Characterizing Pediatric Tuberculosis with and without Human Immunodeficiency Virus Coinfection in Harare, Zimbabwe

Michelle Earley,¹ Joconiah Chirenda,² Alexandra Highet,³ Hilda A. Mujuru,⁴ and Zhenhua Yang^{1*}

¹Department of Epidemiology, School of Public Health, University of Michigan, Ann Arbor, Michigan; ²Department of Community Medicine, College of Health Sciences, University of Zimbabwe, Harare, Zimbabwe; ³Medical School, University of Michigan, Ann Arbor, Michigan;

⁴Department of Paediatrics, College of Health Sciences, University of Zimbabwe, Harare, Zimbabwe

Abstract. Pediatric tuberculosis (TB) represents a major barrier to reducing global TB mortality, especially in countries confronting dual TB and human immunodeficiency virus (HIV) epidemics. Our study aimed to characterize pediatric TB epidemiology in the high-burden setting of Harare, Zimbabwe, both to fill the current knowledge gap around the epidemiology of pediatric TB and to indicate areas for future research and interventions. We analyzed de-identified data of 1,051 pediatric TB cases (0–14 years) found among a total of 11,607 TB cases reported in Harare, Zimbabwe, during 2011–2012. We performed Pearson's χ^2 test and multivariate logistic regression analysis to characterize pediatric TB and to assess predictors of HIV coinfection. Pediatric TB cases accounted for 9.1% of all TB cases reported during 2011–2012. Approximately 50% of pediatric TB cases were children younger than 5 years. Almost 60% of the under-5 age group were male, whereas almost 60% of the 10–14 age group were female. The overall HIV coinfection rate was 58.3%. Odds for HIV coinfection was higher for the 5–9 age group (adjusted odds ratio [AOR]: 2.77, 95% confidence interval [CI]: 1.97–3.94), the 10–14 group (AOR: 3.57, 95% CI: 2.52–5.11), retreatment cases (AOR: 6.17, 95% CI: 2.13, 26.16), and pulmonary TB cases (AOR: 2.39, 95% CI: 1.52, 3.75). In conclusion, our study generated evidence that pediatric TB, compounded by HIV coinfection, significantly impacts children in high-burden settings. The findings of our study indicate a critical need for targeted interventions.

INTRODUCTION

Tuberculosis (TB) has persisted into the twenty-first century as a critical global public health challenge. According to the World Health Organization (WHO), an estimated 10.4 million individuals became infected with TB in 2015.^{1,2} Included in this estimate are 1.0 million children (defined by the WHO as 0–14 years old), accounting for 10% of incident TB cases worldwide. The WHO *Roadmap for Childhood TB* points to targeting childhood TB incidence and infectivity as a key strategy to combating the global TB epidemic.³ Nonetheless, TB infection and mortality among children, an extremely vulnerable population worldwide, have been widely neglected, despite the fact that significant TB morbidity and mortality occurs in childhood.^{1,4,5}

The African continent bears a very severe burden of global TB, accounting for 16 of the 30 countries designated by the WHO as “high TB-burden countries” (HBCs) by incidence rates. According to WHO,¹ the African region accounts for 25% of the 2017 global incident TB cases. Zimbabwe, an HBC within the WHO African Region, had an estimated 2016 TB incidence rate of 376 per 100,000 population, significantly greater than the global incidence of 142 per 100,000 population and nearly 81 times that of the U.S. TB incidence (three per 100,000 population).^{1,6} Of the estimated total incidence of TB (38,000) in Zimbabwe in 2015, 5,000 (or 13.2%) were pediatric cases.¹ Furthermore, Zimbabwe has one of the highest TB and human immunodeficiency virus (HIV) coinfection rates among the 30 HBCs, with a TB/HIV coinfection incidence rate of 139 per 100,000 population and an HIV seropositivity of 58% among all the incident TB cases in 2016.¹ This is alarming, given the well-characterized impact of HIV infection

on the progression of TB in children.^{1,7,8} The persistence of pediatric TB infection and mortality, combined with high rates of TB–HIV coinfection in high-burden, low-resource countries, indicates a vital need for a better understanding of pediatric TB epidemiology. We, therefore, conducted the present study to confront this knowledge gap through a more rigorous characterization of pediatric TB with and without HIV infection in a representative, high-burden country.

