then referring them to a health center for their clinical evaluation (11). Similar results have been reported for 2012 throughout Colombia (17); and in a study conducted in Cuba, 2001-2010 (18). Buenaventura has limitations in sanitary conditions and difficulties in territorial organization, which makes it difficult to classify socio-economic levels, so this study explored the relationship of the health system as a social indicator. This is correlated with the finding of 55% in the subsidized health system, followed by 31% of uninsured persons, situation that evidences the nature of the disease. This is similar to a study carried out in Cali in 2014 (19), where 86.4% of children with TB lived in neighborhoods of low socioeconomic status.

Cases from rural areas represented 18% of the reported cases, and the urban sector presented the highest figures in communes 12, 3 and 11, since these accounted for 43% of the cases. Such information would be useful to generate prevention strategies in high burden communities, as it has been expressed in some studies (18,20) that worked in TB neighborhoods based on the preparation of the communities and health personnel, in order to detect new cases, so diminishing the incidence based on new Public Health strategies (21); this has great importance in the active search of contact sources, since the diagnosis of a child with TB represents a sentinel event that reflects recent transmission within a limited circle of social contact (2). It is defined that the exact quantification of the burden of pediatric TB disease provides a key parameter of control of the epidemic (18).

The clinical diagnosis represents the highest percentage of cases, in addition to a high interrelation with the epidemiological diagnosis, which evidences the gaps mentioned by the Panel of Experts in 2012, since the tests used conventionally do not achieve microbiological confirmation of the disease (22). However, the diagnosis by laboratory showed an increase during the evaluated period, which could be explained by the introduction of microbiological tests to the program. This form of diagnosis is associated in a dependent manner at age >7 years (p -value: 0.0002), since there's a greater possibility of detecting bacilli per field in a smear microscopy in this population, which could also explain the slight increase in notifications of cases for the age of 12 years.

A large percentage of new cases was evidenced thanks to a sieve format, which allowed pulmonary tuberculosis to be detected in respiratory, symptomatic patients. In Colombia, during the last years, about 6% of the new detected cases of TB occurred in the population aged under 15 years (6). It was evidenced re-entry of 7%, something that however does not correlate with the 32% of abandonment, possibly as a consequence of lack of education for parents and environment. According to Médicos sin Fronteras (Médecins Sans Frontières), 58% of abandonment in this population depends on social, family and cultural factors (11); however, new studies are required to expand the possible causes. The abandonment and living in urban or rural areas show dependence (p -value: 0.0007), an association that moves away the compliance of the national goal, according to PAHO (5).

The Pulmonary and Extra-pulmonary Tuberculosis Care Guide – 2007 (23) given by the Ministry of Social Protection, recommends initiation of post-diagnosis treatment in a timely manner, in addition to a treatment based on a 180-day period, divided into two phases of supervision, a situation that varies in Buenaventura. Such behavior possibly occurred due to ignorance of the norm, lack of role of the support networks, and little education to the caregivers (regarding treatment). It is observed that the relationship between the start of treatment and the treatment time do not depend on the Assurance Regime or the Territorial Organization, despite the limitations described for Buenaventura.

The percentage of compliance for phase I in this study was 23%. The lower doses may be part of the Abandonment cases, but those that exceeded the doses would express the little support and control of the follow-up. Alarmingly, for phase II, the study showed no compliance in any of the cases, reflecting seriously the poor application of the regulations.

The exact quantification of pediatric TB provides a key parameter of control of the epidemic; according to the findings of the study, the incidence of Pediatric Pulmonary TB in Buenaventura was 2-4 x 100,000 inhabitants, (a figure) lower than that published in the Epidemiological Report of Colombia of the year 2012 (8), which shows an incidence of 5.5 x 100,000 inhabitants for those aged under 15 years. However, it is a high rate when compared with other countries, such as Cuba, with better prevention and control strategies, where a rate of 2.2 and 2.1 was registered in children from 0 to 14 years in the period 2001 to 2010 (18); or the Netherlands, corresponding to 3.6 for the year 1993 to 1.9 for the year 2012 (24), evidencing that there is much to improve in the prevention of this disease.

