Dear Editor,

Bacille Calmette–Guerin (BCG) vaccine is proposed to have a possible role in preventing or reversing type 1 diabetes (T1D) through its immunomodulatory effects on the islet cells. However, experimental and clinical studies using BCG vaccination in T1D have shown conflicting results. While some studies showed favorable effects of BCG vaccination on T1D autoimmunity or clinical remission, others showed opposite results. Epidemiological surveys from Sweden and Canada suggested no impact of BCG vaccination on the overall incidence of T1D. The BABYDIAB study that followed children from birth to 11 years of age indicated that neonatal BCG vaccination might even accelerate the progression of the autoimmune process in T1D. Thus, the connection of BCG vaccination with islet autoimmunity remains controversial.

We recorded BCG vaccination status (presence or absence of BCG scar) in 300 children with T1D and 300 non-diabetic children visiting the outpatient department. The data on islet autoantibody profiles were retrieved from the clinic files. Children with T1D were older than non-diabetic children (9.2 ± 3.7 yr vs. 6.9 ± 3.8 yr, P value 0.00); however, the proportion of boys and girls in the two groups was similar (169:131 versus 180:120, P value 0.44). The BCG vaccination coverage was high (294/300, 98.0% in both groups). BCG scar formation rate was identical in diabetic (224/294, 76.2%) and non-diabetic children (218/294, 74.1%). In children with T1D, the age at diagnosis was similar in scar-positive and scar-negative. Similarly, the proportion of T1D children with at least one autoantibody positivity was similar (92% vs. 90%) in patients with or without a scar. The frequencies of glutamic acid decarboxylase (GAD65) and islet antigen 2 autoantibodies (IA2) were similar in the two groups, whereas insulin autoantibodies (IAA) positivity was higher in scar-negative children [Table 1].

Our study showed no difference in the age at onset of T1D in scar-positive versus scar-negative children. BCG’s protective immunity is known to start waning with age, especially after 10 years. Hence, the protective impact of neonatal BCG vaccination would be expected to be better in younger children, which was not observed in our study.

The pancreatic autoantibody positivity was similar in the scar-positive and negative children, indicating that a successful neonatal BCG vaccination offered no additional protection for the development of autoimmunity. This finding contrasts two previous studies, which either showed BCG vaccination’s accelerating or protective effect on islet autoimmunity. Although scar formation is considered a surrogate marker for BCG-induced immunity and correlates well with the tuberculin conversion, a negative scar does not necessarily indicate failure of BCG vaccination. Thus, the possibility that BCG’s protective effect occurred in scar-negative children as well cannot be excluded entirely.

The GAD65 and IA2 autoantibodies frequencies were similar in the scar-positive and scar-negative children. Although a higher number of scar-negative children showed IAA autoantibody positivity, the significance of this finding is uncertain due to the low patient numbers available for
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Comparison. In conclusion, successful BCG vaccination did not correlate with islet autoantibody positivity, suggesting that routine BCG vaccination plays no role in T1D autoimmunity.

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Conflicts of interest
There are no conflicts of interest.

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