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ORIGINAL ARTICLE

Association of Factors with Successful Treatment Outcome of Childhood Tuberculosis in Barangay Commonwealth, Quezon City, Philippines: A Two-Year Retrospective Study

ABSTRACT

Background: Tuberculosis remains a public health concern worldwide. Reports on the association of factors of childhood tuberculosis with treatment outcome are limited.

Objectives: To determine the epidemiology and association of factors of childhood tuberculosis with successful treatment outcome in some of the barangays of Quezon City.

Methodology: This is a retrospective cohort study done at Barangay Commonwealth Health Centers including children 0-14 years old with tuberculosis registered and treated from January 1, 2013 to July 15, 2015. Socio-demographic and clinical data were obtained. Patient profile data, treatment cards and medical records were the data sources.

Results: A total of 267 new cases of childhood TB were analyzed. The treatment success rate was 98% (97% completed treatment, 1% cured). The rate of poor treatment outcome including default cases was 2%. There were no reported deaths or treatment failure. On univariate analysis, patients with weight gain ($p=0.001$) had an odds ratio of 8.085 (95% CI:1.310-49.900) to have a successful treatment outcome. On multivariate analysis, weight gain was significantly associated with treatment success ($p=0.042$; OR=12.5, 95% CI: 1.091, 143.244). None of the socio-economic and clinical factors studied was associated with successful treatment outcome.

Conclusion: Weight gain is a factor of a successful treatment in childhood tuberculosis. Children who gained weight after treatment are more likely to have a successful treatment outcome.

KEYWORDS:

Childhood tuberculosis, treatment outcome, weight gain

INTRODUCTION

Tuberculosis (TB) continues to be a public health concern not only in the Philippines but throughout every region in the world. It ranks as the world's second leading cause of death from a communicable disease.¹ As stated in the Global Tuberculosis Report 2014 of the World Health Organization (WHO), an estimated 9.0 million people developed TB and 1.5 million died from the disease in 2013. Childhood TB contributes 6%, equivalent to 550,000 of the total new cases and 7%, equivalent to 80,000 of the total TB deaths from HIV-negative people in the same year.

The Philippines remains one of the 22 highest TB-burden countries worldwide and has one of the highest problems of multidrug resistant TB.² TB in children in our country forms part of the TB burden. The Philippine Health Statistics of 2010 of the Department of Health shows that TB in all forms tops the list of the leading cause of mortality among the immunizable diseases in 0-14 years old.³

TB is a significant cause of morbidity and mortality among children^{4,5,6} and yet there are limited data on the epidemiology of childhood tuberculosis.⁶ Few studies from Asia have also been published.⁷ The World Health Organization has recently expressed the urgent need to address the lack of epidemiological data on pediatric tuberculosis in high-burden countries.⁶

A surveillance report on TB profile of the Philippines from 2003 to 2011 stated that 1% of the new cases were children 0 – 14 years old.² The proportion of their treatment outcome and the factors associated with it, however, were not emphasized.

In a study on the treatment outcomes of childhood TB in Thailand, 200 (72%) out of the 279 (2% of the national

burden) cases completed treatment or were cured; 17(6%) died, 3(1%) failed, 39(14%) defaulted and 20(7%) transferred out.⁷ A 5-year retrospective study in Addis Ababa on TB revealed that the percentage of children with TB was 6.6%. Treatment outcomes were documented for 95.2% of children with treatment success rate of 85.5%. Mortality rate was 3.3% and defaulting was 3.8%.⁸ The data collected in a review of pediatric TB cases in Taiwan from 2002 to 2009 showed that a relatively small number of children ranging from 0.72% to 1.24% were diagnosed with TB.⁹ The nationwide study of TB in Malawi revealed that 11.9% were children from the 22,982 cases registered. Death rate was high at 17%. Forty five percent completed treatment; 13% defaulted and 21% with unknown outcome.¹⁰

The above studies showed that treatment outcomes and incidence of childhood TB vary from one country or region to another even amongst endemic areas. Grange, et al discussed the changing epidemiology of tuberculosis which may result from a complex interplay between social, political, economic, genetic, cultural and environmental factors and the possibility of natural selection of an immune population.¹¹ As presented by Sivanandan, et al, the factors associated with treatment failure in childhood tuberculosis included AFB positivity at diagnosis, non-receipt of Bacille Calmette-Guerin (BCG) vaccination and extrapulmonary tuberculosis (EPTB).¹² The study done in Southern Ethiopia indicated that males, extremes of ages and patients on retreatment were those with poor outcome; smear negative patients had the lowest rate of successful treatment outcome.¹³ Marais, et al pointed out in an article that the determinants of the burden of childhood TB could be extrapolated from community exposure which includes

number and duration of infectiousness and crowding; and community vulnerability which comprises immune compromise, immune stimulation and local defenses.¹⁴ Aside from crowding the other risk factors on childhood TB were identified as parental education and annual household income.⁶ Successful treatment outcome in children was higher in older age group,^{9,11,15} smear-positive and HIV-negative patients.^{11,16}

Childhood TB is a neglected aspect of the TB epidemic because it is usually smear-negative and considered to contribute little to the propagation of the disease.^{17,18,19} However, pediatric cases are important because they provide valuable epidemiologic perspective since they reflect on-going transmission within communities.²⁰

This study determined and investigated the successful treatment outcomes of TB in children and identified the factors affecting them. The results may serve as monitoring tool and may contribute in the modification of existing guidelines, strategies or policies in the management of TB in children to improve the outcome particularly in the community level.

