Distribution Agreement

In presenting this thesis or dissertation as a partial fulfillment of the requirements for an advanced degree from Emory University, I hereby grant to Emory University and its agents the non-exclusive license to archive, make accessible, and display my thesis or dissertation in whole or in part in all forms of media, now or hereafter known, including display on the world wide web. I understand that I may select some access restrictions as part of the online submission of this thesis or dissertation. I retain all ownership rights to the copyright of the thesis or dissertation. I also retain the right to use in future works (such as articles or books) all or part of this thesis or dissertation.

Signature:

_____ _____

Ashley Fell Date

Agreement between Tuberculin Skin Test (TST) and QuantiFERON-TB Gold In-Tube (QFT) Assay When Screening for Latent Tuberculosis Infection (LTBI) in Young Refugee Children

By

Ashley Fell

MPH

Epidemiology

_____

Michael Goodman, MD, MPH

Faculty Thesis Advisor

_____

Alawode Oladele, MD, MPH

Thesis Field Advisor

Agreement between Tuberculin Skin Test (TST) and QuantiFERON-TB Gold In-Tube (QFT) Assay When Screening for Latent Tuberculosis Infection (LTBI) in Young Refugee Children

By

Ashley Fell

BA

St. Olaf College

2011

Faculty Thesis Advisor: Michael Goodman, MD, MPH

An abstract of

A thesis submitted to the Faculty of the

Rollins School of Public Health of Emory University

in partial fulfillment of the requirements for the degree of

Master of Public Health

in Epidemiology

2013

ABSTRACT

Agreement between Tuberculin Skin Test (TST) and QuantiFERON-TB Gold In-Tube (QFT) Assay When Screening for Latent Tuberculosis Infection (LTBI) in Young Refugee Children

By Ashley Fell

Since the early 2000's, foreign-born individuals have begun to make up a majority of cases of TB in the United States. Most of these cases result from the reactivation of latent tuberculosis infection (LTBI). Young children with LTBI are at particularly high risk of reactivation. Recently, interferon-gamma release assays (IGRAs) have been developed as a blood test for LTBI, providing an alternative to traditional tuberculin skin testing (TST). This cross sectional study sought to characterize agreement between QuantiFERON®-TB Gold In-Tube (QFT) and TST results while screening for LTBI in 216 refugee children less than 5 years of age in DeKalb County, Georgia. Medical record review was used to extract relevant test results and characteristics of participants.

Only 11% (4/37) of TST-positive children were QFT-positive and nearly 20% of all children had discordant TST/QFT results. Overall agreement between QFT and TST results was 81% but the kappa statistic indicated very poor concordance (κ=0.09, 95% Confidence Interval (CI): -0.05, 0.23). Concordance was higher in the subset of children 24 months of age or older (Agreement=86%, κ=0.22, 95% CI: -0.01, 0.44). The high discordance of TST and QFT results is likely explained by the high rate of Bacille Calmette-Guerin (BCG) vaccination in the study population and relatively low prevalence of LTBI. Once the use of IGRAs in this population is better understood, testing for LTBI could become simpler and more cost-effective, improving TB control in the United States.

Agreement between Tuberculin Skin Test (TST) and QuantiFERON-TB Gold In-Tube (QFT) Assay When Screening for Latent Tuberculosis Infection (LTBI) in Young Refugee Children

By

Ashley Fell

BA

St. Olaf College

2011

Faculty Thesis Advisor: Michael Goodman, MD, MPH

A thesis submitted to the Faculty of the

Rollins School of Public Health of Emory University

in partial fulfillment of the requirements for the degree of

Master of Public Health

in Epidemiology

2013

INTRODUCTION

In 2008, the World Health Organization (WHO) estimated that tuberculosis (TB) was the 7th leading cause of mortality in the world, accounting for approximately 2% of all deaths (1). Despite the high incidence of TB globally, rates of TB infection have been declining in the United States since the 1990's (2). With the decline in the rate of TB infection in the United States, there has been a change in the demographic profile of individuals at the highest risk of infection. Since the early 2000's, foreign-born individuals have begun to make up the majority of cases of TB in the United States, presenting a set of new challenges for TB control (3).

