

# World Journal of *Diabetes*

Monthly Volume 16 Number 8 August 15, 2025



**EDITORIAL**

Gouda MM. Rheb1 as a novel  $\beta$ -cell regulator connecting mTORC1, AMPK, and NOTCH1 pathways for efficient diabetes therapy. *World J Diabetes* 2025; 16(8): 108310 [DOI: [10.4239/wjd.v16.i8.108310](https://doi.org/10.4239/wjd.v16.i8.108310)]

**MINIREVIEWS**

Rasooly A, Beran D, Ye PP, Joshi S, Yin XJ, Tandon N, Shao RT. Digital health for rural diabetes care: Implementation experience from China and India. *World J Diabetes* 2025; 16(8): 107733 [DOI: [10.4239/wjd.v16.i8.107733](https://doi.org/10.4239/wjd.v16.i8.107733)]

Gumenku L, Erukainure OL, Islam MS, Olaniran AO. Prebiotic, probiotic, and postbiotic properties of fermented corn starch and their application in type 2 diabetes management. *World J Diabetes* 2025; 16(8): 107775 [DOI: [10.4239/wjd.v16.i8.107775](https://doi.org/10.4239/wjd.v16.i8.107775)]

Walia S, Morya AK, Khullar S, Aggarwal S, Kaur R. Role of alternative oral therapy for the management of wet age-related macular degeneration and proliferative diabetic retinopathy. *World J Diabetes* 2025; 16(8): 109231 [DOI: [10.4239/wjd.v16.i8.109231](https://doi.org/10.4239/wjd.v16.i8.109231)]

**ORIGINAL ARTICLE****Case Control Study**

Wu HL, Huang H, Chen BQ, Xia J, Jiang LB. Intraoperative blood perfusion factors in free anterolateral thigh flap repair for diabetic foot ulcers: A retrospective analysis. *World J Diabetes* 2025; 16(8): 105532 [DOI: [10.4239/wjd.v16.i8.105532](https://doi.org/10.4239/wjd.v16.i8.105532)]

Alissa N, Al Zahrani S. Psychological predictors of diabetic ketoacidosis in children: Health belief model-based case-control study. *World J Diabetes* 2025; 16(8): 110088 [DOI: [10.4239/wjd.v16.i8.110088](https://doi.org/10.4239/wjd.v16.i8.110088)]

**Retrospective Cohort Study**

Chen M, Li JT, Gao JB, Zhang L, Gao QH, Zeng X, Liu Q. Autologous platelet rich gel in treatment of lower limb atherosclerotic occlusive disease in diabetic patients. *World J Diabetes* 2025; 16(8): 106215 [DOI: [10.4239/wjd.v16.i8.106215](https://doi.org/10.4239/wjd.v16.i8.106215)]

Wang YR, Gao Y, Liu YC, Xu ZP, Wang YY, Xu HB, Wang JZ, Zhang Y. Higher glycated hemoglobin amplifies the effect of apolipoprotein E epsilon 4-related cognition and olfaction impairments in type 2 diabetes. *World J Diabetes* 2025; 16(8): 106664 [DOI: [10.4239/wjd.v16.i8.106664](https://doi.org/10.4239/wjd.v16.i8.106664)]

Rincon O, Uscategui C, Mancera P, Luna M, Rodriguez A, Alvarez M, Guzman I. Association of social determinants of health and cardiovascular complications in type 2 diabetes in Colombia. *World J Diabetes* 2025; 16(8): 106927 [DOI: [10.4239/wjd.v16.i8.106927](https://doi.org/10.4239/wjd.v16.i8.106927)]

Liu MJ, Xiang SM, Hu XQ. Triglyceride glucose-body mass index is associated with cardiovascular outcomes and overall mortality in type-2 diabetes mellitus patients. *World J Diabetes* 2025; 16(8): 108839 [DOI: [10.4239/wjd.v16.i8.108839](https://doi.org/10.4239/wjd.v16.i8.108839)]

**Retrospective Study**

Shi L, Li NJ. Comprehensive analysis of risk factors associated with carotid plaque in patients with type 2 diabetes mellitus. *World J Diabetes* 2025; 16(8): 104180 [DOI: [10.4239/wjd.v16.i8.104180](https://doi.org/10.4239/wjd.v16.i8.104180)]

Shi YP, Pan ZL, Zhang J, Xue LY, Li MQ. Gut dysbiosis, low-grade inflammation, and renal impairment severity in elderly diabetic nephropathy. *World J Diabetes* 2025; 16(8): 108245 [DOI: [10.4239/wjd.v16.i8.108245](https://doi.org/10.4239/wjd.v16.i8.108245)]

Xin Y, Peng NL, Xin CY, Liao JR, Hu XQ, Dong YH, Zhang XY. Metabolic score for insulin resistance is associated with adverse cardiovascular events in patients with type 2 diabetes. *World J Diabetes* 2025; 16(8): 108671 [DOI: [10.4239/wjd.v16.i8.108671](https://doi.org/10.4239/wjd.v16.i8.108671)]

Carmon L, Bachar Y, Babiev AS, Hazn I, Hershkovitz E, Shaki D, Loewenthal N, Haim A, Hazan G. Impact of COVID-19 outbreak on the seasonality and incidence of type 1 diabetes mellitus: A nationwide cohort study. *World J Diabetes* 2025; 16(8): 108724 [DOI: [10.4239/wjd.v16.i8.108724](https://doi.org/10.4239/wjd.v16.i8.108724)]

**Observational Study**

Lyu L, Huang YL, Huang Y, Wu ZY, Ping F, Li YX. Performance of flash continuous glucose monitoring and glycemic marker correlations in Chinese pregnant women with non-type 1 diabetes. *World J Diabetes* 2025; 16(8): 106967 [DOI: [10.4239/wjd.v16.i8.106967](https://doi.org/10.4239/wjd.v16.i8.106967)]