PATIENTS AND METHODS

Study population. The study population included all the pediatric TB cases diagnosed at Beatrice Road Infectious Diseases Hospital (BRIDH) and Wilkins Infectious Diseases Hospital (WIDH) in Harare between January 1, 2011 and December 31, 2012. These two hospitals diagnose more than 90% of reported TB cases, including both adult and pediatric TB cases, in Harare city, although some of the patients diagnosed in the two centers may often receive TB treatment at one of the local clinics. During the study time period, a total of 11,607 TB cases were reported in Harare. Of these 11,607 reported cases, 1,051 (9.1%) cases younger than 15 years were identified as pediatric cases, following the same age standard for pediatric TB definition used by WHO in their yearly global TB report.¹ Most of the pediatric TB cases included in the study sample were diagnosed on clinical and radiological basis, following the WHO algorithm.⁹ Results of acid-fast bacillus smear microscopy were available for 428 (~41%) of the 1,051 cases either directly or through gastric washings. To characterize pediatric TB cases, our study population included all these 1,051 cases younger than 15 years.

Data collection. This study used existing de-identified TB patient data from the city of Harare electronic TB database. The data analyzed in this study included age, gender, history of TB treatment, location of disease (pulmonary or extrapulmonary), HIV status, and pretreatment sputum smear

* Address correspondence to Zhenhua Yang, Epidemiology Department, School of Public Health, University of Michigan, 1415 Washington Heights, Ann Arbor, MI 48109. E-mail: zhenhua@umich.edu

microscopy (SSM) result. Drug resistance data were not available to the present study. This was because drug susceptibility testing was not part of the routine diagnosis workup for pediatric TB in Harare partly because of the paucibacillary nature of pediatric TB and partly because of the lack of resources required for routine drug susceptibility testing. This study was defined as research not involving human subjects as it did not involve any intervention or interaction with study subjects and was based on an analysis of existing non-identifiable patient data.

Statistical analysis. To characterize childhood TB in Zimbabwe, we computed descriptive statistics of demographic and clinical characteristics for the overall study population.

Specifically, we described the distribution of three age groups in the overall study population: 0–4 years, 5–9 years, and 10–14 years, using Pearson's χ^2 test. These age cohorts align with WHO-designated age categories as well as WHO Sustainable Development Goal (SDG) parameters, notably SDG 3.2 (reducing under-5 mortality by 2030).¹⁰

In addition, we described the distribution of gender and HIV status among these three age groups. Given the high rate of TB and HIV coinfection in Zimbabwe, we assessed the rate of HIV coinfection within our study population and characterized pediatric TB cases with and without HIV coinfection, using Pearson's χ^2 test. We also examined predictors of HIV coinfection, using multivariate logistic regression and obtained adjusted odds ratios (AORs).

Each study patient was classified as either a new or retreatment case. A retreatment case was defined as having received 1 month or more of anti-TB drugs in the past. This includes cases of "relapse," "failed previous treatment" (defined as having positive sputum following 5 months of treatment), and "treatment following a treatment interruption of 2 months or more."¹ Location of disease is classified as either pulmonary TB (PTB), involving the lungs, or extrapulmonary TB (EPTB), involving anatomic sites other than the lungs. All analyses were conducted in R (version 3.2.1; Vienna, Austria).

RESULTS

Study population characteristics. Children younger than 5 years, who are known to be at higher risk of progression to disease than older children, make up about half (536/1,051) of our study population, with the remaining cases distributed similarly between the remaining two older age groups (Table 1). Slightly more than half (553/1,051, 52.6%) of cases were male. Human immunodeficiency virus testing results were available for a total of 929 (88.4%) patients, including 151 (74.8%) of the 202 cases younger than 5 years. Among those with HIV testing data, 58.3% (542/929) were HIV positive.

Tuberculosis disease was predominantly PTB (944/1,051, 89.8%), with a small proportion of EPTB (107/1,051, 10.2%). Of the 428 cases that had an SSM test performed at diagnosis, 18.9% (81/428) had a positive result. Almost all (1,009/1,051, 96.0%) cases were new, with no history of previous treatment.

