How to Cite:
Rafiq, M. N., & Hussein, H. K. (2022). Detection of coxsackie virus B and measurement level of Tumor necrosis factor alpha in patients suffered in T1DM with coxsackie virus infection. *International Journal of Health Sciences*, *6*(S5), 11565–11571. https://doi.org/10.53730/ijhs.v6nS5.11167

Detection of coxsackie virus B and measurement level of Tumor necrosis factor alpha in patients suffered in T1DM with coxsackie virus infection

Meraj Nadhom Rafiq
B.Sc., student, Department of, Pathological Analysis, College of Health and Medical Techniques /Kufa, Al-Furat Al-Awsat Technical University, Iraq
Corresponding authors email: meraj.rafiq.chhu1@student.atu.edu.iq

Humam Kasem Hussein
Technical Institute of Najaf/ Al-Furat Al-Awsat Technical University, 31003 Al-Kufa, Iraq.
Email: kuh.hum@atu.edu.iq

***Abstract*---**Objective. Infection with Coxsackie virus. This virus that damages pancreatic cells, has long been linked to the onset of insulin-dependent diabetic mellitus (IDDM). Pro-inflammatory cytokines can be produced as a result of this illness. Tumor necrosis factor-a is one of these pro-inflammatory cytokines. Materials and Methods. Blood sample were collected from 180 Iraqi participants. Ninety of them is type 1 diabetic patients and other 90 is healthy control .both groups were tested for the incidence of Coxsackie virus B IgG. So the patients groups is divided to two groups according to sero positivity of CVB-IgG .all 180 patients tested to measure of level of TNF-α. Results. The Results showed increasing in levels of TNF-α in CBV positive Type 1 Diabetes mellitus was (34.85 ± 11.00 pg/ml). The level of this interleukin in Type 1 Diabetes mellitus negative to that virus was (26.16 ± 7.79 pg/ml). While the results of this interleukin in control group was (13.82 ± 3.93 pg/ml) with p-value 0. Conclusion. The concentration of TNF-α, according to results, has been shown to be associated with type 1 diabetes mellitus patients infected with CVB-IgG and diabetic patients without CVB.

***Keywords*---**Viral diseases, T1DM, TNF-α, and Coxsackie virus.

Introduction

Diabetes mellitus (DM) is a sever metabolic illness that has been present for a long time that develop as a result of a complex combination of heredity and environmental variables. It is characterized by hyperglycemia, polyuria and polyphagia (1). T1DM (type 1 diabetes mellitus) is a one type of DM, is the most common chronic autoimmune illness defined by gradual loss of pancreatic beta – cell ,leading in a reeducation of insulin output (2). One and the important etiology of T1DM is exposure to virus such as enter virus like Coxsackie virus implicated in the development of T1DM. (3)

Infection with Coxsackie virus recently been linked with to produce some pro-inflammatory cytokine such as TNF-α. Cytokine are small protein produced by cells that play a role in cellular communication and inflammation. Cytokine are protein that regulate pain ,inflammation, immune response and other processes .they are classified as pro-inflammatory and anti- inflammatory cytokine(4). TNF-α producing DCs and macrophage were found in pancreatic islet infiltrate in early investigation, indicating that these cells were the original and main producers of TNF-α. It was discovered that it up regulated MHC-I molecules ,speeding up B – cell death and then induces islet-infiltrating DCs/ macrophages to cross-present an exogenous islet antigen to CD8+ T cells via a CD40/CD154-independent mechanism(5). The aim of this research is measurement of TNF-α in DM patients with viral infection in correlation with those without it.

Materials and Method

Ninety type 1 diabetes mellitus patients were attended to Imam Hassan center for Endocrinology and Diabetes at the holy Karbala province and 90 healthy controls (non-diabetic patients). All of two groups is tested for detection of Coxsackie virus so this groups is divided according to sero –positivity of CVB-IgG to following groups : First groups : Type 1 diabetes mellitus with Coxsackie virus. Second groups: Type 1 diabetes mellitus without Coxsackie virus. Third groups: healthy control. The following step is measurement of level of TNF-α for the three groups. The laboratory diagnosis was done for detection of Coxsackie virus and determination of level of TNF-α is biotek ELISA system.