**Prospective Study**

Zou XL, Zhou C. Persistently high and fluctuating trajectories of total and somatic depressive symptoms increase diabetes risk: Two prospective cohort studies. *World J Diabetes* 2025; 16(8): 106683 [DOI: [10.4239/wjd.v16.i8.106683](https://doi.org/10.4239/wjd.v16.i8.106683)]

**Randomized Controlled Trial**

Gao YQ, Gao YH, Xing JH. Vitamin D supplementation reduces infection rate and promotes wound healing in patients with diabetic foot ulcers. *World J Diabetes* 2025; 16(8): 108166 [DOI: [10.4239/wjd.v16.i8.108166](https://doi.org/10.4239/wjd.v16.i8.108166)]

**Basic Study**

Yuan XJ, Zhang ZC, Li J, Ye SD, Zhou W. Identification and mechanistic insights of ubiquitin-proteasome system and pyroptosis-related biomarkers in type 2 diabetes mellitus. *World J Diabetes* 2025; 16(8): 104879 [DOI: [10.4239/wjd.v16.i8.104879](https://doi.org/10.4239/wjd.v16.i8.104879)]

Tang JY, Chong YJ, Yang L, Li X, Yang Y, Li JC, Mu J. Activation of farnesoid X receptor upregulates binding immunoglobulin protein expression and alleviates diabetic nephropathy. *World J Diabetes* 2025; 16(8): 105228 [DOI: [10.4239/wjd.v16.i8.105228](https://doi.org/10.4239/wjd.v16.i8.105228)]

Li J, Gao M, Wang JX, Li HY, Wang P, Yuan F, Liu AJ, Zhang SY. Troxerutin improves diabetic cognitive dysfunction by inhibiting mitochondrial fission mediated by transient receptor potential melastatin 7/calcineurin/dynamin-related protein 1<sup>ser637</sup>. *World J Diabetes* 2025; 16(8): 106833 [DOI: [10.4239/wjd.v16.i8.106833](https://doi.org/10.4239/wjd.v16.i8.106833)]

Tang YW, Zhang Y, Zhou J, Peng YT, Zi Y, Wei YR, Yue ZH. Electroacupuncture with different current intensities can improve gastrointestinal motility in diabetic gastroparesis *via* vagal and sympathetic pathways. *World J Diabetes* 2025; 16(8): 107779 [DOI: [10.4239/wjd.v16.i8.107779](https://doi.org/10.4239/wjd.v16.i8.107779)]

Wu QG, Zhang MJ, Lan YB, Ma CL, Fu WJ. Hyperglycemia-induced overexpression of CREB3 L3 promotes the epithelial-to-mesenchymal transition in bladder urothelial cells in diabetes mellitus. *World J Diabetes* 2025; 16(8): 108101 [DOI: [10.4239/wjd.v16.i8.108101](https://doi.org/10.4239/wjd.v16.i8.108101)]

**SYSTEMATIC REVIEWS**

Lew LC, Mat Ludin AF, Abdul Manaf Z, Mohd Tohit N, Shahar S. Mapping evidence and identifying risks: A systematic scoping review of meal replacements in type 2 diabetes. *World J Diabetes* 2025; 16(8): 104371 [DOI: [10.4239/wjd.v16.i8.104371](https://doi.org/10.4239/wjd.v16.i8.104371)]

**META-ANALYSIS**

Kamrul-Hasan ABM, Pappachan JM, Nagendra L, Muthukuda D, Dutta D, Bhattacharya S, Shrestha D, Dhakal GP, Sumanatilleke M, Raza SA, Kalra S. Prevalence of diabetes distress among people with type 2 diabetes in South Asia: A systematic review and meta-analysis. *World J Diabetes* 2025; 16(8): 109352 [DOI: [10.4239/wjd.v16.i8.109352](https://doi.org/10.4239/wjd.v16.i8.109352)]

**CASE REPORT**

Gao AM, Deng WL, Yang XP, Wu WY, Ma CY, Liu Y. *WFS1* gene mutation associated with pediatric diabetes mellitus and congenital deafness: A case report. *World J Diabetes* 2025; 16(8): 108946 [DOI: [10.4239/wjd.v16.i8.108946](https://doi.org/10.4239/wjd.v16.i8.108946)]

**LETTER TO THE EDITOR**

Li B. Microglial metabolic reprogramming: Aucubin inhibits aldose reductase to reverse diabetic neuropathic pain. *World J Diabetes* 2025; 16(8): 110285 [DOI: [10.4239/wjd.v16.i8.110285](https://doi.org/10.4239/wjd.v16.i8.110285)]

**ABOUT COVER**

Editorial Board Member of *World Journal of Diabetes*, Jia-Zhong Sun, Professor, Department of Endocrinology, Zhongnan Hospital, Wuhan University, No. 169 Donghu Road, Wuhan 430071, Hubei Province, China.  
sjz300@163.com

**AIMS AND SCOPE**

The primary aim of *World Journal of Diabetes (WJD, World J Diabetes)* is to provide scholars and readers from various fields of diabetes with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

*WJD* mainly publishes articles reporting research results and findings obtained in the field of diabetes and covering a wide range of topics including risk factors for diabetes, diabetes complications, experimental diabetes mellitus, type 1 diabetes mellitus, type 2 diabetes mellitus, gestational diabetes, diabetic angiopathies, diabetic cardiomyopathies, diabetic coma, diabetic ketoacidosis, diabetic nephropathies, diabetic neuropathies, Donohue syndrome, fetal macrosomia, and prediabetic state.