Thousands of refugees arrive in the United States each year. Of the twelve countries that represented 90 to 95% of refugee arrivals to the United States between 2009-2011, four (Burma, Democratic Republic of Congo, Ethiopia and Afghanistan) are considered by the WHO to experience high burden of TB (4, 5). While refugees are screened for active infection before arrival to the United States, they are at much higher risk of latent TB infection (LTBI) than the general US population. LTBI occurs when an individual is infected with *Mycobacterium tuberculosis* bacilli without having active TB disease. Although individuals with LTBI are not infectious, the majority of cases of TB in the United States are the result of reactivation of latent infection. For this reason identification and treatment of LTBI is an important part of the United States TB control and elimination strategy (6). Lifetime risk of LTBI reactivation is 5-10% in older children and adults, but can be as high as 40-50% in infants (7), and therefore identifying

young children with LTBI is especially important. When it is identified, LTBI can be treated to reduce the risk of progression to active TB disease.

Traditionally, diagnosis of LTBI has relied on the tuberculin skin test (TST), which involves injecting tuberculin purified protein derivative (PPD) intracutaneously into the forearm (8). Approximately 48-72 hours after injection, the diameter of induration (raised, hardened area) is measured in millimeters. The cutoff for a positive TST result ranges from 5 to 15 mm, depending on an individual's risk of TB infection. While TST has been the only diagnostic tool available for many years, it has a number of limitations. First, there is variability in how the TST is administered and how the results are evaluated (9). The PPD must be injected properly or the test will not be valid. Reading of the diameter of induration can be subjective and improper readings can lead to inaccurate results. In addition, cut-off values for a positive test significantly impact the sensitivity and specificity of TST. Second, administering and reading a TST requires two visits and patients may not return to have their test result read. Third, there is a high rate of false-positive results in individuals that have received Bacille Calmette-Guérin (BCG) vaccination. While BCG vaccination is not common in the United States, it is widely used in the rest of the world and the WHO recommends that all children born in countries with highly endemic TB receive it (10).

Specificity of the TST varies significantly depending on the population, from approximately 97% in persons unvaccinated with BCG, to about 60%, and with greater variability, in those who received the BCG vaccine (11). TST sensitivity has been reported to range between 71 and 82% (11).

Recently, interferon-gamma release assays (IGRAs) have been developed as an alternative method of diagnosing TB infection (12). IGRAs measure T-cell response to a protein secreted by the *M. tuberculosis* bacterium that is not present in most other mycobacteria or BCG (9). IGRAs require a blood sample and specific laboratory equipment for analysis. Specificity for IGRAs is estimated to reach 96% and 99%, for BCG-vaccinated and unvaccinated populations, respectively, which represents a significant improvement over the specificity of TST (11, 13). The cost of performing IGRAs tests can be prohibitive in low-resource settings (5), but IGRAs have quickly become the standard for LTBI detection in populations with high rates of BCG vaccination in the United States (12). QuantiFERON®-TB Gold In-Tube (QFT) assay is one of the two IGRAs approved by the U.S. Food and Drug Administration for use in the United States and is routinely used at the DeKalb County Board of Health Clinic to screen newly arrived refugees for LTBI.

Previous research has shown that agreement between TST and IGRAs in young children, particularly in those who received BCG vaccination, is low (7, 9, 14). For example, Méndez-Echevarría et al. found that among immigrant children under 5 years of age, discordant results between TST and QFT were more common in children ultimately determined to have LTBI or those who had received BCG vaccination (14). Some studies have also found that young children are more likely to have indeterminate QFT results (15, 16) or possibly less likely to produce TB specific antigen response (17, 18). Because of these indeterminate results, the Centers for Disease Control and Prevention still recommends to rely on TST in young children (12). At present, data on the use of

IGRAs to diagnose LTBI in children less than five years of age are limited, particularly in populations at high risk for TB infection and with high rates of BCG vaccination.

In 2010, the State of Georgia admitted 3,459 refugees, with over 3,000 persons settled in DeKalb County (19). In May 2010, DeKalb County began using QFT to screen all refugees for LTBI during routine health assessment visits that typically occur within the first month of arrival to the United States. Because of the limited data on the use of IGRAs in children, DeKalb County relies on both the TST and QFT results in the diagnosis of LTBI in children. The present study assessed the agreement between TST and QFT results in newly arrived refugee children under the age of five residing in DeKalb County, Georgia.