Statistical analysis

T tests for (cause and control) and ANOVA tests were performed to investigate the difference between the three groups in the study's data using the statistical analysis technique employing social sciences (SPSS) version 20.

Results

The 90 sample of T1DM patients and 90 sample of control groups were tested for Coxsackie virus B ,the result show that 18(28%)patients were positive for specific anti-Coxsackie virus B-IgG(anti CVB-IgG) in T1DM patients. In other hand, all the serum samples of non-diabetes patients were negative to anti CVB-IgG. The Results showed increasing in levels of TNF-α in CBV positive Type 1 Diabetes mellitus was (34.85 ± 11.00 pg/ml). The level of this interleukin in Type 1

Diabetes mellitus negative to that virus was (26.16 ± 7.79 pg/ml). While the results of this interleukin in control group was (13.82 ± 3.93 pg/ml) as shown in Table (1) (Figure 4). There was significant differences (P<0.05) of TNF-α level in CBV positive Type 1 Diabetes mellitus than the others in which negative to them.

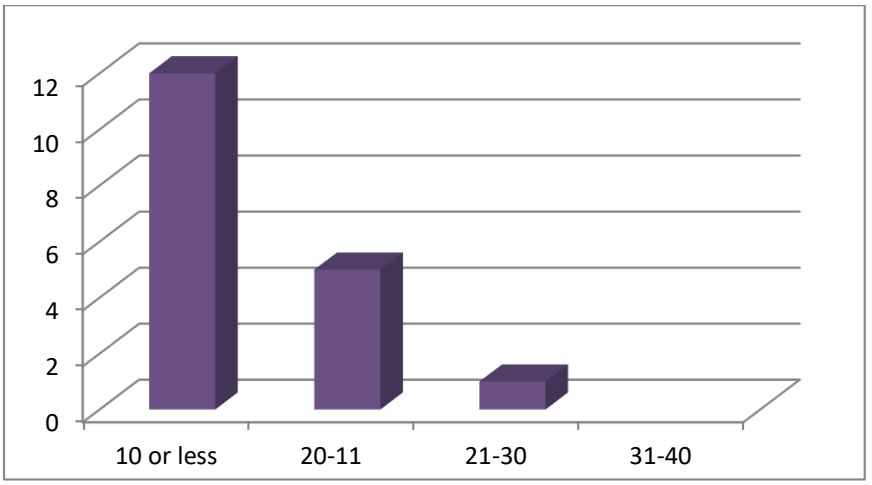

Figure 1 .Distribution of positive CVB-IgG according to age groups

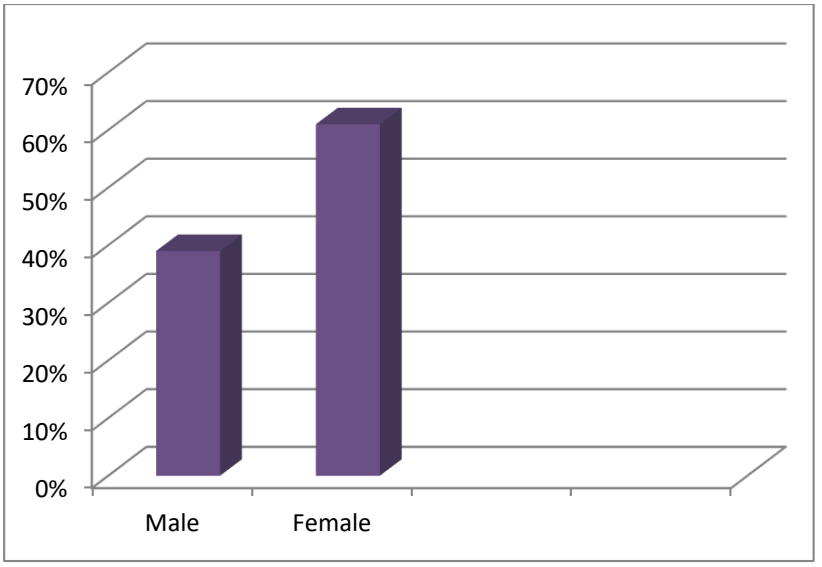

Figure 2 .Distribution of positive CVB-IgG according to gender groups

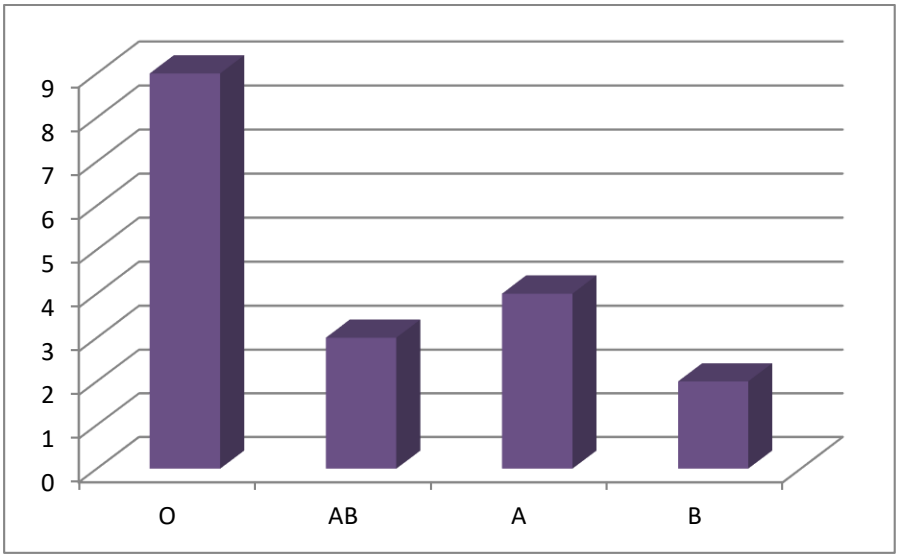

Figure 3.Distribution of positive CVB-IgG according to ABO blood groups.

Measurement of level of serum interleukin (TNF-α)

The result showed the increasing level of TNF-α in CVB positive type 1 diabetes mellitus was (34.85 ± 11.00 pg/ml).the level of this interleukin in type 1 diabetes mellitus negative to that virus was (26.16 ± 7.79 pg/ml).while the result of this interleukin in control groups was (13.82 ± 3.93 pg/ml) .

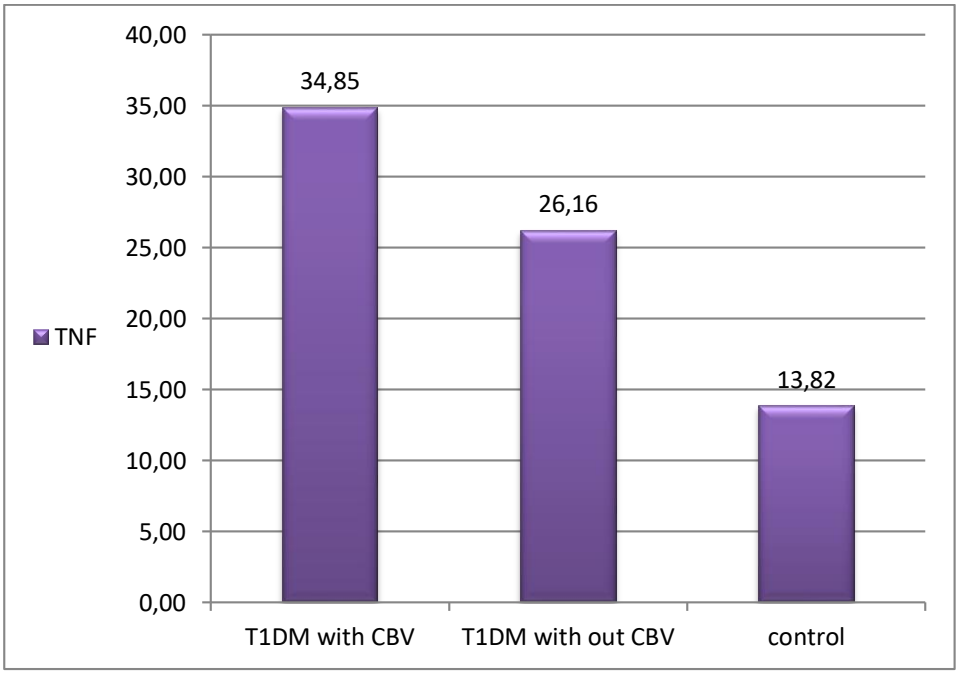

Figure 4. Concentration levels of TNF-α in the presented study: CBV positive Type1 DM, CBV Negative Type1 DM and Control group.