**INDEXING/ABSTRACTING**

The *WJD* is now abstracted and indexed in Science Citation Index Expanded (SCIE, also known as SciSearch®), Current Contents/Clinical Medicine, Journal Citation Reports/Science Edition, PubMed, PubMed Central, Reference Citation Analysis, China Science and Technology Journal Database, and Superstar Journals Database. The 2025 Edition of Journal Citation Reports® cites the 2024 journal impact factor (JIF) for *WJD* as 4.6; JIF without journal self cites: 4.3; 5-year JIF: 5.0; JIF Rank: 43/191 in endocrinology and metabolism; JIF Quartile: Q1; and 5-year JIF Quartile: Q1.

**RESPONSIBLE EDITORS FOR THIS ISSUE**

Production Editor: *Zi-Hang Xu*, Production Department Director: *Xu Guo*, Cover Editor: *Jia-Ru Fan*.

**NAME OF JOURNAL**

*World Journal of Diabetes*

**ISSN**

ISSN 1948-9358 (online)

**LAUNCH DATE**

June 15, 2010

**FREQUENCY**

Monthly

**EDITORS-IN-CHIEF**

Lu Cai, Md. Shahidul Islam, Michael Horowitz

**EDITORIAL BOARD MEMBERS**

<https://www.wjgnet.com/1948-9358/editorialboard.htm>

**PUBLICATION DATE**

August 15, 2025

**COPYRIGHT**

© 2025 Baishideng Publishing Group Inc

**INSTRUCTIONS TO AUTHORS**

<https://www.wjgnet.com/bpg/gerinfo/204>

**GUIDELINES FOR ETHICS DOCUMENTS**

<https://www.wjgnet.com/bpg/GerInfo/287>

**GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH**

<https://www.wjgnet.com/bpg/gerinfo/240>

**PUBLICATION ETHICS**

<https://www.wjgnet.com/bpg/GerInfo/288>

**PUBLICATION MISCONDUCT**

<https://www.wjgnet.com/bpg/gerinfo/208>

**ARTICLE PROCESSING CHARGE**

<https://www.wjgnet.com/bpg/gerinfo/242>

**STEPS FOR SUBMITTING MANUSCRIPTS**

<https://www.wjgnet.com/bpg/GerInfo/239>

**ONLINE SUBMISSION**

<https://www.f6publishing.com>

## Retrospective Study

## Impact of COVID-19 outbreak on the seasonality and incidence of type 1 diabetes mellitus: A nationwide cohort study

Lior Carmon, Yoav Bachar, Amit S Babiev, Itai Hazn, Eli Hershkovitz, David Shaki, Neta Loewenthal, Alon Haim, Guy Hazan

**Specialty type:** Endocrinology and metabolism

**Provenance and peer review:**

Unsolicited article; Externally peer reviewed.

**Peer-review model:** Single blind

**Peer-review report's classification**

**Scientific Quality:** Grade A, Grade B, Grade B, Grade B, Grade B

**Novelty:** Grade A, Grade B, Grade B, Grade C

**Creativity or Innovation:** Grade B, Grade B, Grade B, Grade C

**Scientific Significance:** Grade A, Grade A, Grade B, Grade B

**P-Reviewer:** Horowitz M; Khan A; Ouyang WH

**Received:** April 24, 2025

**Revised:** May 25, 2025

**Accepted:** July 9, 2025

**Published online:** August 15, 2025

**Processing time:** 113 Days and 3.9 Hours



**Lior Carmon, Eli Hershkovitz, David Shaki, Neta Loewenthal, Alon Haim, Guy Hazan,** Pediatric Endocrinology Unit, Soroka University Medical Center, Beer-Sheva 8457108, Israel

**Lior Carmon, Amit S Babiev, Itai Hazn, Eli Hershkovitz, David Shaki, Neta Loewenthal, Alon Haim, Guy Hazan,** Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva 8457108, Israel

**Yoav Bachar, Amit S Babiev, Itai Hazn,** Clinical Research Center, Soroka University Medical Center, Beer-Sheva 8457108, Israel

**Corresponding author:** Lior Carmon, MD, Pediatric Endocrinology Unit, Soroka University Medical Center, 151 Rager Street, Beer-Sheva 8457108, Israel. [liorca2@clalit.org.il](mailto:liorca2@clalit.org.il)

## Abstract

### BACKGROUND

Type 1 diabetes mellitus (T1DM) is an autoimmune disease with a multifactorial pathogenesis. Viral infections have been proposed as contributing triggers, supported by the disease's seasonal pattern, which typically shows higher incidence in autumn and winter. The coronavirus disease 2019 (COVID-19) pandemic and associated lockdowns created a unique context to examine the incidence and seasonality of T1DM during a period characterized by reduced circulation of common viral infections.

### AIM

To investigate the incidence and seasonality of T1DM before and during COVID-19 pandemic in relation to global viral infection rates.

### METHODS

This population-based retrospective study utilized a nationwide computerized database. Extracted data included the number of new T1DM cases over the 8 years preceding and during the COVID-19 pandemic, demographic characteristics of affected individuals, and nationwide respiratory virus polymerase chain reaction data from weekly nasal wash sample collections.

### RESULTS

A total of 2176 patients were diagnosed with new-onset T1DM during the pre-pandemic period, compared to 348 cases during the pandemic. In the same

periods, 33727 respiratory virus-positive polymerase chain reaction results from nasal wash samples were recorded pre-pandemic, compared to 2603 during the pandemic. Additionally, 363399 positive COVID-19 cases were reported during the pandemic period. Seasonality analysis revealed a higher rate of new-onset T1DM cases and a weaker seasonal pattern during the pandemic. Trend analysis showed a consistent increase in T1DM incidence prior to COVID-19, with a more variable trend observed during the pandemic. Correlation analysis between T1DM incidence and respiratory viruses demonstrated a weak correlation between T1DM incidence and a few respiratory viruses.