METHODS

Overview

The goal of this study was to characterize the agreement between TST and QFT results in screening for LTBI in refugee children less than 5 years of age in DeKalb County, Georgia. It was hypothesized that agreement between the tests would be poor because of the high rate of BCG vaccination in this population, resulting in false positive TST and limited IGRA response in young children, leading to false negative QFT. The research protocol was reviewed and approved by the Emory Institutional Review Board (IRB). The Georgia Department of Public Health IRB determined the study was exempt from review.

This cross sectional study involved medical record review to extract the following data elements: quantitative and qualitative TST and QFT results, sex, height, weight, country of origin, country of residence prior to arrival to the US, date of arrival to the US, and BCG vaccination status. The following elements were extracted for children with either a positive TST or QFT result: known contact with an active TB case, chest radiograph results and whether the child was treated for LTBI.

Study Population

Eligible participants were children under the age of 5 who had routine health screening for LTBI at the DeKalb County Board of Health conducted as part of the refugee health program between May 2010 and October 2012. Of 258 age-eligible children, 10 were excluded because they underwent screening before May 2010 and 32

children were excluded because of missing TST or QFT results. Thus the final dataset included 216 children.

Study Variables

Quantitative TST results included the diameter of induration measured in millimeters and recorded upon reading of the TST (approximately 48-72 hours after injection). In addition, the qualitative result (positive or negative) was also recorded. For the purposes of this study, TST was considered positive if the diameter of induration measured ≥10 mm. Quantitative QFT results included the TB specific antigen response, Nil (negative) control and Mitogen response (positive) control, all of which measured the interferon gamma (IFN-γ) concentration in plasma in international units per milliliter (IU/mL). The QFT result was considered positive if the TB specific antigen response (IFN-γ) was ≥0.35 IU/mL and ≥25% of nil, negative if the IFN-γ response was <0.35 IU/mL or <25% of nil with a mitogen response ≥0.5 IU/mL. Any other response was considered indeterminate, as well as any response with a nil >8.0 IU/mL.

Height and weight were measured and recorded as part of the routine pediatric physical exam. BCG vaccination status was reported by the caregiver or ascertained from vaccination records and documented as part of the physical exam record. Country of origin and country of residence prior to arrival to United States were reported on the refugee application physical examination form. All data were entered using EpiInfo 7 (CDC, Atlanta, GA).

Data Analysis

Data cleaning and analyses were performed using SAS 9.3 (SAS Institute, Inc., Cary, NC) statistical software. Age at the time of screening was calculated by subtracting the date of screening from the date of birth. Time in the United States was calculated by subtracting the date of screening from the date of arrival to the United States. Body mass index (in kg/m^2) was calculated for each child using the reported height and weight. BMI categories were assigned using the WHO's child growth standards for BMI-for-age (20). Incidence of TB (as reported by the WHO) for the country of origin and the country residence prior arrival to the US were also included in the analysis (5).

To evaluate the demographic characteristics of the study population, frequency estimates were calculated for the following variables: sex, country of origin, country of residence prior to United States arrival, region of origin, region of residence prior to United States arrival, BMI-for-age category, QFT result, TST result (≥10 mm), known contact with active TB case, treatment for LTBI, chest radiograph result and BCG vaccination status. Summary statistics, including mean, median and standard deviation, were calculated for continuous variables including height, weight, TST induration diameter, concentration of TB specific antigen response, age, and days in the United States at the time of screening.

To determine the concordance between QFT and TST results, frequency tables of QFT by TST results were constructed. Percent agreement and the kappa statistic (κ) were calculated to assess agreement between the tests. κ values less than 0.2 were considered to have poor agreement, values between 0.21-0.4 considered to have fair agreement, values between 0.41-0.6 to have moderate agreement, values between 0.61-0.7 to have

good agreement and values greater than 0.81 to have very good agreement (21). Agreement was calculated for the study population overall, by different TST induration cut-off points and by age group. Linear regression analysis was used to assess the relation of the TB specific antigen response to age and to TST induration diameter. Two sided P-values <0.05 were considered statistically significant.