This study aimed to determine the association of factors of childhood tuberculosis with successful treatment outcome in Barangay Commonwealth, Quezon City from January 2013 to July 2015.

We also determined the socio-demographic, anthropometric and clinical profile of childhood TB patients and the prevalence rates of childhood TB with successful and poor treatment outcomes. The association of socio-demographic, anthropometric and clinical characteristics of childhood TB with successful treatment outcome was studied.

METHODOLOGY

This is a retrospective cohort study that utilized odds ratio to determine association between various socio-demographic, anthropometric and clinical data and treatment outcome of children with TB.

The study was conducted in three health centers of Barangay Commonwealth, the biggest barangay in terms of population size, accounting for 5.6 percent (120,569) of the total population of Quezon City, Philippines²¹ and located in the second district of the city which is administratively divided into seven units.²² The three health centers namely: Commonwealth Health Center (HC), Dona Nicasia HC and National Government Center (NGC) HC are also designated Directly Observed Therapy Short Course (DOTS) facilities under the management and supervision of the Quezon City Health Department (QCHD).

The patients included in the study were children aged zero to fourteen years old diagnosed with tuberculosis based on the NTP standard guidelines and treated from January 1, 2013 to July 15, 2015.

Sample Size

All cases of childhood tuberculosis equivalent to 267 were included in the study.

Inclusion and Exclusion criteria

Patients aged zero to fourteen years old diagnosed with tuberculosis and treated in the above-mentioned centers were included. All patients transferred out were excluded from the study because the outcomes of treatment were indeterminate.

Operational Definition of terms

(as defined in the Manual of Procedures of the National Tuberculosis Control Program 5th ed., 2014 DOH)²³

Children - individuals with age ranging from 0 to 14 years old.

Treatment outcome - the condition of the patient after the prescribed treatment period:

Completed treatment - anti-tuberculous drugs taken and completed during the prescribed course.

Cured - the condition of the patient in which he/she has initially a smear-positive sputum microscopy that turned out to be negative in the last month of treatment and on at least one previous occasion in the continuation phase.

Relapse patient - those previously treated patients for TB and declared cured or treatment completed at the end of the recent course of treatment and are now TB symptomatic with any one of the following: progressive deterioration or worsening of chest radiograph findings, smear positive or culture positive.²⁴

Failed - an initially smear positive who remains or becomes smear positive on the 5th month of treatment or a newly diagnosed TB patient whose TB symptoms persisted and has failed to gain weight after six months of treatment.²⁴

Defaulted - one who has interrupted treatment for two months; lost to follow up.

Retreatment - previously treated case of TB who is started on a treatment regimen after previous treatment has failed or a patient treated for TB who returns to treatment having defaulted; or a patient who was previously declared cured or treatment completed and is diagnosed with bacteriologically positive T5.²⁵

Successful treatment outcome - refers to patients considered as cured or completed treatment; good treatment outcome; treatment success.

Poor treatment outcome - refers to patients considered to have defaulted,

failed in the treatment and died during the treatment period; unsuccessful treatment.

Smear positive PTB - PTB diagnosed through DSSM with two or more initial sputum smear examination for acid-fast bacilli; or one sputum smear examination positive for acid-fast bacilli plus chest radiograph abnormalities consistent with active TB as determined by a clinician; or one sputum smear examination positive for acid-fast bacilli plus sputum culture positive for *M. tuberculosis*; bacteriologically-confirmed case of TB.²⁴

Smear negative PTB - PTB diagnosed through DSSM in 10-14 years old or younger with at least three smear-negative for acid-fast bacilli; and radiologic abnormalities consistent with active pulmonary TB; and no response to a course of broad spectrum antibiotics; and decision by a physician and/or TB Diagnostic Committee to treat the patient with a full course of anti-TB chemotherapy; or a negative DSSM or PTB diagnosed through other diagnostic tests other than DSSM in 0-9 years old who cannot expectorate with any three of the following: TB symptomatic, positive tuberculin skin test, abnormal chest radiograph suggestive of TB, laboratory findings suggestive or indicative of TB; clinically-diagnosed case of TB.²⁴

Poverty threshold - the minimum income required for a family/individual to meet the basic food and non-food requirements which is PhP 8,778.00 monthly for a family of five.^{26,27}

Directly observed treatment short course (DOTS) - a treatment strategy wherein a TB patient takes the anti-TB drugs in the presence of a caregiver whether he be a doctor, a nurse, a midwife, a community health worker or any volunteer who stands as treatment partner of the patient.

Malnutrition – undernutrition in children which is manifested as underweight, wasted or stunted based on the Preventive Pediatric Health Care Handbook 2014²⁸ as follows:

Wasted - children with body mass index (BMI) for age z-score of below -2 to below -3 and weight for length/ height z-score of below -2 to below -3.

Stunted - children with height for age z-score below -2 and below -3.

Underweight - children with weight for age z-score of below -2 to below -3.

