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Detection of Anti-rubella virus, Cytomegalovirus and Chlamydia pneumonia antibodies in patients with type I diabetes mellitus

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ABSTRACT

Type-1 diabetes is defined as destruction of pancreatic beta cell, virus and bacteria are some environmental factor for this disease. The study included 25 patients with type-1 diabetes mellitus aged between 8 – 25 years from Baghdad hospital and 20 healthy persons as control group. Anti-rubella IgG and IgM, anti-*Chlamydia pneumonia* IgG and IgM were measured by ELISA technique while anti-CMV antibody were measured by immunofluorescence technique. The aim of current study was to know the trigger factor for type-1 diabetes. There were significant differences ($P<0.05$) between studied groups according to parameters and the results lead to suggest that *Chlamydia pneumonia*, CMV and rubella virus may trigger type-1 diabetes mellitus in Iraqi patients.

Keywords: diabetes mellitus, viral infection, bacteria

1. INTRODUCTION

Type-1 diabetes results from destruction of pancreatic beta cell; while type-2 diabetes is a bipolar disease characterized by a defect in both insulin secretion and insulin action whose complex interaction leads to a progressive increase of plasma glucose levels [1]. Viruses are one environmental factor that is implicated in the pathogenesis of type-1 diabetes [2]. Rubella virus appears to be involved in the development of type-I diabetes (TID) in patients with congenital rubella syndrome (CRS). Islet cell and anti-insulin antibodies were found in 50-80% of diabetic patients with CRS, whereas these antibodies were present in about 20% of non- diabetic patients with CRS, suggesting an underlying autoimmune disorders [3]. Cytomegalovirus (CMV) has been implicated in TID by a number of clinical studies; Case reports describe a child with congenital CMV infection [4] and a woman with CMV infection [5] who both developed TID. CMV can affect pancreatic beta cell, in a study on children with fatal viral infections, viral cytopathology of the pancreas and characteristic inclusion bodies in the beta cells were found in 20-45 cases of CMV infection [6]. On average, patients with active CMV infection were characterized by a significantly lower insulin secretion than controls without infection [7]. *Chlamydia pneumoniae* is a gram negative bacterium with obligate intracellular life cycle. It can establish persistent in macrophage,associated with alteration of their function and modulate the host immune response [8]. *C. pneumoniae* infection occurs with high frequency in virtually all humans during their lifetime [9] and numerous studies have demonstrated strong links between *Chlamydia pneumonia* infection and metabolic syndrome, insulin resistance, and coronary artery disease [10]. Infection with this bacteria enhances insulin resistances in a genetically and nutritionally restricted fashion in obese B6 mice [11]. Recent studies have shown some evidence linking *C. pneumonia* with coronary heart disease [12]. Patients with type-2 diabetes mellitus have a risk of death from cardiovascular causes that is two to six times that

among persons without diabetes. Multiple modifiable risk factors for late complications in patients with type-2 diabetes, including hyperglycemia, hypertension, and dyslipidemia, increase the risk of a poor outcome [13]. The aim of recent study is to knowing the trigger factor for type-1 diabetes.

2. MATERIALS AND METHODS

The study include (25) patients with diabetic mellitus type-1 of ages (8-25) years from Baghdad hospital and central pediatric hospital from December 2012 to March 2013 and (20) healthy blood donor taken as healthy control groups. All the study group carried out to measure anti-rubella virus IgG and IgM antibodies by ELISA technique according to (Euroimmune, UK), anti-Chlamydia IgG and IgM antibodies by using ELISA technique according to (Euroimmune, UK) and anti-CMV antibodies by using IF technique according to (Euroimmune, UK).

Statistical analysis:

Comparison of paired data from the groups of subjects was done using student t- test, while correlation between groups was analyzed using chi-square. IBM SPSS computer program V. 21 was used to analyze the data [14].

3. RESULTS AND DISCUSSION

The results of the present study showed there was significant elevation (P<0.05) in the concentration of anti-rubella virus antibodies IgG (0.633+0.050) than in control groups (0.411+0.02) as shown in figure (1) significant elevation (P<0.05) in the concentration of anti-rubella virus antibodies IgM (0.522+0.038) than in control groups (0.389+0.021) as shown in figure (2). In addition, there was significant elevation in the level of anti- chlamydia IgG (9.510 ± 0.502) than in the control group (5.417 ± 0.610) (P≤0.05) as shown in figure (3) and significant elevation in the concentration of anti-chlamydia IgM (9.513 ± 0.648) than in the control group (4.649 ± 0.582) (P≤0.05) as shown in figure (4).