## CONCLUSION

The observed increase in new-onset T1DM cases and the disruption of its typical seasonal pattern during the COVID-19 pandemic suggest a potential association between respiratory virus exposure and the development of T1DM.

**Key Words:** Type 1 diabetes mellitus; COVID-19; Seasonality; Pathogenesis; Viral trigger

©The Author(s) 2025. Published by Baishideng Publishing Group Inc. All rights reserved.

**Core Tip:** This population-based study assessed incidence and seasonality of type 1 diabetes mellitus (T1DM) before and during the coronavirus disease 2019 pandemic. A higher rate of new-onset T1DM and diminished seasonal pattern were observed during the pandemic, coinciding with reduced circulation of common respiratory viruses due to lockdown measures. These findings suggest respiratory viruses, including severe acute respiratory distress syndrome corona virus-2, may serve as environmental triggers for T1DM. Weak positive correlations were identified between T1DM incidence and respiratory viruses (*e.g.*, respiratory syncytial virus, influenza). The results support a potential link between viral exposure and T1DM pathogenesis, highlighting the need for further research into underlying mechanisms and preventive strategies.

**Citation:** Carmon L, Bachar Y, Babiev AS, Hazn I, Hershkovitz E, Shaki D, Loewenthal N, Haim A, Hazan G. Impact of COVID-19 outbreak on the seasonality and incidence of type 1 diabetes mellitus: A nationwide cohort study. *World J Diabetes* 2025; 16(8): 108724

**URL:** <https://www.wjgnet.com/1948-9358/full/v16/i8/108724.htm>

**DOI:** <https://dx.doi.org/10.4239/wjd.v16.i8.108724>

## INTRODUCTION

Type 1 diabetes mellitus (T1DM) is a T cell-mediated autoimmune disorder that targets pancreatic beta cells[1,2], leading to insulin deficiency, hyperglycemia, and, in some cases, diabetic ketoacidosis, a life-threatening complication[3]. The global incidence of T1DM has been rising over the past several decades, reaching approximately 15 cases per 100000 individuals per year[4,5]. Both genetic predisposition and environmental exposures contribute to T1DM pathogenesis[1, 2].

Several viruses, including enterovirus, rubella, mumps, rotavirus, parvovirus, and cytomegalovirus, have been proposed as potential environmental triggers for T1DM[1,2]. Suggested mechanisms include molecular mimicry, direct beta cell cytotoxicity, and regulatory T cell dysfunction[2]. Although respiratory viruses are less frequently implicated, some studies suggest they may also play a contributing role[6,7].

Seasonality refers to regular, periodic fluctuations that occur within a 1-year period. In time series analysis, Fourier terms are mathematical components used to model and quantify seasonal variation. Epidemiological studies have shown a seasonal pattern in T1DM incidence, with increased case rates during autumn and winter[8], potentially reflecting seasonal viral exposures[1,2,8-11]. While seasonality may be influenced by geographical position[8] and patient age[9], it has been consistently observed across populations.

The coronavirus disease 2019 (COVID-19) pandemic, which began in March 2020, resulted in widespread public health measures, including lockdowns, movement restrictions, and mandatory face mask use. These interventions led to a marked decline in seasonal respiratory virus infections during the first year of the pandemic[12,13]. This epidemiological shift provided a unique opportunity to examine the relationship between respiratory virus circulation, particularly COVID-19, and the incidence of T1DM, as well as the effect of lockdowns on T1DM seasonality as an indirect indicator of other respiratory viruses as potential triggers. Several studies have reported an increase in T1DM incidence during the pandemic[14-17], while others found no significant change[18-20], and one systematic review yielded inconclusive results [21]. Some studies also noted a reduction in the typical seasonal variation of T1DM incidence during COVID-19 period [14,15,18-20]. One possible explanation is that decreased exposure to respiratory viruses during lockdown may have attenuated their role as environmental triggers for T1DM. This study aimed to investigate the correlation between respiratory virus exposure and the incidence of T1DM before and during the COVID-19 Lockdown, and to assess the impact of viral exposure on the seasonal pattern of T1DM incidence.

## MATERIALS AND METHODS

This population-based retrospective study utilized a nationwide computerized database from Clalit Healthcare Services (CHS) electronic medical records (the MDCLONE system). The CHS database includes extensive demographic data, anthropometric measurements, diagnoses from community clinics and hospitals, medication dispensing records, and comprehensive laboratory results. CHS is the largest health maintenance organization in Israel, serving over 5 million patients. All data were de-identified prior to analysis, and the study involved secondary use of existing clinical records.

The study period was divided into two intervals: The pre-COVID-19 period (“pre-pandemic”, January 2012 to February 2020) and the COVID-19 period (“pandemic”, March 2020 to February 2021), consistent with a previous study [12]. Extracted data included: (1) The number of participants aged 0-18 years with at least two insulin prescriptions, used as a proxy for T1DM diagnosis, following prior methodology [19]. The date of the first insulin prescription was considered the diagnosis date. Demographic variables recorded were age at diagnosis, sex, and ethnicity; and (2) Nationwide respiratory virus polymerase chain reaction (PCR) data from nasal wash samples collected weekly across all Clalit institutions, without age restrictions. Samples were categorized by virus type, and different test methods (*e.g.*, antigen and PCR) were combined. New T1DM diagnoses were defined as those occurring more than 90 days after a previous diagnosis. IgG and IgM antibody test results were excluded. The study protocol was approved by the Medical Ethics Committee of Review Board of Soroka University Medical Center.