Age disparity. To better understand clinical and demographic characteristics of pediatric TB by age, we compared the distribution of demographic and clinical characteristics of the 536 cases younger than 5 years with that of the 515 cases between the ages of 5 and 14 years. These two subgroups were selected in accordance with those reported on by Jenkins and others, who have compared TB fatality rates between the 0–4

TABLE 1

Clinical and demographic characteristics of 1,051 pediatric tuberculosis cases who began treatment between 2011 and 2012 in Harare, Zimbabwe

Variables	Number of cases (%)	
Age (years)		
0–4	536	(51.0)
5–9	241	(22.9)
10–14	274	(26.1)
Gender		
Male	553	(52.6)
Female	498	(47.4)
Treatment history		
New	1,009	(96.0)
Retreatment	35	(3.3)
Location of disease		
Pulmonary	944	(89.8)
Extrapulmonary	107	(10.2)
Human immunodeficiency virus status		
Positive	542	(51.6)
Negative	387	(36.8)
Missing	122	(11.6)
Sputum smear microscopy result		
Positive	81	(7.7)
Negative	347	(33.0)
Not performed	623	(59.3)
Medical center		
BRIDH	700	(66.6)
WIDH	351	(33.4)

BRIDH = Beatrice Road Infectious Diseases Hospital; WIDH = Wilkins Infectious Diseases Hospital.

and 5–14 year age groups.¹¹ Pearson's χ^2 tests of equal proportions reveal significant differences in gender, treatment history, HIV status, location of disease, and SSM result between the two comparative age groups (Table 2). We saw a significantly higher proportion of males than females among cases younger than 5 years (59% versus 41%, $P < 0.001$). In addition, a significantly higher proportion of retreatment cases were found in the 5- to 14-year age group than in the under-5 age group (5.8% versus 0.9%, $P < 0.001$). Furthermore, the 5- to 14-year age group contained a much higher proportion of HIV-positive cases compared with the under-5 age group (66.0% versus 37.7%, P value < 0.001). Extrapulmonary tuberculosis was also found to be significantly more prevalent in the 5- to 14-year age group than in under-5 age group.

To further characterize pediatric TB by age, we divided the older age group into two groups (5–9 years and 10–14 years) and performed the same comparison among the three age groups (Figure 1). This further comparison showed that almost 60% of the under-5 age group is male, which is significantly higher than the proportion of females (P value < 0.001). However, the middle age group (5–9 years) shows no significant gender differences, whereas in the oldest age group (10–14 years), almost 60% is female, which is significantly higher than the proportion of males (P value < 0.001). Comparing these three same age groups, we further found differences in the distribution of HIV status (Figure 2). A significantly higher proportion of cases younger than 5 years were HIV negative (P value = 0.004). By contrast, a significantly higher proportion of cases in each of the two older age groups were HIV positive (P value < 0.001).

Predictors for HIV coinfection. Pearson's χ^2 tests of equal proportions revealed significant differences in age, treatment history, location of disease, and SSM result between cases with and without HIV coinfection (Table 3).

TABLE 2

Comparison of demographics and clinical characteristics between the 0–4 and 5–14 year age groups of the patients who began tuberculosis treatment between 2011 and 2012 in Harare, Zimbabwe

