

BCG protects against tuberculosis irrespective of HIV status: a matched case-control study in Mwanza, Tanzania

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► Additional supplementary files are published online only. To view these files please visit the journal online (<http://dx.doi.org/10.1136/thoraxjnl-2012-201971>).

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Received 28 March 2012

Accepted 3 August 2012

ABSTRACT

While BCG vaccine protects against severe tuberculosis (TB) in children, its effect against adult TB is questionable. Furthermore, it is not known if HIV co-infection modifies the effect of BCG. Among 352 pairs of Tanzanian TB cases and matched controls, the BCG scar was associated with a reduced risk of TB (OR 0.3, 95% CI 0.2 to 0.7, $p=0.005$), irrespective of HIV status (interaction, $p=0.623$). BCG vaccination considerably reduced the risk of TB, both among individuals with and without HIV infection.

BCG vaccination is used in most tuberculosis (TB)-endemic countries, and from 1980 to 2008, the coverage of BCG vaccination in Africa increased from 11% to 84%.¹ However, the data on protection from childhood vaccine against adult TB are inconsistent,² and its role in HIV infection is unclear.³ We conducted an age- and sex-matched case-control study in Tanzania, to assess the protective effect of BCG vaccination and other risk factors for pulmonary TB.

Data were available for 352 pairs of TB patients and non-TB controls ($n=704$). A majority of cases lived alone and worked as farmers or fishermen (see online supplementary table). Fewer cases than controls had a visible BCG scar (78.9 vs 93.1%, $p<0.001$, χ^2), but more cases were HIV co-infected (46.3 vs 9.9%, $p<0.001$, χ^2). The associations between TB and BCG, HIV, smoking and alcohol intake were assessed in a multivariable conditional logistic regression model adjusted for age, diabetes status and sociodemographic factors (table 1). A BCG scar was associated with a considerable reduction in risk of TB (OR 0.3, 95% CI 0.2 to 0.7, $p=0.005$), and this association was not

confounded or modified by any of the other covariates (ie, BCG-HIV interaction test, $p=0.623$). In stratified analysis by HIV status and adjusted for age, diabetes and sociodemographic factors, the BCG scar was associated with TB among both HIV-negative (0.3, 0.1;0.5, $p<0.001$) and HIV-positive (0.1, 0.02;0.95, $p=0.045$) participants. There was a similar effect across all age groups (data not shown), indicating a long-term BCG effect.

The BCG efficacy in 14 prospective trials and 12 case-control studies was 50%, ranging from a zero effect to 80%,⁴ and a recent case-control study from India among 412 pairs of cases and controls reported a protective effect of BCG vaccination (OR 0.47, 95% CI 0.35 to 0.63).⁵ The variations in the observed protective efficacy have been explained as potential differences in the BCG vaccine strains used, the application methods, pre-existing immunity induced by environmental non-tuberculous mycobacteria, or latent TB infection. Our study was not a vaccine efficacy study, but aimed to examine the association between the presence of a BCG scar and developing active TB disease, but the OR of 0.3 does reflect a high efficacy. Since not all BCG-vaccinated individuals develop a BCG scar, the presence of a BCG scar, rather than information on BCG vaccination, might better predict protection, since this indicates that an immunological reaction has actually taken place.

This is the first study providing evidence strongly suggesting that BCG vaccination may prevent TB among both HIV-infected and uninfected participants. We do not have data on the time of HIV infection in the current population, but due to the inclusion criteria (age >15 years),

Table 1 Predictors of pulmonary tuberculosis with OR and 95% CI based on 352 pulmonary tuberculosis cases and 352 controls ($n=704$)

	Crude*		Multivariable†	
	OR (95% CI)	p	OR (95% CI)	p
BCG scar	0.3 (0.2 to 0.5)	<0.001	0.3 (0.2 to 0.7)	0.005
HIV infection	9.0 (5.4 to 15.1)	<0.001	9.6 (4.7 to 19.5)	<0.001
Smoking	3.0 (1.9 to 4.8)	<0.001	2.4 (1.2 to 4.8)	0.017
Alcohol	3.0 (2.1 to 4.3)	<0.001	2.8 (1.6 to 5.2)	0.001

*Univariate conditional logistic regression for matched case-control groups.

†Multivariable conditional logistic regression for matched case-control groups including all covariates from table and adjusted for age, tribe, marital status, occupation, religion and diabetes status.

and since most patients were antiretroviral-treatment naïve, the majority of the HIV infected must have contracted the infection in adulthood.

In conclusion, BCG vaccination seems to have an overall protective effect on the risk of developing active TB, and importantly, the effect is similar among HIV-uninfected and HIV-infected adults.

Contributors HF, NR, JC and ÅBA conceived the study. GP and KJ coordinated the implementation of the study. DFJ analysed the data and wrote the first draft of the manuscript. All authors contributed to the data collection, interpretation of results and commented on drafts and approved the final version. HF (hfr@life.ku.dk) is guarantor of the paper.

Competing interests None.

Ethics approval Ethics Committee of the National Institute for Medical Research (NIMR) in Tanzania.

Provenance and peer review Not commissioned; externally peer reviewed.

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Supplementary table. Background characteristics of 352 pulmonary tuberculosis cases and 352 controls (n=704)

	Cases	(n=352)	Controls	(n=352)	p
Female sex, n (%)	160	(45.5)	160	(45.5)	1.00
Age, years	34.3	(11.5)	33.9	(12.0)	0.713
Bacillus Calmette Guérin scar, n (%)	276	(78.9)	298	(93.1)	< 0.001
HIV infection, n (%)	163	(46.3)	35	(9.9)	< 0.001
Smoke (ever), n (%)	108	(31.0)	57	(16.7)	< 0.001
Take alcohol, n (%)	165	(46.9)	89	(25.4)	< 0.001
Wasukuma tribe, n (%)	172	(48.9)	162	(46.2)	0.472
Other	180	(51.1)	189	(53.8)	
Marital status, n (%)					
Single	98	(28.0)	89	(25.4)	< 0.001
Married/cohabiting	178	(50.9)	240	(68.6)	
Separated/divorced/widow	74	(21.1)	21	(6.0)	
Occupation, n (%)					
Farmer/Fisherman	155	(44.2)	113	(32.2)	0.005
Businessman/Employed	120	(34.2)	142	(40.5)	
Other	76	(21.7)	96	(27.4)	
Religion, n (%)					
Christian	262	(74.4)	276	(78.4)	0.022
Muslim	74	(21.0)	72	(20.5)	
Other	16	(4.6)	4	(1.1)	
Diabetes, n (%)	54	(15.7)	33	(9.5)	0.015
BMI, kg/m ²	18.4	(2.8)	22.6	(4.0)	< 0.001

Data are mean (SD) or %