To identify factors associated with agreement between QFT and TST results, multivariate logistic regression analysis was conducted using agreement between the tests as the binary outcome variable. Because there were so few positive QFT results, agreement was only assessed among QFT-negative children. The results of logistic regression analyses were expressed as adjusted odds ratios (OR) and the corresponding 95% confidence intervals (CI). Collinearity was assessed by calculating condition indices, values over 30 were considered to reflect potential collinearity problems (22). All models were also assessed for two-way interactions among covariates.

RESULTS

Study Population

216 children were included in the study population, with mean ± standard deviation (SD) age of 2.7 ± 1.3 years. Just over one-half of study participants (52.8%) were male. The children were resettled in DeKalb County, between 2010 and 2012 and arrived to the US from 19 countries. Table 1 shows the demographic characteristics of the study population by gender. The most commonly listed country of origin among participants was Burma (35%), followed by Bhutan (28%), Somalia (9%) and Iraq (9%). The median amount of time in the United States at the time of LTBI screening was 21 days (mean=30 days, SD =37 days). A vast majority (94%) of the study participants were BCG vaccinated. Most children had a healthy BMI-for-age, but almost 20% were underweight (Table 1). Among the 216 children, 17% (37) were TST-positive, 5.6% (12) were QFT-positive and one had an indeterminate QFT result.

Table 2 shows the demographic characteristics of the study population by region of origin. Most notably, children from Africa were more likely to be male and have a BMI-for-age considered to be overweight. Children from Africa had the lowest proportion of positive TST results (10%) but the highest proportion of positive QFT results (12%).

Agreement between QFT and TST results

Only 11% (4/37) of TST-positive children were QFT-positive and 19% of the children had discordant TST/QFT results (41/216). Overall agreement was 81% (κ=0.09,

95% Confidence Interval (CI): -0.05, 0.23). In children under the age of 24 months, agreement was 72% (κ=-0.07, 95% CI: -0.15, 0.00). In children 24 months of age or older, agreement was 86% (κ=0.22, 95% CI: -0.01, 0.44). Agreement did not vary when different induration diameter cut-off points were used for defining a positive TST result.

QFT response

To investigate the relation between age and response to the QFT assay, TB specific antigen (IFN-γ) response was plotted against age for all children (Figure 1) and children with a positive QFT result (Figure 2). Linear regression showed no statistically significant association between age and IFN-γ response in all children (β_1=0.007, 95% CI: -0.002, 0.016, p=0.13, R^2=0.04) or in QFT-positive children (β_1=0.076, 95% CI: -0.085, 0.237, p=0.32, R^2=0.10).

A similar analysis examined the association between induration diameter of TST and IFN-γ response (Figure 3). There was a statistically significant association between induration diameter of TST result and IFN-γ response in all children (β_1=0.041, 95% CI: 0.014, 0.068, p=0.003, R^2=0.04) but the R-squared value is low, indicating poor fit. In QFT-positive children, the association between induration diameter of TST and IFN-γ response was not statistically significant (β_1=0.310, 95% CI: -0.021, 0.641, p=0.063, R^2=0.30) (Figure 4).

Logistic Regression Analysis

The logistic regression model included sex, age and the total number of days since arrival to the US at the time of testing (Table 3). As only QFT-negative children were

included in the model, the dependent variable was negative TST result. Agreement was not statistically significantly higher among females compared to males (OR=1.7, 95% CI: 0.8, 3.8), but increased with increasing age (average OR per each year =1.04, 95% CI: 1.01, 1.06). Increasing days spent in the United States at the time of testing was associated with less agreement (average OR per each additional day=0.99, 95% CI: 0.98, 0.99).

DISCUSSION

Prevalence of positive QFT results in the study population was low. While overall percent agreement between QFT and TST results was relatively high, κ indicated very poor concordance. Compared to the results for the entire study population, estimates of concordance were higher in children 24 months of age or older. There was no significant association between IFN-γ response and age; however older age was associated with a higher probability of a negative TST among QFT-negative participants. One other factor found to be associated with a higher likelihood of agreement between TST and a negative QFT was duration of residence in the US.