### Statistical analysis

Descriptive analyses were performed to compare T1DM incidence between the pre-pandemic and pandemic periods. Population-based incidence rates were calculated by dividing the number of new T1DM diagnoses by the total number of CHS members. Statistical analysis began with an assessment of data distribution and measures of central tendency. Temporal trends in T1DM incidence were evaluated using Poisson regression models adjusted for time periods. Seasonal patterns were analyzed using an additive generalized linear regression model incorporating Fourier terms. The time series model was defined as: “ $Y_t = \alpha_0 + \alpha_1 t + \alpha_2 t^2 + \alpha_3 t^3 + b_1 \cos(\omega t) + c_1 \sin(\omega t) + \epsilon_t$ ” where  $Y_t$  is the number of diabetes cases at time  $t$ ,  $\alpha$  terms represent polynomial trend components,  $\omega$  denotes yearly periodicity ( $\omega = 2\pi/365$ ), and sine and cosine terms (Fourier terms) capture seasonal variation. The term  $\epsilon_t$  represents random variation. Poisson regression was used to account for count-based data.

For the pre-pandemic period, associations between respiratory viruses and T1DM incidence were analyzed using weekly aggregated data. Spearman correlation tests were conducted between the number of T1DM diagnoses and each type of viral infection. This was followed by individual Poisson regression analyses that controlled for seasonal effects. The analysis was performed at the population level, not at the level of individual T1DM patients. All statistical analyses were conducted using R software (version 4.2.3; R Core Team, 2023).

## RESULTS

### Demographics

A total of 2524 patients with new-onset T1DM were included, comprising 2176 cases during the pre-pandemic period and 348 during the pandemic period. Approximately half of the participants were female, 39% were of Bedouin ethnicity, and the median age at diagnosis was 11 years (interquartile range: 7-14). No significant demographic differences were observed between the two groups (Table 1).

### Viral PCR data

Seasonality analysis of T1DM was conducted separately for the pre-pandemic and pandemic periods. During the pre-pandemic period, 33727 viral-positive PCR results from nasal wash samples were recorded, compared to 2603 during the pandemic. Additionally, 363399 positive COVID-19 cases were reported throughout the pandemic period. A clear seasonal pattern was observed pre-pandemic, with higher T1DM incidence during autumn and winter (Figure 1).

### Seasonality analysis

During the pre-pandemic period, the seasonality analysis yielded a log value of 0.728094, with a small positive cosine term and a larger sine term, indicating a moderate seasonal pattern characterized by rhythmic sinusoidal waves (Figure 1A). In contrast, the pandemic period showed an increased average log value of 0.953425, reflecting a higher rate of new-onset T1DM cases. However, the cosine term was negative and the sine term was minimal, indicating a weakened seasonal pattern during this time (yellow line in Figure 1B).

### Trend analysis and correlation analysis

Trend analysis revealed a steady increase in T1DM incidence throughout the pre-pandemic period, whereas the trend during the pandemic period was more variable (Supplementary Figure 1). Correlation analysis using Spearman’s method showed weak positive correlations between T1DM incidence and several respiratory viruses, including respiratory syncytial virus (RSV) (commonly referred to as RSV), parainfluenza, influenza, and adenovirus (Table 2, Supplementary Figure 2).

**Table 1 Demographic characteristics of diabetes mellitus type 1 diagnosis cohort**

Characteristic	Pre-COVID-19 period (n = 2176)	COVID-19 period (n = 348)	P value <sup>1</sup>	Overall (n = 2524)
Gender, male, n (%)	1132 (52)	186 (53)	0.6	1318 (52)
Ethnicity, Arab, n (%)	858 (39)	122 (35)	0.12	980 (39)
Age at diagnosis (years), median (IQR)	11.0 (7.0-14.0)	11.0 (8.0-13.0)	0.7	11.0 (7.0-14.0)

<sup>1</sup>Pearson's  $\chi^2$  test; Wilcoxon rank sum test; Wilcoxon rank sum exact test.  
 COVID-19: Coronavirus disease 2019; IQR: Interquartile range.

**Table 2 Correlation between type 1 diabetes mellitus incidence and respiratory viruses cases per week**

Value	Total viruses	Adeno	Entero	Influenza A	Influenza B	Parainfluenza	HMPV	RSV	Rhino
Rho	0.193	0.196	0.045	0.196	0.165	0.151	0.032	0.130	0.077
P value	< 0.001	< 0.001	0.343	< 0.001	< 0.001	0.001	0.49	0.006	0.107

HMPV: Human metapneumovirus; RSV: Respiratory syncytial virus.

## DISCUSSION

This study identified a moderate seasonal pattern of new-onset T1DM cases during the pre-pandemic period, characterized by higher incidence in autumn and winter. In contrast, during the pandemic period, there was an almost complete loss of this seasonal pattern. The question of triggers and causality in T1DM pathogenesis remains unresolved[22,23]. However, the potential role of respiratory viral infections as contributing factors has been widely explored[6,7], with supporting evidence from the observed seasonality of T1DM incidence, which peaks in autumn and winter[8,9].

