Detection of Human Parvovirus B19 IgG in a Group of Iraqi Children with Newly onset Type 1 Diabetes Mellitus

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Abstract

Background   Type 1 diabetes mellitus (T1DM) is a complex disease that is caused by a combination of genetic and environmental factors. One of environmental factor that has been linked to T1DM is Parvovirus B19 (B19V), a virus that can infect erythroid progenitor cell. Studies have assumed that people with T1DM are more likely to have been infected with B19V, which suggest that B19V may play a role in the development of T1DM.

Objective   To detect B19V IgG in patients with T1DM.

Methods   A total of 50 children with newly diagnosed T1DM and 50 non-diabetic children were recruited as controls. B19V was detected using enzyme linked immunosorbent assay (ELISA) technique.

Results   B19V infections had been detected in T1DM patients and control group with exposure rate 6% and 10% respectively. However, results were statistically not-significant.

Conclusion   Current study concluded that B19V infection might not be considered as a risk factor for T1DM.

Keywords   Parvovirus B19, T1DM, ELISA

Citation   Khudair EA, Al-Shuwaikh AM, Abdoun DS. Detection of Human Parvovirus B19 IgG in a group of Iraqi children with newly onset type 1 diabetes mellitus. Iraqi JMS. 2024; 22(2): 212-216. doi: 10.22578/IJMS.22.2.4

List of abbreviations: B19V = Parvovirus B19, ELISA = Enzyme-Linked Immunosorbent assay, T1DM = Type 1 Diabetes Mellitus

Introduction

Type 1 diabetes mellitus (T1DM), formerly known as insulin-dependent diabetes mellitus (IDDM), is an autoimmune disease that typically develops in children and adolescents. This disease causes the body to destroy its own insulin-producing cells in the pancreas, which lead to deficiency of insulin production due to the destruction of pancreatic beta cells and require lifelong insulin administration for survival. T1DM is one of the most common chronic diseases of childhood, accounting for about 10% of all diabetes cases [1,2].

T1DM is emerging as a very heterogeneous disease driven by a complex network of multiple factors, including genetic and environmental interactions [3].

There is a strong association between viruses and T1DM. Several studies have shown that people with T1DM are more likely to have been infected with certain viruses in the past, such as enteroviruses, mumps virus, and cytomegalovirus [4,5].

Data from experimental animals as well as in vitro studies indicate that various viruses are clearly able to modulate the development of T1DM via different mechanisms. The earliest

observations for the suggestion of virus contribution to T1DM are that the beginning of T1DM sometimes follows acute viral infections and happens with greater frequencies at certain times of the year, which often indicate a viral reason [6].

Parvovirus B19 (B19V) have was considered a candidate in the pathophysiology of T1DM. For numerous reasons, its peak incidence in children, prevalent subclinical presentation, and endemic frequency with irregular outbreak intervals are consistent with the characteristics of an environmental viral agent connected to the development of T1DM [7].
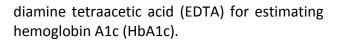
Current study aimed to detect B19V IgG in patients with T1DM to shed light on cause of the disease. This could lead to new ways to prevent or delay the onset of T1DM, or to improve the treatment of people with T1DM.

Methods

A case-control study was conducted in Baghdad, Iraq, to investigate the possible link between viral infection and T1DM in children. From October 2020 to February 2023, 50 newly diagnosed children with T1DM and 50 non-diabetic children as a control group their age were ranged from less than 1 year to 15 years were included in the study at Central Teaching Hospital of Pediatrics in Baghdad. The research project was approved by the Institutional Review Board (IRB) of Al-Nahrain College of Medicine on 14 November 2022, with approval declaration number 202207/76. The written consent of the child's guardian was obtained prior to conducting the research.

Specimens' collection

Five milliliters of blood was drawn from each child enrolled in this study. The sample was divided into two parts; three milliliters was placed in a sterile gel tube and allowed to clot. The serum was then separated by centrifugation at 4000 rpm for 15 minutes. The serum was stored at -20°C and used to estimate the levels of B19V IgG, the remaining 2 milliliters of blood was kept in ethylene diamine tetraacetic acid (EDTA) for estimating hemoglobin A1c (HbA1c).

Diagnosis of T1DM

Blood samples were collected from 50 children who had just been diagnosed with T1DM and were being attended to the Central Teaching Hospital of Pediatrics. The diagnosis was confirmed according to the World Health Organization (WHO) criteria, which include random blood sugar (RBS) and HbA1c levels.

Viral diagnosis

B19V IgG was diagnosed by enzyme-Linked Immunosorbent assay (ELISA).

Interpretation of the results

B19V IgG the calculated absorptions for the sera of the study groups were compared with the cut off value. The cut off value = absorbance of negative control + 0.15. If the absorbance of the sample is equal or higher than the cut off value, the test sample is considered positive, otherwise the test sample is considered negative.

