

## A Study of Relation between BCG Scar and Atopy in Schoolchildren of Zanjan City

Akefeh Ahmadiashar, Mohammad Reza Parchegani, Nooredin Moosavinasab, and Ali Koosha

*Department of Pediatric, Vali-e-Asr Hospital, Zanjan University of Medical Sciences, Zanjan, Iran*

### ABSTRACT

The prevalence of atopic disease in recent decades has been dramatically increased. It has been suggested that BCG vaccination may protect against development of allergic diseases.

The purpose of this study was to identify relation between scar of BCG vaccine and atopy. This cross-sectional study was done in 1000 children, 10-15 years of age, in Zanjan city. One thousand children (501 girls and 499 boys) were recruited in this study, 137, 121 and 141 cases of asthma, atopic dermatitis and allergic rhinitis, respectively were detected.

Three hundred and three subjects had at least one of these disorders, which were diagnosed as atopy. There was reverse correlation between BCG scar and asthma ( $P=0.013$ ), atopic dermatitis ( $P<0.01$ ), and atopy ( $P<0.01$ ). We did not find any association between the diameter of BCG scar and allergic rhinitis.

Reverse correlation of asthma, atopic dermatitis and atopy with BCG scar are significant. This relied on history and symptoms of patients. Further studies with skin tests, measurements of total and specific IgE levels and spirometry are recommended.

**Key words:** Allergy; Asthma; BCG vaccine; Dermatitis, Atopic

### INTRODUCTION

The prevalence of allergic disorders has considerably increased in recent decades.<sup>1,2</sup> It may be due to changes in lifestyle and exposure to certain infections.<sup>3,4</sup> Changes in human microbial flora, declining exposure to food borne and orofecal infections, reduction of lactobacillus and higher levels of aerobic bacteria such as gram negative bacilli and staphylococci may be as putative contributors to rise of allergy and asthma.<sup>2,5</sup> Skewing the immune response towards a Th1 phenotype has been shown to suppress allergic inflammation. One of the ways this could be achieved is by administration of BCG vaccine early in life.<sup>6</sup>

This could alter local cytokine production and decrease expression of adhesion molecule (VCAM-1) in the lung.<sup>7,8</sup>

In support of this theory, some studies showed the protective role of BCG in reduction of allergic disorders,<sup>9-12</sup> but some other studies showed conflicting results,<sup>13-15</sup> thus more prospective and intervention studies seem to be desirable.

BCG is a vaccine that is routinely administered to all newborns after birth in Iran. In the present study the diameter of BCG scar as a marker of Th1 cell activity in relation with atopy was measured

### MATERIALS AND METHODS

This cross sectional study was done from May to August 2004. One thousand schoolchildren from 20 guidance schools of Zanjan city had been randomly

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**Corresponding Author:** Akefeh Ahmadiashar, MD;  
Department of Pediatric, Vali-e-Asr Hospital, Zanjan University of  
Medical Sciences, Zanjan, Iran. Tel: (+98 241) 7270 801-9, Fax:  
(+98 241) 7270 751, E-mail: akefeh@yahoo.com

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selected and recruited in this study. One physician visited the subjects and asked questions about their allergic status and another examiner just measured the diameter of BCG scar on their arms separately by one ruler that was used for this purpose. Subjects were considered to have allergic rhinitis if at least two symptoms of running nose, itching of nose, sneezing and stuffiness were present. Asthma was described as having at least two symptoms of cough longer than two weeks, night cough, exercise induced cough or having wheezing or dyspnea after exclusion of other diseases. The diagnosis of atopic dermatitis was based on the criteria of Hanifin and Rojka.<sup>16</sup> All data were analyzed by using statistical package of Mini Tab. Results presented as scar size difference (95%CI) and P value of <0.05 was considered to be significant.