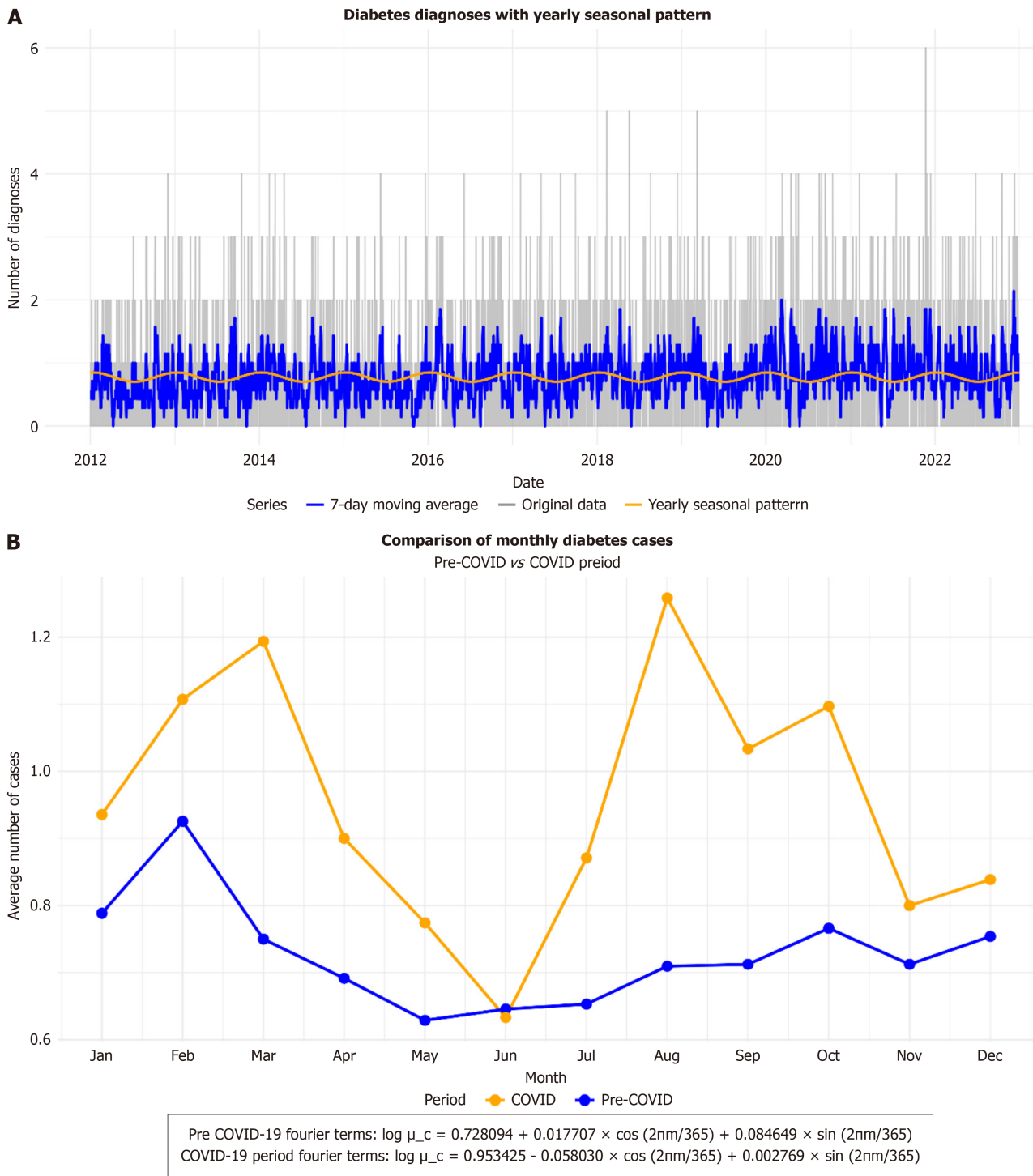
During the pandemic period, the incidence of new-onset T1DM was higher compared to the pre-pandemic period, consistent with findings from previous studies[14-17]. This increase may suggest COVID-19 as a potential trigger for T1DM[24]. Proposed mechanisms for COVID-19's impact on pancreatic beta cells include direct cellular damage as well as enhanced autoimmunity through epitope spreading, molecular mimicry, and bystander activation[24].

However, alternative explanations for the shifts in T1DM incidence during the COVID-19 pandemic have been proposed, including limited access to medical care, changes in healthcare-seeking behavior, and increased stress[16,18]. The seasonal pattern observed in the pre-pandemic period was diminished during the pandemic, consistent with findings from other studies[18-20]. Given the marked reduction in respiratory virus transmission during COVID-19 Lockdowns [12], our results suggest that exposure to respiratory viruses may influence T1DM seasonality and contribute to its development. Moreover, the increased incidence of T1DM during the pandemic and the potential role of COVID-19 as a trigger support this hypothesis. Initial post-pandemic trend data indicating a decline in T1DM incidence may further reinforce this theory[25].

Influenza, parainfluenza, adenovirus, and RSV were found to have a weak positive correlation with T1DM incidence in the pre-pandemic period. These viruses are known to follow distinct seasonal patterns[26], and our findings suggest they may contribute to the observed seasonality of T1DM incidence. This study's strengths include a large, population-based cohort and an extended pre-pandemic observation period, enabling robust trend and seasonality analyses. However, several limitations should be noted. The relatively short duration of the pandemic period (1 year) restricts the depth of seasonal trend evaluation during this time frame. Additionally, the use of insulin prescription as a proxy for new-onset T1DM, while consistent in previous studies[19], may lead to misclassification, as insulin is occasionally prescribed for type 2 diabetes. Nonetheless, limiting the cohort to individuals aged 0-18 years likely mitigated this concern. Further research is needed to clarify the role of respiratory viruses in T1DM pathogenesis, elucidate underlying causal mechanisms, and identify potential preventative strategies.

## CONCLUSION

This study suggests that the diminished seasonal variation in T1DM incidence observed during the COVID-19 Lockdown, alongside an overall increase in new cases, may reflect the potential role of respiratory viruses, including severe acute respiratory distress syndrome corona virus-2, as environmental triggers for T1DM. These findings underscore the need for further research to confirm causal relationships and to inform preventive and public health strategies.



**Figure 1 Type 1 diabetes mellitus incidence.** A: Type 1 diabetes mellitus incidence in the pre-pandemic [coronavirus disease 2019 (COVID-19)] period; B: Comparison of type 1 diabetes mellitus incidence in the pre-pandemic (COVID-19) period and in the pandemic (COVID-19) period. COVID-19: Coronavirus disease 2019.