	0–4 years		5–14 years		Difference	(95% CI)	P value*
	N	(%)	N	(%)			
Gender							
Male	316	(59.0)	237	(46.0)	13.0	(6.8, 19.1)	< 0.001
Female	220	(41.0)	278	(54.0)	–13.0	(–19.1, –6.8)	< 0.001
Treatment history							
New	530	(98.9)	479	(93.0)	5.9	(3.3, 8.4)	< 0.001
Retreatment	5	(0.9)	30	(5.8)	–4.9	(–7.3, –2.5)	< 0.001
Human immunodeficiency virus status							
Positive	202	(37.7)	340	(66.0)	–28.3	(–34.3, –22.3)	< 0.001
Negative	250	(46.6)	137	(26.6)	20.0	(14.1, 26.6)	< 0.001
Location of disease							
Pulmonary	501	(93.5)	443	(86.0)	7.5	(3.6, 11.3)	< 0.001
Extrapulmonary	35	(6.5)	72	(14.0)	–7.5	(–11.3, –3.6)	< 0.001
Sputum smear microscopy result							
Positive	22	(4.1)	59	(11.5)	–7.4	(–10.8, –3.9)	< 0.001
Negative	62	(11.6)	285	(55.3)	–43.7	(–49.0, –38.5)	< 0.001
Not performed	452	(84.3)	171	(33.2)	51.1	(45.8, 56.4)	< 0.001
Medical center							
BRIDH	377	(70.3)	323	(62.7)	7.6	(1.7, 13.5)	0.01
WIDH	159	(29.7)	192	(37.3)	–7.6	(–13.5, –1.7)	0.01

BRIDH = Beatrice Road Infectious Diseases Hospital; CI = confidence interval; WIDH = Wilkins Infectious Diseases Hospital.

* P value from Pearson's χ^2 test of equal proportions.

Multivariate logistic regression identified several statistically significant predictors for HIV coinfection. Compared with the youngest (younger than 5 years) age group, the odds of HIV coinfection drastically increase for both the five to nine age group (AOR: 2.77, 95% confidence interval [CI]: 1.97–3.94) and the 10–14 age group (AOR: 3.57, 95% CI: 2.52–5.11). Furthermore, compared with new cases, retreatment cases had a significant odds for having HIV coinfection (AOR: 6.17, 95% CI: 2.13, 26.16) (Table 4). In addition, PTB was more likely to be associated with HIV coinfection than EPTB (AOR: 2.39, 95% CI: 1.52, 3.75). Gender was not found to be a significant predictor for HIV coinfection.

DISCUSSION

Although the world has seen major advances in TB control in recent years, the burden of pediatric TB has largely escaped attention, and data on pediatric TB epidemiology are lacking. We conducted the present study to better understand the characteristics of pediatric TB in Harare, Zimbabwe, a WHO-designated HBC and low-resource urban setting.

Our study generated several important findings. First, we found that 9.1% (1,051/11,607) of the total TB cases diagnosed at BRIDH and WIDH were younger than 15 years, which extends the current knowledge about the epidemiology of pediatric TB in HBCs. Although previous studies have quantified the incidence of pediatric and adolescent HIV in

FIGURE 1. Comparison of the gender distribution among three age groups of pediatric tuberculosis patients who began treatment between 2011 and 2012 in Harare, Zimbabwe. White bars correspond to females and hatched bars correspond to males. The x axis represents age categories and the y axis represents the proportion of children in a given age/gender category. Each bar contains a 95% confidence interval for its respective proportion. The P values from χ^2 tests of equal proportions were < 0.001, > 0.99, and < 0.001 for the 0–4, 5–9, and 10–14 year groups, respectively.

FIGURE 2. Comparison of human immunodeficiency virus (HIV) status among three age groups of pediatric tuberculosis patients who began treatment between 2011 and 2012 in Harare, Zimbabwe. White bars correspond to HIV-negative children and hatched bars correspond to HIV-positive children. The x axis represents age categories and the y axis represents the proportion of children in a given HIV/age category. Each bar contains a 95% confidence interval for its respective proportion. The P values from χ^2 tests of equal proportions were 0.004, < 0.001, and < 0.001 for the 0–4, 5–9, and 10–14 year groups, respectively.

Harare, to our knowledge, no such study has carried out the same for TB.¹²

The relatively low rate of pediatric TB cases among all TB cases determined by the present study (9.1%), as compared with the proportion of children within the overall Zimbabwean population (41.1%), should be interpreted with caution, given the high likelihood for underdiagnosis of pediatric TB due to the challenges in diagnosing pediatric TB, especially in the setting where acute childhood pneumonia occurs frequently.^{13,14} The other factor that may also have contributed to the under-detection of pediatric TB in our study is that the suspected infant TB cases and severe forms of pneumonia cases in Harare were often referred to Harare Central Hospital, the pediatric teaching hospital for the University of Zimbabwe

for diagnosis, instead of either of the two Harare city infectious disease hospitals from which the study data were obtained, and thus were not captured by our statistic.