Data and information were extracted from the National Tuberculosis Program (NTP) TB registry, treatment cards and the health center patient profile and medical records. The following data were collected: socio-demographic such as age, sex, educational attainment of parents, employment status and occupation of parents, family income, and family size; anthropometric data: weight, BMI and height; and clinical information as to the classification of TB cases, category of patients, close TB contact, BCG vaccination, Tuberculin Skin Test (TST), chest radiograph findings, co-morbid conditions, exposure to cigarette smoke and treatment outcomes. Pre-treatment and post treatment weight were taken to determine the presence of weight gain, average weight gain and percentage of weight gain from baseline. Post treatment height was unavailable; hence, post treatment BMI was not calculated. The presence of malnutrition in every patient was determined by getting the height/length for age, BMI for age, weight for age, and weight for height/length. Z-scores of the anthropometric record of each patient were taken using the WHO Z-score charts. Data from the treatment cards were rechecked in the TB registry. Missing information on the patient profile and medical records were verified by the

community health workers who stood as treatment partners of the patients. Hence, the TB registration number, the names, addresses and telephone numbers were initially gathered for this purpose but disregarded in the final tally of data prior to analysis to ensure confidentiality. Data were listed in a data extraction form and saved using EXCEL

Data from all evaluable subjects who satisfy the inclusion/exclusion criteria were included in the analysis. Missing values were not replaced or estimated during the statistical analysis of outcome variables. Summary statistics were presented in tables and reported as n (%). Column percentages were computed relative to total data excluding missing values. Checks for homogeneity of sample population was done. Yates' chi-square test was used to compare proportions. Univariate analysis was performed to determine independent significant associations of sociodemographic, anthropometric and clinical characteristics with success of treatment outcome. Significant variables from the univariate analysis were included in the multivariate logistic regression analysis to determine significant associations considering effects of other independent characteristics. Odds-ratios and 95% confidence intervals were estimated. Statistical significance was based on p-values ≤ 0.05 . Statistical Package for the Social Sciences version 20 (SPSS v20) was used in data processing and analysis.

ETHICAL CONSIDERATIONS

A waiver of consent for the conduct of this study was given by the East Avenue Medical Center Institutional Ethics Review Board (EAMC IERB). An approval from the QCHD was obtained prior to the initiation of the study.

RESULTS

A. Socio-demographic, Anthropometric and Clinical Profile

Data from 267—eligible subjects were included in the analysis. Most of the children were 4 years or younger with majority of the parents either finished grade school or high school, most had both or either parent employed and belonged to families with 2-5 members. Socio-demographic characteristics are summarized in Table 1.

Table 1. Socio-demographic Profile of Children with TB in Barangay Commonwealth, Quezon City, 2013 – 2015

	Successful Treatment Outcome		Poor Treatment Outcome	Total n = 267	p-value
	Cured n = 3	Completed n = 259	Defaulted n = 5		
Age in years, n (%)					
0 – 4	-	152 (56%)	5 (100%)	157 (59%)	0.000*
5 – 9	-	85 (33%)	-	85 (32%)	
10-14	3 (100%)	22 (8%)	-	25 (9%)	
Gender, n (%)					
Male	-	131 (51%)	4 (80%)	135 (51%)	0.665
Female	3 (100%)	128 (49%)	1 (20%)	132 (49%)	
Educational Attainment of Parents, n (%)					
Grade School/ High School	2 (67%)	158 (65%)	5 (100%)	165 (66%)	0.000*
Vocational/ College	1 (33%)	86 (35%)	-	87 (34%)	
Employment of Parents, n (%)					
Employed	2 (67%)	239 (98%)	5 (100%)	246 (98%)	0.000*
Unemployed	1 (33%)	5 (2%)	-	6 (2%)	
Family size, n (%)					
2-5 members	3 (100%)	174 (71%)	3 (60%)	180 (71%)	0.000*
≥ 6 members	-	70 (29%)	2 (40%)	72 (29%)	
Economic status, n (%)					
Equal/ below poverty threshold**	3 (100%)	127 (52%)	5 (100%)	135 (54%)	0.609
Above poverty threshold	-	116 (48%)	-	116 (46%)	

*Non-homogeneity of sample population: significant at 5% level
 ** Approximately PhP8,000.00 to PhP9,000.00 estimate of average monthly income based on 2014 National Statistical Coordination Board Poverty threshold equivalent to PhP8,778.00 monthly income for a family of five
 ---The total number of cases in some parameters was less than 267 due to missing data

The median weights of cured patients before and after treatment were 37kg and 40kg, respectively. Patients who completed treatment and defaulted both had a median weight of 14kg prior to treatment. The median weight after treatment among those with complete treatment was 15kg. No weight change was seen among those who defaulted. The BMI of patients with successful treatment outcome and poor treatment outcome was comparable prior to treatment. Among those who completed treatment,

50 (50/262) were stunted (Z-score below -2 to Z-score below -3) and 64 (64/262) were wasted (Z-score below -2 to Z-score below -3). Among those with poor treatment outcome, only 1 (1/5) was wasted. All cured patients had gained weight with a median percentage of 7.53% from baseline. Eighty four percent among those who completed treatment gained weight of 5.71% from baseline. Two patients who defaulted had a weight gain of 4.16%. Anthropometric characteristics are summarized in Tables 2 and 3.