It is important to point out that our results seem to be in general agreement with previous reports. Similar studies in children report percent agreement between QFT and TST results to be between 55 and 95% (9, 14, 16, 18), with lower agreement among BCG-vaccinated children. With overall agreement at 81%, the results of this study are consistent with the previous literature; however, our κ estimate was only 0.09, which is lower than the previously reported range of 0.17-0.63 among BCG-vaccinated children (9, 14, 18). The better agreement observed in children 24 months and older in our population is also concordant with previous reports (16). While the association between age and IFN-γ response is disputed in the literature (16, 17), to our knowledge no study examined the relation between time since arrival to the US and QFT/TST results.

Although our study is similar to previous reports, its contribution to the literature is important because it specifically focused on children 5 years old or younger. In addition, nearly all children in the present study were BCG vaccinated. In other studies,

children were generally recruited because of a risk factor for TB infection, while refugees are at higher risk for TB, the children in this study did not necessarily have known exposure to a TB contact. These factors would likely contribute to a higher number of TST false-positive results, leading to lower agreement and κ values.

Strengths of this study include reliability and consistency in testing for both QFT and TST. TSTs are used regularly at the clinic and the staff is well trained in administering and evaluating test results. QFT results were processed in the on-site laboratory and the low rate of indeterminate results indicates good laboratory practices.

The main weaknesses of this study are small sample size and the low prevalence of positive QFT results, which limited our ability to assess agreement with TST. In addition, analyses of factors associated with agreement between TST and QFT were limited by lack of information about specific risk factors for TB infection such as contact with active TB infection.

Some of the issues brought up in this and other similar reports may only be resolved in a large, prospective study with sufficient follow up that allows evaluating the validity of both TST and IGRA assay as predictors of TB reactivation. In addition, whether IFN-γ response is associated with age has been disputed in the literature and this study was not in a position to resolve this question due to a narrow age range of its participants. Expanding the study population to include children of all ages might be helpful in this regard. Once the use of IGRAs in BCG-vaccinated children is better understood, testing for LTBI could become simpler and more cost-effective, improving TB control in the United States.

REFERENCES

1. WHO. The top 10 causes of death. 2011. (http://www.who.int/mediacentre/factsheets/fs310/en/index.html). (Accessed 2013).
2. CDC. Reported Tuberculosis in the United States, 2010. Atlanta, GA: U.S. Department of Health and Human Services, CDC, 2011.
3. Trends in tuberculosis--United States, 2010. *MMWR Morbidity and mortality weekly report* 2011;60(11):333-7.
4. Martin DC, Yankay JE. Annual Flow Report: Refugees and Asylees: 2011. U.S. Department of Homeland Security, 2012.
5. WHO. Global tuberculosis report 2012. Geneva, Switzerland: World Health Organization, 2012.
6. Horsburgh CR, Jr., Rubin EJ. Clinical practice. Latent tuberculosis infection in the United States. *The New England journal of medicine* 2011;364(15):1441-8.
7. Cruz AT, Geltemeyer AM, Starke JR, et al. Comparing the tuberculin skin test and T-SPOT.TB blood test in children. *Pediatrics* 2011;127(1):e31-8.
8. Lee E, Holzman RS. Evolution and current use of the tuberculin test. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America* 2002;34(3):365-70.
9. Lighter J, Rigaud M, Eduardo R, et al. Latent tuberculosis diagnosis in children by using the QuantiFERON-TB Gold In-Tube test. *Pediatrics* 2009;123(1):30-7.
10. WHO. BCG Vaccine. *Weekly epidemiological record* 2004;79(4):27-38.

11. Pai M, Zwerling A, Menzies D. Systematic review: T-cell-based assays for the diagnosis of latent tuberculosis infection: an update. *Annals of internal medicine* 2008;149(3):177-84.

12. Mazurek GH, Jereb J, Vernon A, et al. Updated guidelines for using Interferon Gamma Release Assays to detect Mycobacterium tuberculosis infection - United States, 2010. *MMWR Recommendations and reports : Morbidity and mortality weekly report Recommendations and reports / Centers for Disease Control* 2010;59(RR-5):1-25.

13. Diel R, Goletti D, Ferrara G, et al. Interferon-gamma release assays for the diagnosis of latent Mycobacterium tuberculosis infection: a systematic review and meta-analysis. *The European respiratory journal : official journal of the European Society for Clinical Respiratory Physiology* 2011;37(1):88-99.