Approximately 90% of cases in the study were diagnosed with PTB. This is in accordance with the WHO's estimate that the most common form of childhood TB is PTB (EPTB is estimated to occur in 20–30% of all cases in children).¹ However, our results must be interpreted with caution. Since pediatric TB is particularly challenging to diagnose, EPTB, which is likely sputum smear negative and more difficult to diagnose than PTB, is largely underreported.¹⁵ In addition, Wiseman and others have pointed out that the PTB/EPTB classification system is ineffective because it does not characterize the true severity of the disease among pediatric patients.¹⁶ Given

TABLE 3

Comparison of demographics and clinical characteristics between HIV-positive and HIV-negative groups of pediatric tuberculosis cases who began treatment between 2011 and 2012 in Harare, Zimbabwe

	HIV+		HIV–		Difference	(95% CI)	<i>P</i> value*
	<i>N</i>	(%)	<i>N</i>	(%)			
Age (years)							
0–4	202	(37.3)	250	(64.6)	–27.3	(–33.8, –20.8)	< 0.001
5–9	153	(28.2)	72	(18.6)	9.6	(4.0, 15.3)	< 0.001
10–14	187	(34.5)	65	(16.8)	17.7	(12.0, 23.4)	< 0.001
Gender							
Male	274	(50.6)	205	(53.0)	–2.4	(–9.1, 4.3)	0.51
Female	268	(49.4)	182	(47.0)	2.4	(–4.3, 9.1)	0.51
Treatment history							
New	503	(92.8)	384	(99.2)	–6.4	(–9.0, –3.9)	< 0.001
Retreatment	32	(5.9)	3	(0.8)	5.1	(2.7, 7.5)	< 0.001
Location of disease							
Pulmonary	495	(91.3)	333	(86.0)	5.3	(0.9, 9.7)	0.01
Extrapulmonary	47	(8.7)	54	(14.0)	–5.3	(–9.7, –0.9)	0.01
Sputum smear microscopy result							
Positive	39	(7.2)	33	(8.5)	–1.3	(–5.1, 2.4)	0.53
Negative	230	(42.4)	86	(22.2)	20.2	(14.1, 26.3)	< 0.001
Not performed	273	(50.4)	268	(69.3)	–18.9	(–25.3, –12.4)	< 0.001
Medical center							
BRIDH	360	(66.4)	272	(70.3)	–3.9	(–10.0, 2.4)	0.24
WIDH	182	(33.6)	115	(29.7)	3.9	(–2.4, 10.0)	0.24

BRIDH = Beatrice Road Infectious Diseases Hospital; CI = confidence interval; HIV = human immunodeficiency virus; WIDH = Wilkins Infectious Diseases Hospital.

* P value from Pearson's χ^2 test of equal proportions

TABLE 4
Predictors for TB-HIV coinfection determined by multivariate logistic regression analysis

	HIV coinfection		
	Adjusted odds ratio	(95% CI)	P value
Age (years)			
5–9 (vs. 0–4)	2.77	(1.97, 3.94)	< 0.001
10–14 (vs. 0–4)	3.57	(2.52, 5.11)	< 0.001
Gender			
Female (vs. male)	1.08	(0.82, 1.43)	0.58
Treatment history			
New (vs. retreatment)	6.17	(2.13, 26.16)	0.003
Location of disease			
Pulmonary (vs. extrapulmonary)	2.39	(1.52, 3.75)	< 0.001

CI = confidence interval; HIV = human immunodeficiency virus.

these limitations, the association of PTB with HIV coinfection found here, which is in contrast to the well-established EPTB and HIV coinfection by studies of adult TB, remains to be further investigated in future studies.¹⁷

Within our study, about 59% cases did not have a sputum sample taken, and of those who had a sample taken, a small percentage (7.7%) was smear positive. This is expected given that children are known to be often paucibacillary and mostly sputum negative, representing a major limitation in studying childhood TB. Kunkel et al.¹⁸ also reported a similar low smear positivity rate of 6.6% in children treated for PTB. Our study, therefore, adds to the growing list of research in support of the need for more effective diagnostic criteria for pediatric TB in low-resource settings.