## FOOTNOTES

**Author contributions:** Carmon L and Hazan G designed the study; Carmon L wrote the original draft of the manuscript; Bachar Y, Babiev AS, Hazn I, and Hazan G performed the research and statistical analysis; Hershkovitz E, Shaki D, Loewenthal N, and Haim A reviewed the manuscript; Hazan G reviewed manuscript and made major contributions to the final version; Haim A and Hazan G edited the manuscript; and all authors approved the final version of the manuscript.

**Institutional review board statement:** This study was approved by the Medical Ethics Committee of Review Board of Soroka University Medical Center, approval No. 0167-23-SOR.

**Informed consent statement:** This population-based retrospective study utilized a nationwide computerized database. All data were de-

identified before analysis.

**Conflict-of-interest statement:** All the authors report no relevant conflicts of interest for this article.

**Data sharing statement:** Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

**Open Access:** This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <https://creativecommons.org/licenses/by-nc/4.0/>

**Country of origin:** Israel

**ORCID number:** Lior Carmon [0000-0002-4551-5708](https://orcid.org/0000-0002-4551-5708).

**S-Editor:** Bai Y

**L-Editor:** A

**P-Editor:** Xu ZH

## REFERENCES

- 1 **Filippi CM**, von Herrath MG. Viral trigger for type 1 diabetes: pros and cons. *Diabetes* 2008; **57**: 2863-2871 [RCA] [PMID: 18971433 DOI: 10.2337/db07-1023] [FullText] [Full Text(PDF)]
- 2 **van der Werf N**, Kroese FG, Rozing J, Hillebrands JL. Viral infections as potential triggers of type 1 diabetes. *Diabetes Metab Res Rev* 2007; **23**: 169-183 [RCA] [PMID: 17103489 DOI: 10.1002/dmrr.695] [FullText]
- 3 **Dhatariya KK**, Glaser NS, Codner E, Umpierrez GE. Diabetic ketoacidosis. *Nat Rev Dis Primers* 2020; **6**: 40 [RCA] [PMID: 32409703 DOI: 10.1038/s41572-020-0165-1] [FullText]
- 4 **Gomez-Lopera N**, Pineda-Trujillo N, Diaz-Valencia PA. Correlating the global increase in type 1 diabetes incidence across age groups with national economic prosperity: A systematic review. *World J Diabetes* 2019; **10**: 560-580 [RCA] [PMID: 31915518 DOI: 10.4239/wjd.v10.i12.560] [FullText] [Full Text(PDF)]
- 5 **Mobasser M**, Shirmohammadi M, Amiri T, Vahed N, Hosseini Fard H, Ghajzadeh M. Prevalence and incidence of type 1 diabetes in the world: a systematic review and meta-analysis. *Health Promot Perspect* 2020; **10**: 98-115 [RCA] [PMID: 32296622 DOI: 10.34172/hpp.2020.18] [FullText] [Full Text(PDF)]
- 6 **Beyerlein A**, Wehweck F, Ziegler AG, Pflueger M. Respiratory infections in early life and the development of islet autoimmunity in children at increased type 1 diabetes risk: evidence from the BABYDIET study. *JAMA Pediatr* 2013; **167**: 800-807 [RCA] [PMID: 23818010 DOI: 10.1001/jamapediatrics.2013.158] [FullText]
- 7 **Lönnrot M**, Lynch KF, Elding Larsson H, Lernmark Å, Rewers MJ, Törn C, Burkhardt BR, Briese T, Hagopian WA, She JX, Simell OG, Toppari J, Ziegler AG, Akolkar B, Krischer JP, Hyöty H; TEDDY Study Group. Respiratory infections are temporally associated with initiation of type 1 diabetes autoimmunity: the TEDDY study. *Diabetologia* 2017; **60**: 1931-1940 [RCA] [PMID: 28770319 DOI: 10.1007/s00125-017-4365-5] [FullText]
- 8 **Moltchanova EV**, Schreier N, Lammi N, Karvonen M. Seasonal variation of diagnosis of Type 1 diabetes mellitus in children worldwide. *Diabet Med* 2009; **26**: 673-678 [RCA] [PMID: 19573115 DOI: 10.1111/j.1464-5491.2009.02743.x] [FullText]
- 9 **Samuelsson U**, Carstensen J, Löfman O, Nordfeldt S. Seasonal variation in the diagnosis of type 1 diabetes in south-east Sweden. *Diabetes Res Clin Pract* 2007; **76**: 75-81 [RCA] [PMID: 16963147 DOI: 10.1016/j.diabres.2006.07.023] [FullText]
- 10 **Afoke A**, Ludvigsson J, Hed J, Lindblom B. Raised IgG and IgM in "epidemic" IDDM suggest that infections are responsible for the seasonality of type 1 diabetes. *Diabetes Res* 1991; **16**: 11-17 [RCA] [PMID: 1818792] [FullText]
- 11 **Principi N**, Berioli MG, Bianchini S, Esposito S. Type 1 diabetes and viral infections: What is the relationship? *J Clin Virol* 2017; **96**: 26-31 [RCA] [PMID: 28934695 DOI: 10.1016/j.jcv.2017.09.003] [FullText]
- 12 **Hazan G**, Fox C, Mok H, Haspel J. Age-dependent rebound in asthma exacerbations after COVID-19 lockdown. *J Allergy Clin Immunol Glob* 2022; **1**: 314-318 [RCA] [PMID: 36377231 DOI: 10.1016/j.jacig.2022.06.001] [FullText]
- 13 **Amram T**, Duek OA, Golan-Tripto I, Goldbart A, Greenberg D, Hazan G. The Interplay Between Respiratory Syncytial Virus and Asthma Inception: Insights Gained From the COVID-19 Pandemic. *Pediatr Pulmonol* 2025; **60**: e27474 [RCA] [PMID: 39760467 DOI: 10.1002/ppul.27474] [FullText]
- 14 **McKeigue PM**, McGurnaghan S, Blackburn L, Bath LE, McAllister DA, Caparrotta TM, Wild SH, Wood SN, Stockton D, Colhoun HM. Relation of Incident Type 1 Diabetes to Recent COVID-19 Infection: Cohort Study Using e-Health Record Linkage in Scotland. *Diabetes Care* 2023; **46**: 921-928 [RCA] [PMID: 35880797 DOI: 10.2337/dc22-0385] [FullText]
- 15 **Schiaffini R**, Deodati A, Rapini N, Pampanini V, Cianfarani S. Increased incidence of childhood type 1 diabetes during the COVID-19 pandemic. Figures from an Italian tertiary care center. *J Diabetes* 2022; **14**: 562-563 [RCA] [PMID: 35916392 DOI: 10.1111/1753-0407.13298] [FullText] [Full Text(PDF)]
- 16 **Rahmati M**, Keshvari M, Mirnasuri S, Yon DK, Lee SW, Il Shin J, Smith L. The global impact of COVID-19 pandemic on the incidence of pediatric new-onset type 1 diabetes and ketoacidosis: A systematic review and meta-analysis. *J Med Virol* 2022; **94**: 5112-5127 [RCA] [PMID: 35831242 DOI: 10.1002/jmv.27996] [FullText] [Full Text(PDF)]
- 17 **Vlad A**, Serban V, Timar R, Sima A, Botea V, Albai O, Timar B, Vlad M. Increased Incidence of Type 1 Diabetes during the COVID-19 Pandemic in Romanian Children. *Medicina (Kaunas)* 2021; **57**: 973 [RCA] [PMID: 34577896 DOI: 10.3390/medicina57090973] [FullText]