14. Mendez-Echevarria A, Gonzalez-Munoz M, Mellado MJ, et al. Interferon-gamma release assay for the diagnosis of tuberculosis in children. *Archives of disease in childhood* 2012;97(6):514-6.

15. Ferrara G, Losi M, D'Amico R, et al. Use in routine clinical practice of two commercial blood tests for diagnosis of infection with Mycobacterium tuberculosis: a prospective study. *Lancet* 2006;367(9519):1328-34.

16. Pavic I, Topic RZ, Raos M, et al. Interferon-gamma release assay for the diagnosis of latent tuberculosis in children younger than 5 years of age. *The Pediatric infectious disease journal* 2011;30(10):866-70.

17. Connell TG, Curtis N, Ranganathan SC, et al. Performance of a whole blood interferon gamma assay for detecting latent infection with Mycobacterium tuberculosis in children. *Thorax* 2006;61(7):616-20.

18. Dogra S, Narang P, Mendiratta DK, et al. Comparison of a whole blood interferon-gamma assay with tuberculin skin testing for the detection of tuberculosis infection in hospitalized children in rural India. *The Journal of infection* 2007;54(3):267-76.

19. Georgia Refugee Arrivals by Country of Origin and County of Residence. State of Georgia Refugee Health Program, 2010.

20. WHO. Child growth standards. 2013. (http://www.who.int/childgrowth/en/). (Accessed).

21. Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics* 1977;33(1):159-74.

22. Kleinbaum DG, Kupper LL, Nizam A, et al. Regression Diagnostics. *Applied Regression Analysis and Other Multivariable Methods*: Thomson Higher Education, 2008.

FIGURES AND FIGURE LEGENDS

Table 1. Demographic characteristics of refugee children screened for LTBI at the DeKalb County Board of Health Clinic, 2010-2012

Characteristic	Male N (%)	Female N (%)
Country of Origin (N=216)		
Africa		
Somalia	13 (11)	7 (7)
Sudan	6 (5)	4 (4)
Other	7 (6)	4 (4)
Americas	0 (0)	1 (1)
Asia		
Bhutan	30 (26)	31 (30)
Burma	40 (35)	35 (34)
Other	3 (3)	5 (5)
Middle East		
Iraq	8 (7)	11 (11)
Other	7 (6)	4 (4)
WHO High Burden Country (N=216)		
Yes	62 (54)	50 (5)
BCG vaccinated (N=205)		
Yes	109 (99)	94 (99)
BMI category (N=212)		
Underweight	17 (15)	23 (23)
Healthy	90 (79)	75 (77)
Overweight	7 (6)	0 (0)
TST Result (N=216)		
<10 mm	91 (80)	88 (86)
≥10 mm	23 (20)	14 (14)
QFT Result (N=216)		
Positive	8 (7)	4 (4)
Negative	106 (93)	97 (95)
Indeterminate	0 (0)	1 (1)

Table 2. Demographic characteristics of refugee children screened for LTBI at the DeKalb County Board of Health Clinic by region of origin, 2010-2012

	Region		
	Africa	Asia	Middle East
Characteristic	N (%)	N (%)	N (%)
Total	41 (19.0)	144 (66.7)	30 (13.9)
Males	26 (63.4)	73 (50.7)	15 (50.0)
TST ≥10	4 (9.8)	26 (18.1)	7 (23.3)
Positive QFT	5 (12.2)	6 (4.2)	1 (3.3)
BMI-for-age			
Wasted	6 (14.6)	31 (21.5)	3 (10.0)
Healthy	32 (78.1)	106 (73.6)	26 (86.7)
Overweight	3 (7.3)	4 (2.8)	0 (0)

Table 3. Unadjusted and adjusted odds ratios for agreement between QFT and TST results, among QFT-negative children

	Unadjusted				Adjusted			
Predictor	OR	95% CI	β	*P*	OR	95% CI	β	*P*
Sex (female)	1.75	0.81, 3.78	0.280	0.155	1.71	0.76, 3.83	0.269	0.192
Age (months)	1.03	1.00, 1.06	0.030	0.029	1.04	1.01, 1.07	0.036	0.015
Time in US (days)	0.99	0.98, 0.99	-0.012	0.011	0.99	0.98, 0.99	-0.013	0.008