Second, we found that approximately half (51%) of the 1,051 pediatric TB cases were in the 0- to 4-year age group. This is significant when compared with the overall Zimbabwean population demographics: only 36.8% of the total population of children younger than 15 years is 0–4 year old.¹³ This suggests that the 0- to 4-year age group in Harare (and possibly in Zimbabwe) was disproportionately affected by TB compared with children in the older age groups. Young age has been established as an important risk factor for progression to active TB disease following infection by previous studies.^{19,20} Although the risk of developing active TB among adults is between 5% and 10%, this risk is estimated to be 15% in adolescents, 25% in children between the ages of 1 and 5 years, and 43% in infants younger than 1 year.^{19,20} Research conducted in South Africa attributes this increased risk to the immature immune systems of children, resulting in an inability to control infection. The WHO and several research groups have pointed to the high risk of complications (such as TB meningitis) seen with infant TB and the importance of early disease detection.³ Our finding that the 0- to 4-year age group was disproportionately affected by TB compared with the children in the older age groups extends the evidence for the age-related risk for TB from a previously understudied HBC country. An early study conducted in Uganda also reported that about 54% of pediatric TB cases in their study population were attributed to cases younger than 5 years.²¹ However, in settings with high HIV positivity, challenges in the diagnosis of TB in children younger than 1 year could have led to the overestimation of TB in our study setting.^{7,8,22} Our study proves that by continuing to overlook this age group, the global health community will miss a critical opportunity to combat infant mortality.

Third, significant gender differences were noted between the age subgroups studied (Figure 1). Worldwide, the male-to-female ratio of notified TB cases is known to be 2:1, indicating gender as a risk factor for TB.^{20,22} Within our pediatric cohort, 60% of the under-5 age group was male, whereas the middle subgroup (5–9 years) was not statistically different and the oldest subgroup (10–14 years) was 60% female. There has been much debate about the gender differences associated with global TB incidence, with some researchers speculating that these differences are a result of underreporting TB among women because of lifestyle factors, stigmatization, or awareness and others pointing to the biological effects of sex hormones on the immune response to infection or genetic background.²³ Less research has been conducted on the role of gender in pediatric TB. In the early 1950s, WHO prevalence surveys conducted in Africa found that the prevalence among males began to exceed that of females between the ages of 10 and 16 years, with no gender differences between children younger than 10 years.²⁴ Our results do indicate that gender may play a role in dictating when TB-HIV coinfection is likely to be identified, but further research is needed to elicit reasons for this. Furthermore, our data suggest that among young children, males were disproportionately affected by TB, whereas among the older children, females were disproportionately affected by TB, given that there is a fairly equal male-female gender distribution among Zimbabwean children of these age groups.¹³

Finally, our most alarming finding is the 58.3% coinfection rate of HIV among the children in the study who were tested for HIV. The complementary effects of TB and HIV infection and progression have been firmly established. Studies estimate that among HIV-infected children in Africa, TB may account for up to 20% of deaths.⁷ Worldwide, approximately 11% of incident TB cases in 2015 were HIV positive; for the WHO African region, this estimate rises to 31% and exceeds 50% for southern Africa (WHO Global TB report, 2016). Of the new and relapse TB patients reported in Zimbabwe in 2015, 70% of these patients knew their HIV status and were HIV positive, one of the highest such rates for the 30 high-burden countries.⁵ According to Zimbabwe's National TB Control Program, the country's TB epidemic is being driven in part by its high burden of HIV.²⁵