Table 2. Anthropometric Profile of Children with TB in Barangay Commonwealth, Quezon City, 2013 – 2015

	Successful Treatment Outcome		Poor Treatment Outcome	Total n = 267	p-value
	Cured n = 3	Completed n = 259	Defaulted n = 5		
Weight (kg), median (range)	37 (34-37)	14 (6-52)	14 (8-15)	14 (6-52)	0.009*
Height (cm), median (range)	160 (158-162)	102 (57-155)	99 (75-109)	102 (57-162)	0.008*
Height for age before treatment, n (%)					
Z-score above 3	-	6 (2%)	1 (20%)	7 (3%)	0.000*
Z-score above 2	-	7 (3%)	-	7 (3%)	
Z-score above 1	-	2 (1%)	-	2 (1%)	
Z-score 0	3 (100%)	170 (66%)	4 (80%)	177 (66%)	
Z-score below -1	-	22 (8%)	-	22 (8%)	
Z-score below -2	-	30 (12%)	-	30 (12%)	
Z-score below -3	-	20 (8%)	-	20 (8%)	
BMI (kg/m²), median (range)	14 (13-15)	14 (6-23)	15 (13-15)	14 (6-23)	0.820
BMI for age before treatment, n (%)					
Z-score above 3	-	2 (1%)	-	2 (1%)	0.000*
Z-score above 2	-	10 (4%)	-	10 (4%)	
Z-score above 1	-	22 (8%)	-	22 (8%)	
Z-score 0	-	96 (37%)	1 (20%)	97 (36%)	
Z-score below -1	-	68 (26%)	3 (60%)	71 (26%)	
Z-score below -2	2 (67%)	31 (12%)	1 (20%)	34 (13%)	
Z-score below -3	1 (33%)	30 (12%)	-	31 (12%)	

*Non-homogeneity of sample population: significant at 5% level

Table 3. Anthropometric Data After Treatment of Children with TB in Barangay Commonwealth, Quezon City, 2013 – 2015

	Successful Treatment Outcome		Poor Treatment Outcome	Total n = 267	p-value
	Cured n = 3	Completed n = 259	Defaulted n = 5		
Weight (kg), median (range)	40 (37-40)	15 (6-52)	14 (8-16)	15 (5-52)	0.006*
Weight gain, n (%)	3 (100%)	218 (84%)	2 (40%)	223 (84%)	0.000*
Weight gain in kg, median (range)	2.8 (2.5-3.0)	0.8 (0.10-7.80)	0.5 (0.3-0.7)	0.8 (0.10-7.80)	0.009*
% weight gain relative to baseline weight, median (range)	7.53 (7.25-8.11)	5.71 (0.30-35.21)	4.16 (3.66-4.67)	5.71 (0.30-35.21)	0.443

*Non-homogeneity of sample population: significant at 5% level

All children were new cases of childhood tuberculosis and classified as pulmonary TB. Of the 267 cases, two children had both pulmonary and extrapulmonary types of TB. One had scrofula and the other, TB peritonitis. There were no cases of extrapulmonary TB alone. Two hundred sixty-four (99%) are smear-negative or clinically diagnosed TB. Comparable results were seen in children exposed (126/262, successful treatment; 3/5, poor treatment) and not exposed (109/262, successful

treatment; 2/5, poor treatment) to a known source case of TB. Majority received BCG vaccination and most of the children (163/262, successful treatment; 4/5, poor treatment) had a positive skin test or TST size of equal to or more than 10mm. Most common comorbidity reported was malnutrition (3/3, cured; 108/262, completed; 1/5, defaulted). Clinical characteristics are summarized in Table 4.

Table 4. Clinical Profile of Children with TB in Barangay Commonwealth, Quezon City, 2013 – 2015

	Successful Treatment Outcome Cured n = 3	Completed n = 259	Poor Treatment Outcome Defaulted n = 5	Total n = 267	p-value
Category of Patients, n (%)					
New	3 (100%)	259 (100%)	5 (100%)	267 (100%)	-
Classification of TB, n (%)					
PTB Smear +/- BC ^a	3 (100%)	-	-	3 (1%)	-
PTB Smear -/ CD ^{aa}	-	259 (100%)	5 (100%)	264 (99%)	
Close TB contact, n (%)					
Negative	3 (100%)	106 (41%)	2 (40%)	111 (42%)	0.199
Positive	-	126 (49%)	3 (60%)	129 (48%)	
BCG Vaccination, n (%)					
Positive	2 (67%)	240 (95%)	5 (100%)	247 (95%)	0.000*
Negative	1 (33%)	11 (4%)	-	12 (5%)	
Tuberculin Skin Test size (mm), n (%)					
< 10	-	51 (24%)	1 (20%)	52 (24%)	0.000*
≥ 10	-	163 (76%)	4 (80%)	167 (76%)	
Chest X-ray, n (%)					
Without findings	3 (100%)	121 (47%)	4 (80%)	128 (48%)	0.341
With findings	-	138 (53%)	1 (20%)	139 (52%)	
Cigarette smoke exposure, n (%)					
Yes	-	97 (40%)	2 (40%)	99 (39%)	0.000*
No	3 (100%)	147 (60%)	3 (60%)	153 (61%)	
Comorbidity, n (%)					
Without	-	145 (56%)	3 (60%)	148 (55%)	0.019*
With	3 (100%)	114 (44%)	2 (40%)	119 (45%)	
Malnutrition, n (%)					
Without	-	151 (58%)	4 (80%)	155 (58%)	0.076
With	3 (100%)	108 (42%)	1 (20%)	112 (42%)	
Asthma, n (%)					
Without	3 (100%)	240 (93%)	5 (100%)	248 (93%)	0.000*
With	-	19 (7%)	-	19 (7%)	
Recurrent URTI^{aaa}, n (%)					
Without	3 (100%)	237 (92%)	5 (100%)	245 (92%)	0.000*
With	-	22 (8%)	-	22 (8.2%)	
Pneumonia, n (%)					
Without	3 (100%)	232 (90%)	5 (100%)	240 (90%)	0.000*
With	-	27 (10%)	-	27 (10%)	
Acute tonsillopharyngitis, n (%)					
Without	3 (100%)	257 (99%)	5 (100%)	265 (99%)	0.000*
With	-	2 (1%)	-	2 (1%)	