Statistical analysis

The statistical analysis was performed using the statistical package for the social sciences (SPSS) software version 25.0. The data were first tested for normality. Categorical data were presented as counts and percentages Chi-square test (χ^2-test) was used to describe the association between categorical variables. Numerical data were presented as mean ± standard deviation and t test was used to calculate the difference in mean, the level of significance (P value) was set at ≤0.05. The results were presented in tables.

Results

Study population demographics and clinical features

This study included 50 children with T1DM and 50 apparently healthy children as a control group, their age were ranged from less than 1 year to 15 years with median of 8 years and

mean of (8.08±4.65 vs. 7.88±4.42) respectively. Thirty (60%) of T1DM patients were girls and 20 (40%) were boys, while in control group 23 (46%) were girls and 27 (54%) were boys. Patients with T1DM had weight range from 8 to 62 kg and controls group had weight range from 8 to78kg and their mean of weight were (28.88±14.02 vs.33.24±18.40), respectively. The differences between the two groups in mean of age, sex, and weight of the participants were statistically not significant (P >0.05). However, 35 (70%) of T1DM patients were from urban and 15 (30%) from rural, while 48 (96%) of control group were from urban and 2 (4%) from rural with a significant difference between both groups (P <0.01). Regarding family history of DM, 32 (64%) of patients and 13 (26%) of control group had a family history of DM with significant difference (P <0.01). In T1DM patients, disease duration ranged from 1 day to 23 days with a mean of 3.98±3.30 days.

Biochemical tests related to T1DM
Levels of RBS and HbA1c in patients were higher (217.20±87.7 mg/dl and 10.27±1.8%) respectively) than in control group (88.7±7.3 mg/dl and 4.92±0.5%) respectively, with statistically significant differences (P <0.05) (Table 1).

Table 1. Biochemical tests related to study population

Tests		Patient (n=50)	Control (n=50)	P value*
RBS, mg/dl	Mean±SD	217.20±87.7	88.7±7.3	< 0.001*
	Median	207.5	89.0	
	Range	75-539	73-100	
HbA1c, %	Mean±SD	10.27±1.89	4.92±0.5	0.004*
	Median	10.0	4.9	
	Range	5.7-15	4.0-6.1	

Normal values: RBS <200 mg/dl, HbA1c 5.7-6.4%, P value by Mann Whitney test

Detection of ani-B19V IgG antibody
Three patients (6%) tested positive for anti-B19V IgG antibodies, and five of the children in the control group (10%) tested positive, the difference was statistically not significant (P >0.05) as shown in table (2).

Table 2. Frequency of anti-B19V IgG antibodies in the study groups

Study population	No.	Anti-B19V IgG antibodies	
		Positive No. (%)	Negative No. (%)
Patients	50	3 (6.0%)	47 (94.0%)
Control	50	5 (10.0%)	45 (90.0%)
P value*		0.461	

*Chi-square test (χ2-test)

Discussion

Viral infections have long been suspected as a possible environmental trigger for T1DM. However, the evidence for this association is still largely circumstantial. There are a number of viruses that have been linked to T1DM, including enteroviruses, rotavirus, mumps virus, and cytomegalovirus. Enteroviruses are the most well-studied such as Coxsackievirus have been shown to induce or accelerate T1DM, also several studies considered a link between B19V infection and the pathogenesis of T1DM [8-9].

According to the findings of the present study T1DM patients had significantly greater levels of RBS, HbA1c than control group (Table 1). The findings of the current study are consistent with those of previous studies conducted in Iraq, Iran, Morocco and United Kingdom [10-13].

The present study revealed that the presence of B19 IgG did not differ significantly between the diabetic and the control groups. The present finding is similar with other studies such as in Pennsylvania, and in Iraqi population a cross-sectional study includes 45 patients with T1DM that showed no significant association between B19V with T1DM [9,14].

In this study, the higher prevalence of anti-B19V IgG antibodies in the control group (10%) compared to the T1DM group (6%) was not statistically significant, suggesting greater past exposure in the control group without a direct link to disease development. This result is consistent with a study in Iraq, where the prevalence of anti-B19V IgG and IgM antibodies was 33.33% and 0%, respectively, and a study in Egypt, which reported a 20% seropositivity rate for IgG in healthy children. Overall, B19V antibody prevalence increases with age [15-17].

A limitation of this study is the lack of anti-B19V IgM antibody testing, which would have helped identify recent infections. However, IgM detection is challenging due to its transient nature. As a result, IgG testing is often preferred, as it provides more reliable evidence of past exposure or immunity.

Current study concluded that the presence of anti-B19V IgG antibodies might not be considered as a risk factor for T1DM. Further research is needed to confirm these findings and to determine whether B19V infection may play a role in the development of T1DM.

Author contribution

Khudair: conducted the laboratory experiments, performed the statistical analysis, and drafted the initial version of this manuscript as part of her PhD thesis. Dr. Al-Shuwaikh: conceptualized and supervised the study, and oversaw the preparation of the final manuscript. Dr. Abdoun: contributed to sample collection and provided expertise on the clinical aspects of the work. All authors reviewed and approved the final version of the manuscript.

Conflict of interest

There is no conflict of interest.

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Received Sep. 21st 2023
Accepted May 9th 2024