At the beginning of the study, there was a 51% correlation between the Tuberculosis Program data and the National Public Health Surveillance System, but despite the shortcomings, a tendency towards improvement was observed, a situation that was unified in 2013, with a 100% correlation.

Due to the lack of data, a fact the researchers are not accountable for, it was possible to analyze (only) 68% (163/238) of the records of pediatric patients with pulmonary TB reported by the TB program, estimating the epidemiological situation of the TB children in Buenaventura.

One of the strengths of this study was the active search for information, managing to recover 93% of the records of patients not notified, which ensured the quality of the information.

The diagnosis, treatment and follow-up of the children population with pulmonary tuberculosis is a challenge for clinicians and for tuberculosis control programs. It is worth highlighting the role of Médicos sin Fronteras (Médecins Sans Frontières, France), which contributed to the reduction of the incidence of pulmonary tuberculosis in children, in Buenaventura.

In conclusion, the social and political difficulties in depressed areas of Buenaventura have a negative impact on the control

strategies of pulmonary tuberculosis in children, which are based on diagnosis and timely treatment, effective case monitoring, contact study, and efficient, timely and truthful notification.

References

1. Dheda K, Barry CE, Maartens G. Tuberculosis. *Lancet*. 2016; 387(10024): 1211-26.
2. Lee SH. Tuberculosis infection and latent tuberculosis. *Tuberc Respir Dis (Seoul)*. 2016;79(4):201. Doi: 10.4046/trd.2016.79.4.201
3. Zumla A, Raviglione M, Hafner R, Fordham von Reyn C. Tuberculosis. *N Engl J Med*. 2013; 368(8): 745-55. doi: 10.1056/NEJMra1200894.
4. Perez-Velez CM, Marais BJ. Tuberculosis in children. *N Engl J Med*. 2012; 367(4): 348-61.
5. WHO. Guidance for national tuberculosis programmes on the management of tuberculosis in children – 2nd ed. Geneva, Switzerland: WHO; 2014.
6. Instituto Nacional de Salud. Protocolo de vigilancia en salud pública Tuberculosis. Bogotá: INS; 2014. http://www.ins.gov.co:81/lineas-de-accion/Subdireccion-Vigilancia/sivigila/Protocolos_SIVIGILA/PRO_Tuberculosis.pdf
7. Suarez RF. Buenaventura: una ciudad-puerto, globalizante, diversa y multicultural. Rey TE; Calvo GP. XIV Encuentro de Latinoamericanistas Españoles: congreso internacional, Sep 2010, Santiago de Compostela, España. Universidad de Santiago de Compostela, Centro Interdisciplinario de Estudios Americanistas Gumersindo Busto; Consejo Español de Estudios Iberoamericanos; 2010. pp.2488-2507.
8. Instituto Nacional de Salud. Informe Epidemiológico Nacional 2012. Bogotá (Colombia); 2015. <http://doi.org/10.1017/CBO9781107415324.004>
9. Panqueva COP, Morales dLJE. Tuberculosis en niños. *Precop SCP*. 2011; 10(2) :62-69.
10. OPS. Detección oportuna de tuberculosis permitirá reducir la mortalidad en niños y niñas. Bogotá; 2013. Available from: https://www.paho.org/col/index.php?option=com_docman&view=download&category_slug=pubblicaciones-ops-oms-colombia&alias=1403-tb-24-marzo-2013&Itemid=688.
11. Prada S, Sarría M, González J. ¿Y usted, como lo haría?: El programa de tuberculosis de Médicos sin Fronteras en Buenaventura; 2017. Available at SSRN: <https://ssrn.com/abstract=2931161>.