	Successful Treatment Outcome Cured n = 3	Completed n = 259	Poor Treatment Outcome Defaulted n = 5	Total n = 267	p-value
Scabies, n (%)					
Without	3 (100%)	257 (99%)	5 (100%)	265 (99%)	0.000*
With	-	2 (1%)	-	2 (1%)	
Otitis, n (%)					
Without	3 (100%)	256 (99%)	5 (100%)	264 (99%)	0.000*
With	-	3 (1%)	-	3 (1%)	
Parasitism, n (%)					
Without	3 (100%)	259 (100%)	4 (80%)	266 (99.6%)	0.000*
With	-	-	1 (20%)	1 (0.4%)	
Hearing defect, n (%)					
Without	3 (100%)	258 (99.6%)	5 (100%)	266 (99.6%)	0.000*
With	-	1 (0.4%)	-	1 (0.4%)	
Brain cyst, n (%)					
Without	3 (100%)	258 (99.6%)	5 (100%)	266 (99.6%)	0.000*
With	-	1 (0.4%)	-	1 (0.4%)	

*Non-homogeneity of sample population: significant at 5% level---The total number of cases in some parameters was less than 267 due to missing data

^aBacteriologically confirmed

^{aaa}Upper Respiratory Tract Infection

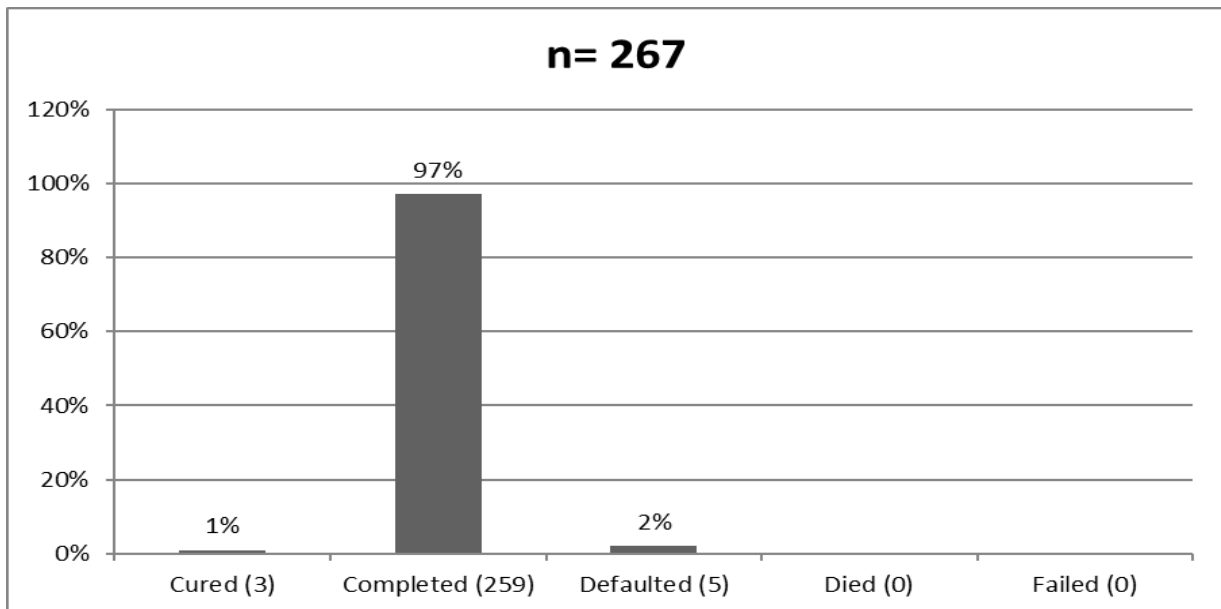
^{aa}Clinically diagnosed

B. Treatment Outcome

Majority of children with tuberculosis in this study had a successful treatment outcome. Two hundred fifty-nine (97%) completed treatment and three (1%) were cured. A negligible number had

unsuccessful treatment outcome (5, 2%). All of those with poor outcome defaulted. There were no reported cases of death or treatment failure (Figure 1).

Figure 1. Rates of Outcome of Treatment in 267 Children with Tuberculosis



C. Factors Associated with Successful Treatment Outcome

On univariate analysis (Table 5), the successful treatment outcome was 8.085-fold (95% CI, 1.310-49.000) higher in

children with weight gain ($p=0.001$). The percent weight increase ($p=0.422$) of patients with successful treatment outcome (5.73%) was not significant compared to the percent weight increase of those with poor treatment outcome (4.16%). The absence of comorbid conditions namely: acute tonsillopharyngitis ($p=0.015$), scabies ($p=0.015$), parasitism ($p=0.019$), hearing

defect ($p=0.000$) and brain cyst ($p=0.000$) was a factor independently related with the treatment outcome among children with tuberculosis. On multivariate analysis (Table 5), the successful treatment outcome was 12.5-fold (95% CI, 1.091-143.244) higher in patients with weight gain ($p=0.042$).