Table 1 .centration levels of TNF-α, in the study groups: CBV positive Type1 DM, CBV Negative Type1 DM and Control group.

cytokines	groups	NO.	Mean	Std. Deviation	F .test	P-V*alue
TNF-α	T1DM with CBV	18	34.85	11.00	33.522	0.000
	T1DM without CBV	72	26.16	7.79		
	control	90	13.82	3.93		

*P-value 0.05

Discussion

The result of of anti –CVB-IgG of this research which was 28% sera –positivity of anti CVB-IgG results ,would refer to previous Coxsackie virus B infection that had been neutralized by adaptive immune response. IgG antibody response are crucial for adaptive immunity because they reflect the immunological memory for previous pathogen exposure (6). The induction of adaptive immunity is associated with clearness of virus .B cell regulate and conduct the production of specific antibodies .which ether deactivates the virus opsonisation and neutralization processes or initiates destruction of infected cells (7).

According to figure 1, the result showed showed that the age group less or 10 years had the highest percentage (66.7%). The high prevalent within 1-10 years age might be due to more predisposing related to poor hygiene habits in that age ,which increased transmission of viral infection among them readily(8). According to figure 2, sex showed that the highest percentage of them which constituted 64.28% female groups.

According to figure 3, ABO blood system results of type 1 diabetic patients with Coxsackie virus, the highest percentage O blood group 50%. Human blood is organized into 34 groups, each of which carries hundreds of genes and antigens that are inherited as polymorphic features. Changes in expressed blood group antigens can affect a person's ability to withstand infectious illnesses in a variety of situations. Blood groups may play a key role in the acquisition of viral illnesses by increasing cellular adhesion and virus engulfment as virus receptors and co-receptors. (9)

According to figure 4,and table 1 , The Results showed increasing in levels of TNF-α in CBV positive Type 1 Diabetes mellitus was (34.85 ± 11.00 pg/ml). The level of this interleukin in Type 1 Diabetes mellitus negative to that virus was (26.16 ± 7.79 pg/ml). While the results of this interleukin in control group was (13.82 ± 3.93 pg/ml) as shown in Table (4.1) (Figure 4). There was significant differences ($P<0.05$) of TNF-α level in CBV positive Type 1 Diabetes mellitus than the others in which negative to them. Experimental infection of human peripheral blood mononuclear cells with CBV resulted in increased production of cytokines such as TNF-α and IL-6 (10), that CBV is able to infect β-cells and The similarity of human and viral proteins might provide another reason, and the coxsackie-B

virus does include a protein that is comparable to human glutamic acid decarboxylase-65 (GAD65) (11).

Although, TLR4-dependent mechanism, viral infections cause the production of pro-inflammatory cytokines in human pancreatic cells, including IL-1BETA and TNF-α. Some research has suggested that these cytokines may have a negative effect on pancreatic function, and TNF-α has been linked to cell damage in the early stages of T1DM development by inducing endoplasmic reticulum stress, despite the fact that they appear to play a protective role in the host's defense against infection. (12). The -cells are infected by T1DM, CBV, which causes them to produce CXCL8 and stimulates Th1 and Th2 cells to generate TNF-.α (13).

Conclusions

This study show, the Coxsackie virus B(CVB)was detected 28% from the serum of type 1 diabetes mellitus. The result of CVB- IgG antibodies revealed that IgG antibody has levels were higher age group less than 10 years than other age groups. The result showed that CVB was predominant in females patients more than male patients. Also the result shows the O blood groups is more susceptible to Coxsackie virus infection. The concentration of the TNF-α, according to our results, has been shown to be associated with the type 1 diabetes mellitus patients infected with CVB –IgG and diabetic patient without CVB.