12. DANE: Mercado laboral de la ciudad de Buenaventura 2016; 2017. https://www.dane.gov.co/files/investigaciones/boletines/ech/ech_buenaventura/boletin_buenaventura_16.pdf.
13. DANE. Censo General de Colombia: 2005. 2005; <http://www.dane.gov.co/index.php/estadisticas-por-tema/demografia-y-poblacion/censo-general-2005-1>.
14. Fundación Panamericana para el Desarrollo. Buenaventura, ciudad puerto de clase mundial. Plan local de empleo 2011-2015. 2012. <http://www.mintrabajo.gov.co/documents/20147/18956918/Plan+Local+de+Empleo+de+Buenaventura+2012.pdf/7c1a4b61-4952-aeaf-f014-9f03bbd3c754?download=true>.
15. Perez PT, Perez GL, Ghaddar FN. Caracterización clínico epidemiológica de la tuberculosis en la edad pediátrica. Santa Clara. 2009-2011 (Cuba). Universidad de Ciencias Médicas “Dr. Serafin Ruíz de Zárate Ruíz” de Villa Clara; 2013. <http://files.sld.cu/enfermeria-pediatria/files/2013/03/mencion-3-caracterizacion-clinico-epidemiologica-de-la-tuberculosis-en-la-edad-pediatria-santa-clara-2009-2011.pdf>.
16. Ministerio de Protección Social, OMS. Capítulo 7: Tuberculosis Infantil. Aten Integr a las Enfermedades Prevalentes la Infanc. 2009; http://www.saludinfantilvalledelcauca.com/uploads/1/3/7/8/13787752/capitulo_7_tuberculosis_infantil.pdf
17. Mecanismo coordinador de País. Fortalecer la estrategia Alto a la Tuberculosis en 46 municipios prioritarios del Litoral Pacífico colombiano. 2013. <http://www.mcpcolombia.co/tuberculosis/alto-a-la-tb>
18. Gladys DC, Suárez A, Lázara IL, Cabrera C, Elizabeth L, Rodríguez R, et al. Tuberculosis en menores de 15 años. *Rev Cubana Pediatr*. 2014;86(1):59-67. <http://pesquisa.bvsalud.org/portal/resource/es/lil-709193>
19. Villegas SL, Ferro BE, Rojas CM, Perez-Velez CM. Assessment of children exposed to adult pulmonary tuberculosis in Cali, Colombia. *Paediatr Int Child Health*. 2014; 34(3): 170-7. <http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=medl&NEWS=N&AN=24939365>
20. Zorzenon dSRM, Amador A, de Souza WV, de Albuquerque MFPM, Ponce DS, Ruffino-Netto A, et al. A dynamic analysis of tuberculosis dissemination to improve control and surveillance. *PLoS ONE*. 2010; 5(11): e14140. Doi: 10.1371/journal.pone.0014140
21. Cegielski JP, Griffith DE, McGaha PK, Wolfgang M, Robinson CB, Clark PA, et al. Eliminating Tuberculosis One Neighborhood at a Time. *Am J Public Health*. 2013; 103(7):1292-1300. doi:10.2105/AJPH.2012.300781
22. Graham SM, Ahmed T, Amanullah F, Browning R, Cardenas V, Casenghi M, et al. Evaluation of tuberculosis diagnostics in children: 1. Proposed clinical case definitions for classification of intrathoracic tuberculosis disease. Consensus from an expert panel. *J Infect Dis*. 2012; 205(suppl 2):199-208. Doi: 10.1093/infdis/jis008
23. Ministerio de Protección Social. Guía II: guía de la atención de tuberculosis pulmonar y extrapulmonar. Bogotá. (Colombia); 2007. https://www.minsalud.gov.co/Documentos_y_Publicaciones/GUIAS_DE_ATENCION-TOMO_DOS.pdf
24. Erkens CGM, de Vries G, Keizer ST, Slump E, van den Hof S. The epidemiology of childhood tuberculosis in the Netherlands: still room for prevention. *BMC Infect Dis*. 2014; 14(1): 295.

© Universidad Libre. 2018. Licence Creative Commons CC-BY-NC-ND-4.0. <https://creativecommons.org/licenses/by-nc-nd/4.0/legalcode>.