Table 5. Univariate and Multivariate Association of Sociodemographic, Anthropometric and Clinical Characteristics with the Treatment Outcome of Childhood TB in Barangay Commonwealth, Quezon City, 2013 – 2015

	Successful Treatment Outcome n = 262	Poor Treatment Outcome n = 5	p-value (Univariate Analysis)	Odds Ratio (95% CI**)	p-value (Multivariate Analysis)	Odds Ratio (95% CI**)
Age in years, n (%)						
0 – 4	152 (58%)	5 (100%)	0.447	-	-	-
5 – 9	85 (32%)	-				
10-14	25 (10%)	-				
Gender, n (%)						
Male	131 (50%)	4 (80%)	0.380	0.250	-	-
Female	131 (50%)	1 (20%)		(0.028,2.267)		
Educational Attainment of Parents, n (%)						
Grade School/ High School	160 (65%)	5 (100%)	0.224	-	-	-
Vocational/ College	87 (35%)	-				
Employment of Parents, n (%)						
Employed	241 (98%)	5 (100%)	0.259	-	-	-
Unemployed	6 (2%)	-				
Family size, n (%)						
2-5 members	177 (72%)	3 (60%)	0.944	1.686	-	-
≥6 members	70 (28%)	2 (40%)		(0.276,10.305)		
Economic status, n (%)						
Below/equal to poverty threshold	130 (53%)	5 (100%)	0.101	-	-	-
Above poverty threshold	116 (47%)	-				
Weight (kg), median (range)						
Before treatment	14 (6-52)	14 (8-15)	0.307	-	-	-
After treatment	15 (6-52)	14 (8-16)	0.160	-	-	-
Weight gain, n (%)						
With	221 (84%)	2 (40%)	0.001*	8.085	0.042*	12.5
Without	41 (16%)	3 (60%)		(1.310,49.900)		(1.091, 143.244)
Weight gain in kg, median(range)	0.8 (0.10-7.80)	0.5 (0.3-0.7)	0.204	-	-	-
% weight gain relative to baseline weight, median (range)	5.73 (0.30-35.21)	4.16 (3.66-4.67)	0.422	-	-	-
Height for age before treatment, n (%)						

	Successful Treatment Outcome n = 262	Poor Treatment Outcome n = 5	p-value	Odds Ratio (95% CI**)	p-value	Odds Ratio (95% CI**)
				(Univariate Analysis)		(Multivariate Analysis)
Z-score above 3	6 (2%)	1 (20%)	0.243	-	-	-
Z-score above 2	7 (3%)	-				
Z-score above 1	2 (1%)	-				
Z-score 0	173 (66%)	4 (80%)				
Z-score below -1	22 (8%)	-				
Z-score below -2	30 (12%)	-				
Z-score below -3	20 (8%)	-				
BMI (kg/m²), median (range)	14 (6-23)	15 (13-15)	0.569	-	-	-
BMI for age before treatment, n (%)						
Z-score above 3	2 (1%)	-	0.682	-	-	-
Z-score above 2	10 (4%)	-				
Z-score above 1	22 (8%)	-				
Z-score 0	96 (37%)	1 (20%)				
Z-score below -1	68 (26%)	3 (60%)				
Z-score below -2	33 (13%)	1 (20%)				
Z-score below -3	31 (12%)	-				
Category of Patients, n (%)						
New	262 (100%)	5 (100%)	-	-	-	-
Classification of TB, n (%)						
PTB Smear +/- BC ^a	3 (1%)	-	0.057	-	-	-
PTB Smear -/ CD ^{aa}	259 (99%)	5 (100%)				
Close TB contact, n (%)						
Negative	109 (46%)	2 (40%)	0.865	1.298	-	-
Positive	126 (54%)	3 (60%)		(0.213,7.909)		
BCG Vaccination						
Positive	242 (95%)	5 (100%)	0.564	-	-	-
Negative	12 (5%)	-				
Tuberculin Skin Test size (mm), n (%)						
< 10	51 (24%)	1 (20%)	0.739	1.252	-	-
≥ 10	163 (76%)	4 (80%)		(0.137,11.452)		
Chest X-ray, n (%)						
Without findings	124 (47%)	4 (80%)	0.319	0.225	-	-
With findings	138 (53%)	1 (20%)		(0.025,2.037)		
Cigarette smoke exposure, n (%)						
No	150 (61%)	3 (60%)	0.668	1.031	-	-
Yes	97 (39%)	2 (40%)		(0.169,6.283)		
Co-morbid condition, n (%)						
Without	145 (55%)	3 (60%)	0.805	0.826	-	-
With	117 (45%)	2 (40%)		(0.136,5.027)		
Malnutrition, n (%)						
Without	198 (76%)	4 (80%)	0.749	0.790	-	-
With	64 (24%)	1 (20%)		(0.087,7.195)		
Asthma, n (%)						
Without	243 (93%)	5 (100%)	0.879	-	-	-
With	19 (7%)	-				
Recurrent URTI^{aaa}, n (%)						
Without	240 (92%)	5 (100%)	0.885	-	-	-
With	22 (9%)	-				