The TB-HIV coinfection rate among children in sub-Saharan African studies was estimated to be between 11% and 64%, placing Zimbabwe's estimates on the high end of these figures.⁷ These results are especially important because TB is a major cause of mortality among children over the age of 1 year who are HIV infected.²⁶ Although most adults will acquire latent TB before HIV, some studies have found that children are more likely to be infected with HIV perinatally from an HIV-positive mother and later become infected with TB.⁷ Children born with HIV are severely immunocompromised early in life and are unable to fight off TB infection and subsequent disease; thus, pediatric TB-HIV coinfection represents an additional critical barrier to improving child mortality globally. According to the most recent estimate of WHO, 21% (52,000/253,000) of pediatric TB deaths occur in HIV coinfecting children.¹ Carlucci et al.²⁷ reported that the sub-Saharan African population of children with HIV/TB coinfection treatment is not managed in accordance with WHO guidelines and indicated that favorable TB outcomes can result from early antiretroviral therapy (ART) initiation. The finding of a high proportion of TB

and HIV coinfection in Harare Zimbabwe indicates a particularly important role of early initiation of ART in reducing childhood TB mortality in Zimbabwe. A better understanding of the characteristics of pediatric TB cases with and without HIV coinfection in a population can assist in the effort.

Interestingly, our study shows that a lower proportion of TB cases younger than 5 years are coinfecting with HIV, compared with the older age groups. This is surprising, given the susceptibility of the infant immune system to both infections, mother-to-child TB transmission, and the established association between maternal TB and increased mother-to-child transmission of HIV. One possible explanation for this difference is the inadequate reporting and delayed diagnosis of pediatric HIV cases, including mother-to-child infections, in Zimbabwe before the rollout of the United Nations' AIDS Prevention of Mother To Child HIV Transmission (PMTCT) program in 2011.²⁸ As our data were collected from 2011 to 2012, when the enhanced population-level surveillance and diagnosis of maternal and perinatal HIV initiated by PMTCT had not been achieved, it is possible that our statistics underestimate the true burden of HIV–TB coinfection in the 0- to 4-year age group.

In addition, given the high mortality of infantile TB and HIV, it is possible that the cohort of children aged 0–4 years who are coinfecting and survivors is reduced.¹¹

One major limitation of the present study is that HIV testing results were missing for 11.6% of the study patients. To assess the potential bias resulting from the lack of HIV testing results for some of the patients, we compared the distribution of patient characteristics between cases with and without HIV testing results. We found that the 0- to 4-year age group is more likely not to have HIV testing results (accounting for 69% of cases without HIV test results versus 49% of cases with HIV test results, P value < 0.001). By contrast, the 5- to 9-year age group are more likely to have HIV testing results (accounting for 13% of cases without HIV test results versus 24% of cases with HIV test results, P value = 0.01). Similarly, the 10- to 14-year age group is also more likely to have HIV test results (accounting for 18% without HIV test results versus 27% of cases with HIV test results, P value = 0.04). In addition, we found that cases diagnosed in one of the two health centers involved were more likely to have HIV test results (68% versus 56% having, P value = 0.01). These findings indicate the possibility that the actual HIV coinfection rate for the 0- to 4-year age group could have been higher or even lower than what we found in this study. Further research and analysis are needed to better understand why HIV rates appear to be lower in the 0- to 4-year age category.

CONCLUSION

As the most comprehensive characterization to date of pediatric TB and HIV coinfection in the high-burden, low-resource setting of Harare, Zimbabwe, to our knowledge, our study demonstrated an extremely high rate of HIV coinfection in our study population, especially among older children. Our data extend the knowledgebase of pediatric TB and TB/HIV coinfection and indicate that the pediatric population in high-burden countries such as Zimbabwe is in crucial need of improved interventions for both TB and HIV. This study provides motivation for further research into this population and directed resources to vulnerable, at-risk subpopulations.

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Authors' addresses: Michelle Earley, The Biostatistics Center, The George Washington University, Rockville, MD, E-mail: mearley@bsc.gwu.edu. Joconiah Chirenda, Department of Community Medicine, College of Health Sciences, University of Zimbabwe, Harare, Zimbabwe, E-mail: joconiahc@gmail.com. Alexandra Highet, Medical School, University of Michigan, Ann Arbor, MI, E-mail: ahighet@med.umich.edu. Hilda A. Mujuru, Department of Pediatrics, College of Health Sciences, University of Zimbabwe, Harare, Zimbabwe, E-mail: hmujuru@mweb.co.zw. Zhenhua Yang, Epidemiology Department, School of Public Health, University of Michigan, Ann Arbor, MI, E-mail: zhenhua@umich.edu.

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