### RESULTS

One thousand subjects (499 girls and 501 boys), aged 11-15 years with the mean age of  $12.97 \pm 1.12$  were recruited. The diameter of BCG scar was measured by one ruler: 3.1% of cases did not have BCG scar, 22.8% had scar 1-5 mm, and 71.1% had diameter scar of more than 5 mm (mean diameter:  $7.13 \pm 2.86$ ). One hundred and forty one subjects had allergic rhinitis; the medium size of BCG scars was  $6.77 \pm 2.07$  mm in these patients and  $7.15 \pm 2.92$  mm in healthy subjects. This difference was not significant (P-value= 0.16, estimate for difference: 0.388, 95%CI: -0.097-0.872).

One hundred and thirty seven subjects had asthma symptoms according to above-mentioned the criteria and remaining 863 cases were considered as controls; the difference of BCG scar diameters in two groups was significant ( $6.61 \pm 2.40$  mm versus  $7.18 \pm 2.92$  mm, P = 0.013, estimate For difference: 0.572, 95%CI: 0.122-1.022). We also detected 121 subjects with atopic dermatitis. The mean size of BCG scar in this group was  $6.14 \pm 2.87$  mm and in other 879 children was  $7.23 \pm 2.88$  mm (P< 0.01, estimate for difference: 1.091, 95%CI: 0.540-1.641). This difference was significant. Three hundred and three subjects who had at least one symptom of allergic rhinitis, asthma or atopic dermatitis; they were considered as atopic children. Other cases did not have any of these disorders. The size of BCG scar in atopic group was  $6.58 \pm 2.76$  mm, which was significantly lower than  $7.32 \pm 2.92$  mm in

control group (P < 0.01, estimate for difference: 0.744, 95%CI: 0.364-1.125).

### DISCUSSION

In this study, we found significant reverse correlation between BCG scar and asthma, atopic dermatitis and atopy. BCG scar diameter is a marker of Th1 lymphocyte activity; which has inhibitory effect on Th2 lymphocytes and induction of allergy.<sup>6</sup>

Similar results were shown in other studies such as a double blind study in Korea in which BCC had beneficial effect in patients with asthma.<sup>9</sup> Such as one study in Australia.<sup>10</sup> In a multicentre study there was reverse correlation between atopy and PPD diameter in Turkey and Thailand but not in Argentina<sup>17</sup> and also one study showed the better results of immunotherapy accompanied by BCG.<sup>18</sup> In another study PPD responses in BCG immunized allergic patients was higher than non-allergic children, which is in contrast to our study.<sup>19</sup> In several other studies this correlation have not been shown.<sup>20-23</sup> In one study in India the same as our study BCG scar of asthmatic children was smaller than control.<sup>12</sup> With regard to these studies and different types of reaction and presence of the different sizes of BCG scar, the influence of other factors such as ethnic or genetic factors in modulating the immune system even in first days of birth was postulated, as study that was done in Germany in which non German children had reverse correlation between atopy and PPD reaction, but Germany children did not show this relation.<sup>24</sup> In our study, we did not find any correlation between allergic rhinitis and BCG scar. It may be due to either existence of atopy in control group or presence of other non-allergic rhinitis disorders in positive group or both, because of reliance of study is based on objective symptoms and absence of measurement of total or specific IgE and skin prick test measures. In one study BCG had protective effect on allergic rhinitis<sup>25</sup> and in one study the prevalence of asthma in allergic rhinitis patients in respect to the presence of BCG scar was low.<sup>11</sup> In the study of Gruber et al early immunization especially in neonatal period was found as a protective factor for allergy.<sup>26</sup> Immunogenicity of different strains of BCG vaccine may be different.<sup>27</sup> Subjects of our study were immunized in the first day after birth and immunization was done by Health Centers. We proposed that all children be vaccinated with the same strain of vaccine in the same ages, but

the size of scar was different. It might be due to other factors especially genetic ones as mentioned above, that cause different responses in similar conditions. The significant reverse correlations between BCG scar and atopy, asthma and AD in our study indicate the protective effect of Th1 lymphocytes activity that was shown by the diameter of BCG scar. Th1 lymphocytes activation lead to inhibition of Th2 lymphocytes in producing cytokines that promote atopy, but the effect of BCG vaccination by this way was not revealed. Other prospective studies with skin prick test, measurement of total and specific IgE level and cytokine profile of them could be useful and are recommended.

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