	Successful Treatment Outcome n = 262	Poor Treatment Outcome n = 5	p- value (Univariate Analysis)	Odds Ratio (95% CI**)	p- value (Multivariate Analysis)	Odds Ratio (95% CI**)
Pneumonia, n (%)						
Without	235 (89%)	5 (100%)	1.000	-	-	-
With	27 (10%)	-				
Acute tonsillopharyngitis, n (%)						
Without	260 (99%)	5 (100%)	0.015*	-	-	-
With	2 (1%)	-				
Scabies, n (%)						
Without	260 (99%)	5 (100%)	0.015*	-	-	-
With	2 (1%)	-				
Otitis, n (%)						
Without	259 (99%)	5 (100%)	0.057	-	-	-
With	3 (1%)	-				
Parasitism, n (%)						
Without	262 (100%)	4 (80%)	0.019*	-	-	-
With	-	1 (20%)				
Hearing defect, n (%)						
Without	261 (99.6%)	5 (100%)	0.000*	-	-	-
With	1 (0.4%)	-				
Brain cyst, n (%)						
Without	261 (99.6%)	5 (100%)	0.000*	-	-	-
With	1 (0.4%)	-				

DISCUSSION

Tuberculosis is an infection that leads to wasting caused by loss of appetite and body weight, nutrient malabsorption, micronutrient malabsorption and altered metabolism as a response to the infectious process in which a complex interaction between the host and the virulence of the organism modulates the overall metabolic response and the various degrees of tissue breakdown.^{29,30} The presence of weight gain after therapy indicates a satisfactory response to treatment.^{31,32} wherein the virulence of mycobacteria has been successfully targeted by the anti-tuberculosis drugs.

As seen in our study, weight gain has a significant association with successful treatment outcome based on univariate and multivariate analyses. Children with TB who gained weight after treatment have an 8.085-fold to 12.5-fold probability of having a successful treatment outcome. However, the median

weight gain of 0.8kg or 5.73 % weight increase seen among those with successful treatment in this study is not significant compared to the 0.5kg weight gain or 4.16% weight increase among those with poor outcome.

This study shows that the socio-demographic and clinical factors such as age, gender, educational attainment and employment of parents, family size, economic status, patient category, TB classification, TST size, chest x-ray, cigarette smoke exposure and co morbid conditions namely malnutrition, asthma, recurrent URTI and pneumonia have no significant association with successful treatment outcome.

Several studies have demonstrated an association between age and gender and successful treatment outcome such as those done in Addis Ababa⁸ and southern region of Ethiopia.^{13,15} Fifty nine percent of patients in this study are children 0-4 years old. Age plays one of the most significant

roles in determining which children will progress to disease.¹⁸ Young children under 2-3 years of age in whom the immune system is still immature are likely susceptible to developing disease following the primary *Mycobacterium tuberculosis* infection.^{7,14} This study parallels the research done in Cape Town, South Africa where children <3 years old have the most number of cases (52%),³³ in contrast to the research done in Thailand where the least number of cases belongs to the under 4 years of age (26%).⁸ There is no significant difference in the distribution of cases across genders in this study which is different from the data at national level which show a male to female ratio of 1.8 in 2014.³⁴

Majority (98%) of the parents are employed but more than half (54%) of them still belong to the poverty threshold or below threshold, 68% acquired a low level of education and 72% with successful treatment belong to families with few members. No association between parental education, socio-economic background and crowding to treatment success of patients is created with these data found in the present study. Previous literatures show that there is a higher incidence of childhood tuberculosis found among parents with lower level of education and low annual household income such as those found in a cross-sectional study in South Africa⁶ and a hospital-based study in Pakistan.³⁵ The odds ratio of successful treatment outcome is only 1.686-fold higher in families with 2-5 members in contrast to a previous study where crowding is a factor for unsuccessful treatment outcome.⁵

All cases of childhood tuberculosis in this study are newly diagnosed, which matches the study done in Malawi where 99% of the childhood TB patients were new cases.¹⁰ The studies conducted in Thailand

and Addis Ababa had 78% and 88% as new cases, respectively. Almost all are PTB smear-negative or clinically diagnosed, opposing other studies where sputum smear-negativity ranges from 29%-66% of all childhood TB cases evaluated.^{7,8,36} Only 1% is PTB smear-positive or bacteriologically confirmed belonging to the 10-14-year age group. This finding is congruent to the study done in Malawi where 5% of the studied population had sputum smear-positive belonging to the 5-14 year age group as compared to the studies done in Congo and Thailand which has a higher percentage of 14% and 20%, respectively.^{7,8,36} Adolescence is associated with an increased risk of the development of TB, which usually presents as adult-type pulmonary disease and is often sputum smear-positive.⁷ Most of the patients in the present study belong to the 0-4 age group, therefore, expectoration is not expected and the collection of good quality sputum in the 5-9 year age group is hard. The association of TB classification and patient category with successful treatment outcome is not established in this study. Some researches show that successful treatment outcome is lower in smear-negative children¹⁶ and in re-treatment adult patients.^{13,37}

The diagnosis of TB infection supported by a positive TST was seen in 76% and chest radiograph findings were remarkable in one half of the study population. Eighty three percent of children assessed in a study in Congo had a pathologic chest radiograph results and is associated with treatment outcome.³⁶ Positive Tuberculin skin test was observed in 52% of children with TB studied in Rio de Janeiro and 59% in Cape Town, South Africa.^{38,39} This study showed that chest radiograph findings and TST size have no association with the treatment outcome.