Figure 1. Responses to QFT TB-specific antigen versus age for all children

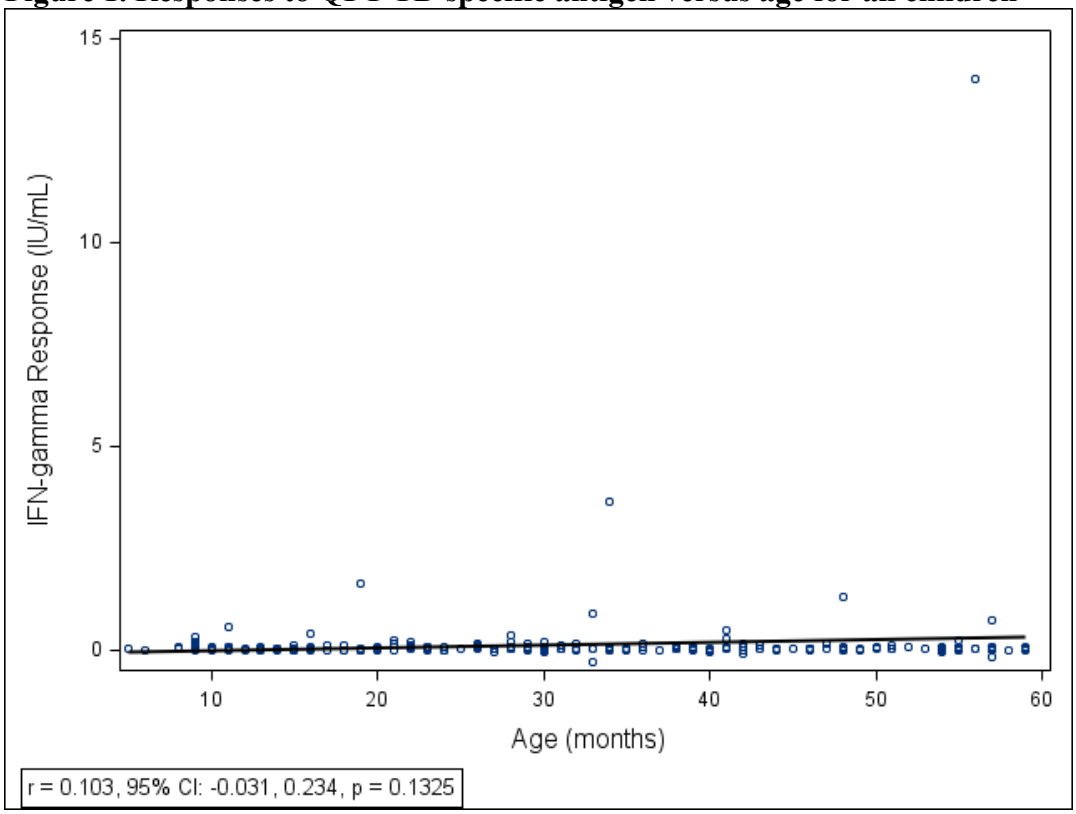

Figure 2. Responses to QFT TB-specific antigen versus age for QFT-positive children