On the other hand, there were 3(1.2%) positive results of anti-CMV antibodies by IF test compared with control groups as shown in figure (5).

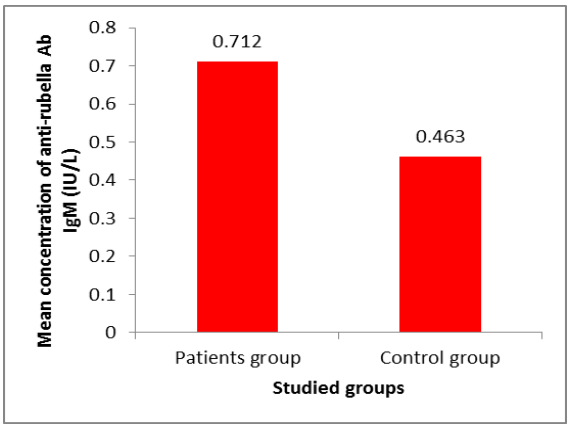

Figure 1: The concentration of anti-rubella virus Antibody IgG

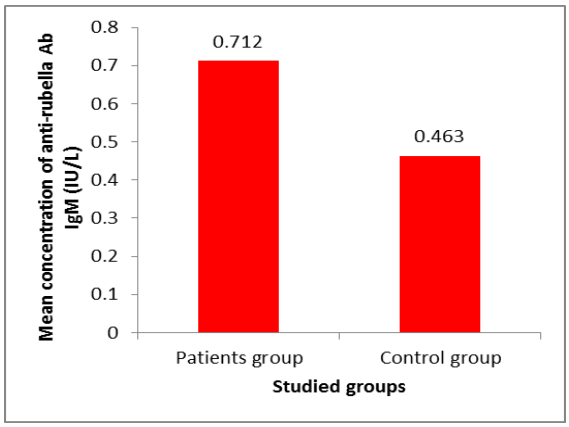

Figure 2: The concentration of anti-rubella virus Antibody IgM

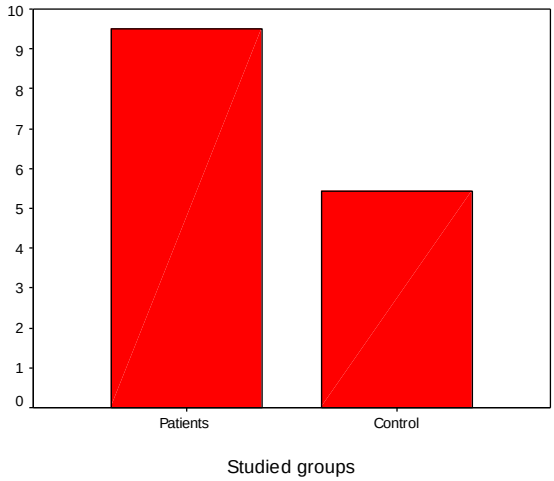

Figure 3: The concentration of anti-chlamydia antibody (IgG) in the sera of patients with diabetes mellitus.

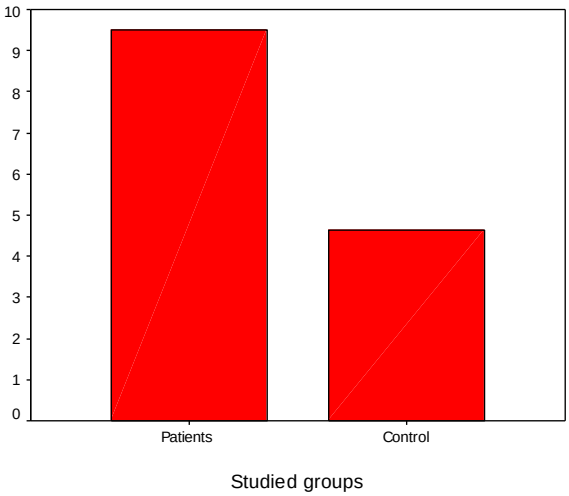

Figure 4: The concentration of anti-chlamydia antibody (IgM) in the sera of patients with diabetes mellitus.