Almost one half of our study population (48%) was exposed to a source case. The odds ratio of a successful treatment is only 1.298-fold higher among patients with no exposure as found in this study and not significant. Children in household or other close contact with an adult with pulmonary tuberculosis especially smear-positive or culture-positive pulmonary TB are at higher risk of getting infected.⁷ The result of a study done by Singh, et al, suggests that there is a high prevalence of infection among children in household contact with adult cases and that the risk is higher for contacts of smear-positive patients but is significant for sputum-negative patients.⁴⁰ Singh also stated that there is higher incidence of transmission of infection with exposure to environmental tobacco smoke. This study showed that 39% were exposed to cigarette smoke and has the odds ratio of successful treatment of only 1.031-fold higher than the non-exposed. In a meta-analysis study done by Patra, J., et al, second-hand smoke exposure is associated with an increase in the relative risk of latent TB infection and active TB after controlling for age, biofuel mass use, and contact with a TB patient.⁴¹ Cigarette smoke impairs pulmonary defense mechanisms, making airways more susceptible to infection.⁴⁰

Several medical conditions are risk factors for TB and for poor TB treatment results, while TB can complicate the disease course of some diseases.⁴² Forty five percent of the children in this study have medical conditions other than TB. The co-morbid conditions present were as malnutrition, bronchial asthma, recurrent upper respiratory tract infection, pneumonia and otitis media and all these did not show any association on the success of treatment outcome. The other comorbidities found in the study

population are as follows: acute tonsillopharyngitis ($p=0.015$), scabies ($p=0.015$), parasitism ($p=0.019$), hearing defect ($p=0.000$) and brain cyst ($p=0.000$); and their absence based on univariate analysis reveals an independent relationship with the treatment outcome.

Malnutrition is the most prevalent co-morbidity in this study. The WHO states that malnutrition is a significant risk factor for childhood tuberculosis⁷ and is associated with worse outcomes. Although the mechanisms underlying its association with TB remain unclear, some evidences suggest that it affects genetic expression and immune function that predisposes children to tuberculosis progression that results in a disease and inflammatory response that further worsens the nutritional state.⁴³

Only two patients were found to have extrapulmonary TB (EPTB) namely scrofula and TB peritonitis concomitant with pulmonary TB. The WHO states that extrapulmonary TB occurs in approximately 20–30% of all cases in children. In this study, the high coverage of almost 100% BCG vaccination among the study population can be a possible explanation for the low rate of EPTB. BCG vaccine has been shown to prevent about 60% to 90% of cases of the more severe forms of TB such as meningeal TB and disseminated TB in young children.⁴⁴ Another most likely explanation is that EPTB are generally more severe in terms of signs and symptoms and would usually be referred to or seen immediately in hospitals or referral center instead of being diagnosed and managed in DOTS facilities. As mentioned in the literature, non-receipt of BCG during infancy and EPTB are factors associated with poor treatment outcome. In this study, however, BCG is not associated with successful treatment outcome.

This study showed that children 0-14 years with tuberculosis comprise 23%⁴⁵ from the total TB cases both in adult and children which is two-fold higher than the 2014 national estimate of 12% for the same age group.³⁴ In a study by Marais, et al, a global estimate of 15% occurs in children <15 years of age in low income countries.³³ The treatment success rate in this study is 98%. This has contributed in the high treatment success rate of the entire city which is 91%⁴⁶ in 2014 exceeding the national and WHO targets of 90%⁴⁷ and 87%⁴⁸, respectively for the Millennium Development Goal 2015. The high treatment success rate can be attributed to the efforts of the local health officials to improve case holding through various NTP strategies such as the administration of DOTS in workplaces, homes and other acceptable venues in the community other than the health facility involving community volunteers as treatment partners.²

CONCLUSION

Weight gain in general is the single factor of a successful treatment in childhood tuberculosis established in this study. However, the median percentage weight increase of those with successful treatment outcome is not significant compared to the weight increase seen among patients with poor treatment outcome.

The socio-demographic and clinical factors such as patient category, TB classification, TST size, chest x-ray, cigarette smoke exposure and co morbid conditions namely malnutrition, asthma, recurrent URTI and pneumonia have no significant association with successful treatment outcome.

The prevalence rates of successful and poor treatment outcome in this study were 98% and 2%, respectively.

Follow-up on patients after treatment is a vital strategy in achieving and sustaining a TB-free community.

LIMITATIONS AND RECOMMENDATIONS

The limitation of this study is that it was done retrospectively. A prospective study that focuses on the other aspects of childhood tuberculosis such as co-infection with HIV, drug resistance and the factors that affect poor treatment outcome such as defaulting, failure and death is recommended. A larger population is also suggested by doing a multi-center study composed of more than 5 institutions or multi-barangay setting and longer study period of 5 years or more. Studies on weight gain in relation to TB are mostly done among adult patients. Further prospective research on weight and body mass index in childhood tuberculosis with emphasis on the percentage of monthly weight gain is, likewise, recommended. Some variables are found to be missing in the course of data collection. A complete patient profile and medical record should be obtained and recorded electronically to avoid missing data and result to easy access of a more reliable and valid information for future research studies.

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