References

1. Alam, S.; Hasan, M.; Neaz, S.; Hussain, N.; Hossain, M. and Rahman, T. (2021). Diabetes Mellitus: insights from epidemiology, biochemistry, risk factors, diagnosis, complications and comprehensive management. Diabetology, 2(2), 36-50.
2. Alberts, B.; Johnson, A.; Lewis, J.; Raff, M.; Roberts, K. and Walter, P. (2002). The Adaptive Immune System, Chapter 24. In: Molecular Biology of the Cell, 4th ed. New York: Garland Science.
3. Alidjinou E. K.; Sane, F.; Engelmann, I. and Hober D. (2013). Serum-dependent enhancement of coxsackievirus B4-induced production of IFNalpha, IL-6 and TNFalpha by peripheral blood mononuclear cells. J Mol Biol. 425:5020–31. doi: 10.1016/j.jmb.2013.10.008
4. Ariwibowo, M. F., Wahab, Z., Isnanta, R., & Isnurhadi, I. (2020). Physical evidence promotion on consumer decisions in using bowling sport services. International Journal of Social Sciences and Humanities, 4(3), 22–28. https://doi.org/10.29332/ijssh.v4n3.445
5. Bergamin, C. S.; Pérez-Hurtado, E.; Oliveira, L.; Gabbay, M.; Piveta, V.; Bittencourt, C. and Dib, S. A. (2020). Enterovirus Neutralizing Antibodies, Monocyte Toll Like Receptors Expression and Interleukin Profiles Are Similar Between Non-affected and Affected Siblings From Long-Term Discordant Type 1 Diabetes Multiplex-Sib Families: The Importance of HLA Background. Frontiers in Endocrinology, 662.
6. Cooling, L. (2015). Blood Groups in Infection and Host Susceptibility. Clin Microbiol Rev. 28(3): 801-870.
7. Corrales-Aguilar, E.; Trilling, M.; Reinhard, H.; Falcone, V.; Zimmermann, A.; Adams, O.; Hengel, H. *et al.* (2016). Highly individual patterns of virus-

immune IgG effector responses in humans. Medical microbiology and immunology, 205(5): 409-424.
8. De Beeck, A. O. and Eizirik, D. L. (2016). Viral infections in type 1 diabetes mellitus—why the β cells?. Nature Reviews Endocrinology, 12(5), 263-273.
9. Gomez-Díaz, R. A. (2019). Pathophysiology of Type 1 Diabetes. In: The Diabetes Textbook, 89-99. Cham: Springer
10. Hussein. H. K. (2019). Detection the infection with viral hepatitis C in Suwayrah/Wasit Governorate /Iraq. Journal of Global Pharma Technology, 251-255
11. Kahaly, G. J. and Hansen, M. P. (2016). Type 1 diabetes associated autoimmunity. Autoimmunity reviews, 15(7): 644-648.
12. Lien, E., and Zipris, D. (2009). The role of Toll-like receptor pathways in the mechanism of type 1 diabetes. Current molecular medicine, 9(1), 52-68.
13. Lu, J.; Liu, J.; Li, L.; Lan, Y. and Liang, Y. (2020). Cytokines in type 1 diabetes: mechanisms of action and immunotherapeutic targets. Clinical & translational immunology, 9(3), e1122
14. Masriadi, M., Mahmud, N. U., Muriyati, M., Adam, R. K., Alawiyah, T., Safruddin, S., Amir, H., & Asnidar, A. (2022). Determinant of metabolic syndrome: Case study hypertension and diabetes mellitus type II. International Journal of Health Sciences, 6(2), 1046–1057. https://doi.org/10.53730/ijhs.v6n2.10800
15. Ramos-Morcillo, A.; Moreno-Martínez, F.; Hernández Susarte, A.; Hueso-Montoro, C. and Ruzafa-Martínez, M. (2019). Social Determinants of Health, the Family, and Children's Personal Hygiene: A Comparative Study. International journal of environmental research and public health, 16(23): 4713.
16. Suryasa, I. W., Rodríguez-Gámez, M., & Koldoris, T. (2021). Health and treatment of diabetes mellitus. International Journal of Health Sciences, 5(1), i-v. https://doi.org/10.53730/ijhs.v5n1.2864