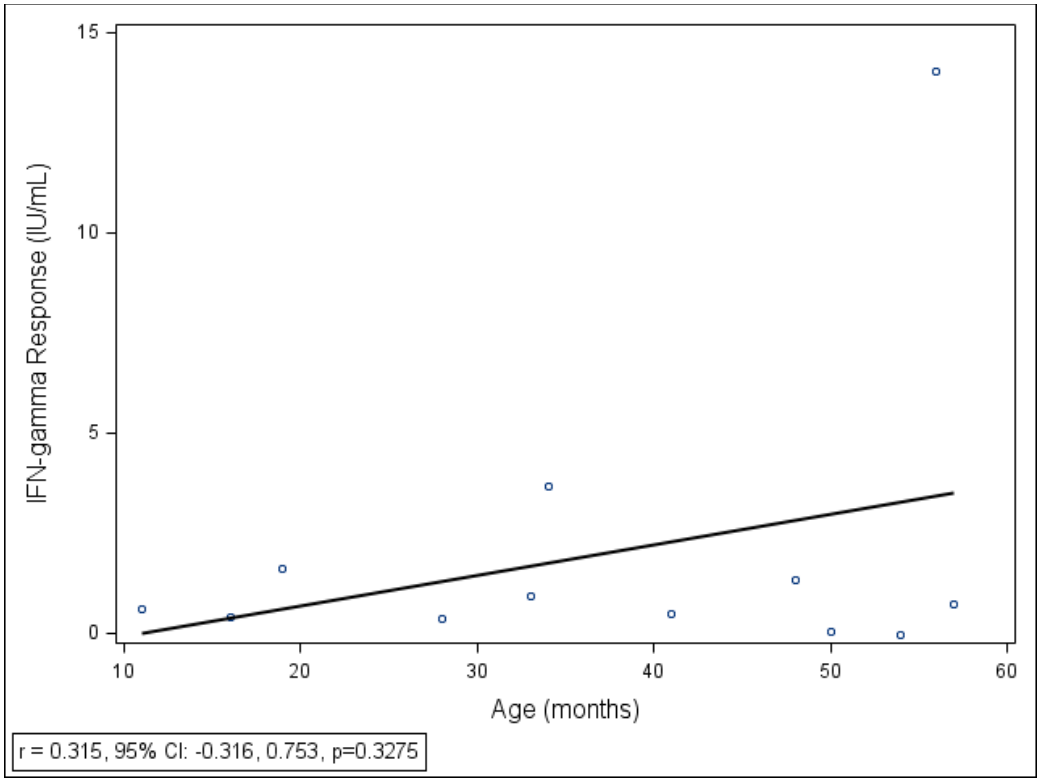

Figure 3. Responses to QFT TB-specific antigen versus induration diameter of TST result for all children

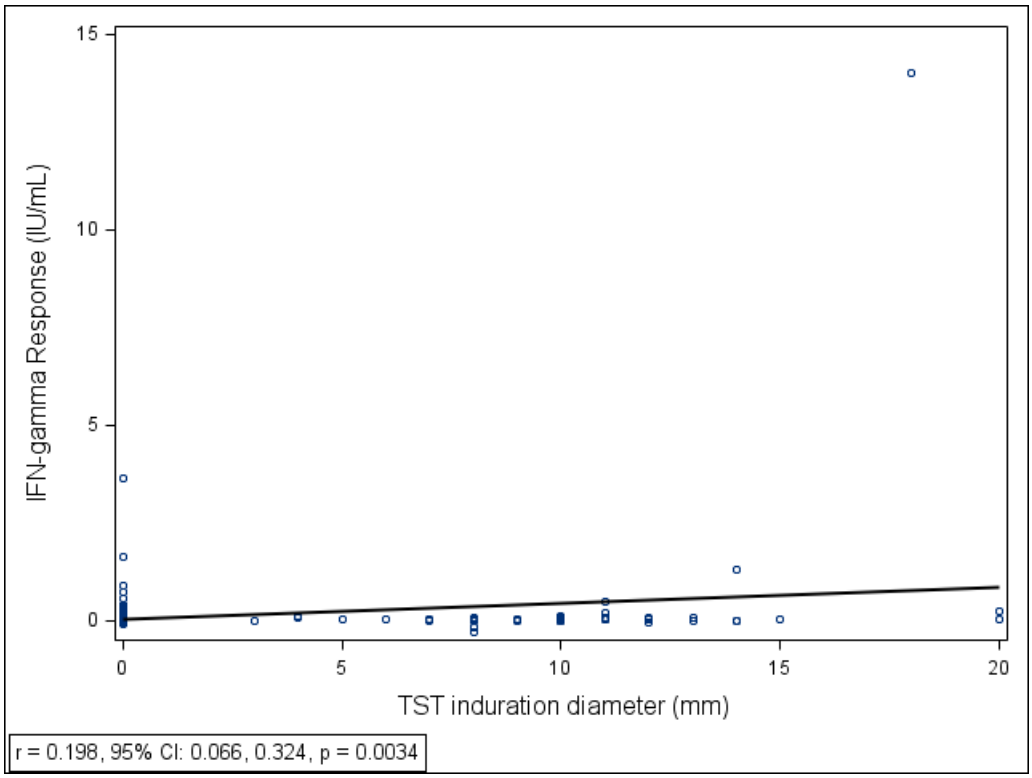

Figure 4. Responses to QFT TB-specific antigen versus induration diameter of TST result for QFT-positive children