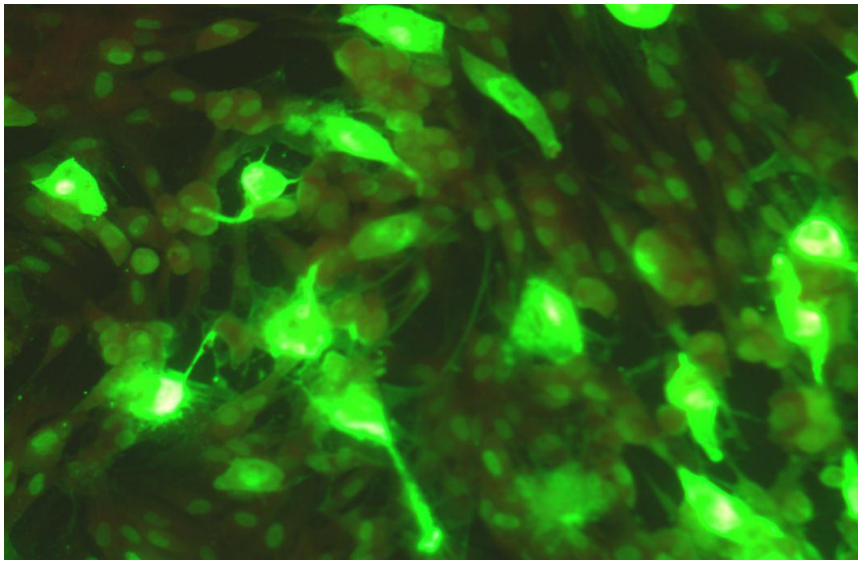

Figure 5: Positive results of anti-CMV antibodies by IF test

The results of the present study is in agreement with other studies, it has been implicated that TID as patients with congenital rubella syndrome (CRS) had a higher incidence of TID than the general population ,approximately 10-20% developing diabetes between the ages of 5-20 years [15], high incidence of subsequent onset of diabetes has been found among children previously afflicted with CRS, persistent rubella virus infection in the pancreas of patients with CRS has also been reported in some cases [16]. Rubella

virus appears to be able to directly infect B-cell, as shown by *in vitro* and *in vivo* studies. It is possible that the virus may insert, expose, or alter antigens in the plasma membrane of the infected host, the mechanism of rubella virus-induced diabetes is known [3]. Virus associated with diabetes in animals cause disease by directly lysing the B-cell, trigger an autoimmune response, specifically impairing secretory process of B-cell through a persistent infection [17]. Correlation between CMV infection and TID also has been found by studies using molecular biological methods. A study using both dot and in situ hybridization techniques showed that 20% of TID patients had CMV genomic DNA in their lymphocytes, compared to only 2% of normal controls [18]. It is possible that molecular mimicry may involve in some cases of CMV–induced diabetes. In this situation, immune responses against similar epitopes shared by antigenic determination of CMV and islet cell-specific protein may lead to islet cell-specific autoimmunity. Evidence for this is the finding that human CMV can induce an islet cell antibody that react with a 38 KD auto antigen expressed in human pancreatic islets [19]. Case reports from fatal CMV infections in children have shown that the pancreas may be a major target organ as CMV has been discovered in various types of pancreas cell [20], and characteristic inclusion bodies and virus Ag/ DNA/RNA have been detected in B-cell [21]. Thus, viral induction of apoptosis and pro inflammatory cytokines may have a pivotal role in the pathogenesis of both type1 and type-2 diabetes [22].

These results harmonized with other studies in which antibodies against *C. pneumonia* are present in more than 70% of the adult population and specific antibodies to *C. pneumoniae* have been found in more than half of the adult population [23]. Others revealed that asymptomatic infection with *C. pneumonia* is worldwide and surveys in various parts of the world have demonstrated that preexisting antibodies to C*. pneumonia* occur in 40-60% of the adult populations . Among them, recent study using PCR showed that *C pneumonia* was detected in 3.5% of samples of those positive for *C pneumonia***;** In contrast, in the control group, none of them was positive for *C pneumoniae* [24].

Numerous recent studies have demonstrated that type-1 and 2 diabetes mellitus is an independent risk factor for cardiovascular disease including coronary heart disease (CHD), myocardial infarction, stroke, and peripheral arterial disease. Since myeloperoxidase is an important neutrophilic mediator of oxidative stress; recent studies showed that its increase activity in the blood can be an additional marker of oxidative stress and cardiovascular risk in patient with diabetes mellitus [25].

The biological properties of both CMV and *C pneumoniae* are consistent with a potential role in the pathogenesis of atherosclerosis. However, our present results do not suggest a direct role for *C pneumonia* in the pathogenesis of atherosclerosis, while determining the *C pneumonia* specific antibody may be a valuable parameter in the management of patients with diabetes. From all these results lead us to suggest that *Chlamydia pneumonia*, CMV and rubella virus may trigger type-1 diabetes mellitus in Iraqi patients

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