- [Full Text(PDF)]
- 18 **Kostopoulou E**, Eliopoulou MI, Rojas Gil AP, Chrysis D. Impact of COVID-19 on new-onset type 1 diabetes mellitus - A one-year prospective study. *Eur Rev Med Pharmacol Sci* 2021; **25**: 5928-5935 [RCA] [PMID: 34661251 DOI: 10.26355/eurrev\_202110\_26869] [Full Text]
  - 19 **van den Boom L**, Kostev K, Kuss O, Rathmann W, Rosenbauer J. Type 1 diabetes incidence in children and adolescents during the COVID-19 pandemic in Germany. *Diabetes Res Clin Pract* 2022; **193**: 110146 [RCA] [PMID: 36347421 DOI: 10.1016/j.diabres.2022.110146] [FullText] [Full Text(PDF)]
  - 20 **Reschke F**, Lanzinger S, Herczeg V, Prahalad P, Schiaffini R, Mul D, Clapin H, Zabeen B, Pelicand J, Phillip M, Limbert C, Danne T; SWEET Study Group. The COVID-19 Pandemic Affects Seasonality, With Increasing Cases of New-Onset Type 1 Diabetes in Children, From the Worldwide SWEET Registry. *Diabetes Care* 2022; **45**: 2594-2601 [RCA] [PMID: 36166593 DOI: 10.2337/dc22-0278] [FullText]
  - 21 **Nassar M**, Nso N, Baraka B, Alfishawy M, Mohamed M, Nyabera A, Sachmechi I. The association between COVID-19 and type 1 diabetes mellitus: A systematic review. *Diabetes Metab Syndr* 2021; **15**: 447-454 [RCA] [PMID: 33592371 DOI: 10.1016/j.dsx.2021.02.009] [FullText] [Full Text(PDF)]
  - 22 **Duncan LJP**, Clarke BF. Changing Concepts of the Cause of Diabetes Mellitus. *Res Medica* 2013; **5** [DOI: 10.2218/resmedica.v5i3.466] [Full Text]
  - 23 **Buschard K**. What causes type 1 diabetes? Lessons from animal models. *APMIS Suppl* 2011; 1-19 [RCA] [PMID: 21615797 DOI: 10.1111/j.1600-0463.2011.02765.x] [FullText] [Full Text(PDF)]
  - 24 **Wang Y**, Guo H, Wang G, Zhai J, Du B. COVID-19 as a Trigger for Type 1 Diabetes. *J Clin Endocrinol Metab* 2023; **108**: 2176-2183 [RCA] [PMID: 36950864 DOI: 10.1210/clinem/dgad165] [FullText]
  - 25 **Kamrath C**, Eckert AJ, Lignitz S, Hillenbrand N, Dost A, Warncke K, Klose D, Grohmann-Held K, Holl RW, Rosenbauer J. Wave in Pediatric Type 1 Diabetes Incidence After the Emergence of COVID-19: Peak and Trough Patterns in German Youth-A Population-Based Study From the Prospective Multicenter DPV Registry. *Diabetes Care* 2025; **48**: e47-e48 [RCA] [PMID: 39887349 DOI: 10.2337/dc24-2026] [FullText]
  - 26 **Moriyama M**, Hugentobler WJ, Iwasaki A. Seasonality of Respiratory Viral Infections. *Annu Rev Virol* 2020; **7**: 83-101 [RCA] [PMID: 32196426 DOI: 10.1146/annurev-virology-012420-022445] [FullText]



Published by **Baishideng Publishing Group Inc**  
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA  
**Telephone:** +1-925-3991568  
**E-mail:** [office@baishideng.com](mailto:office@baishideng.com)  
**Help Desk:** <https://www.f6publishing.com/helpdesk>  
<https://www.wjgnet.com>

