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# Examining the Relationship between SARS-CoV-2 Infection and Type 1 Diabetes: A Reanalysis of Recent Findings

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## Introduction

Type 1 diabetes (T1D), an autoimmune disease mediated by T cells, has long been associated with various viral infections [1-4]. Among these infections, enterovirus infection [5-7] was more consistently reported to contribute to the development of T1D, while some virus infection might mitigate the T1D by suppressing the autoimmune responses [8-10]. In the studies on recent COVID19 pandemic, the findings [1,11-17] from most investigators and us demonstrated COVID patients have higher risk for type 1 and type 2 diabetes. However, a study [18] recently published in New England Journal of Medicine (NEJM) yielded conflicting results, suggesting that SARS-CoV-2 infection does not have impact on the incidence of pediatric T1D. This commentary aims to provide a nuanced reanalysis of pertinent data to contribute clarity to this ongoing discourse.

## Methods

In the study [18] published in NEJM, the authors investigated the relationship between SARS-CoV-2 infection, islet autoimmunity, and T1D in young individuals. They analyzed the data from 4,586 participants by categorizing patients into those with islet autoantibodies and those without, and comparing their positive rates for SARS-CoV-2 nucleocapsid antibodies.

They concluded that SARS-CoV-2 infection does not increase islet autoimmunity or T1D in teenagers [18]. It is evident that the authors have wrongly analyzed and misinterpreted their data. In our reanalysis, we employed a focused approach by categorizing patients into those with SARS-CoV-2 nucleocapsid antibodies and those without, and comparing their positive rates for islet autoantibodies. This methodological adjustment aimed to address the potential impact of SARS-CoV-2 infection on islet autoimmunity and T1D more accurately.

## Results

Our reanalysis of the data from the study [18] in NEJM revealed a statistically significant difference ($P<0.05$, $\chi2=3.9833$) in the positive rates of islet autoantibodies between the SARS-CoV-2 nucleocapsid antibody-positive population (11.63%) and the SARS-CoV-2 nucleocapsid antibody-negative population (9.22%). These findings align with existing perspectives suggesting a heightened risk of islet autoimmunity and T1D following SARS-CoV-2 infection.

## Discussion

Some potential pathogenesis of SARS-CoV-2 infection for T1D development has been discussed in some studies [11-16] and it needs more direct evidence for how SARS-CoV-2 infection causes β cell damage [1].

While acknowledging the limitations of our analysis due to the unavailability of raw data, we contend that a multiple correlation analysis, if feasible in future studies, could

provide a more robust foundation for drawing conclusions. Transparency regarding these limitations underscores the necessity for more comprehensive investigations into the intricate relationship between SARS-CoV-2 infection and T1D.

In addition, although the study [18] published in NEJM did not demonstrate that SARS-CoV-2 virus infection does not increase T1D as authors stated, the correct interpretation of results from the authors' original analysis should be that the children with T1D do not have higher risk for SARS-CoV-2 infection.

## Conclusion

Contrary to the initial interpretation of the study [18] in NEJM, our reanalysis substantiates the hypothesis that SARS-CoV-2 infection indeed increases the morbidity of T1D. By addressing methodological nuances, we contribute valuable epidemiological evidence that aligns with the challenges posed by the ongoing pandemic. A meticulous understanding of this association remains pivotal for effective public health strategies.

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