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Serum immunoglobulin E is associated with glycated hemoglobin in human with diabetic mellitus

Parsian Heshmatolah*, Faraji Gholamreza, Zand Alireza, Imanzadeh Reza

Department of Physical Education and Sport Science, Shahre - e - Qods Branch, Islamic Azad University, Iran

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Abstract

Recent evidence suggests the importance of molecules secreted by mast cell in diabetes. This study's purpose was to determine whether serum *Immunoglobulin E* is associated with glycated hemoglobin and insulin resistance in human with diabetic mellitus. For this purpose, fasting serum *Immunoglobulin E*, glycated hemoglobin and insulin resistance were measured in forty five sedentary adult males (age 41±6 yrs, body weight 95±12 Kg) with diabetic mellitus. Pearson correlation coefficients were used to determine the associations between IgE with HbA1C and insulin resistance. A p-value less than 0.05 were considered statistically significant. A significant positive correlation was found between serum *Immunoglobulin E* with glycated hemoglobin (P= 0.000, r = 0.68). Serum *Immunoglobulin E* was also correlated positively with insulin resistance in studied patients (P= 0.000, r = 0.56). Based on high correlation in IgE with insulin resistance and HbA1C, It can be concluded that mast cell–related molecules can be affect pre-diabetes and diabetes mellitus, although more research is needed to further explore the physiopathological mechanisms underlying these associations.

***Corresponding Author:** Parsian Heshmatolah ✉ heshmatprasian@yahoo.com

Introduction

What is clear is that progressive deterioration of beta cell function leads to an inability to secrete sufficient insulin to compensate for insulin resistance in the pathogenesis of type 2 diabetes (Bergman *et al.,* 2002; Weyer *et al.,* 1999). In addition, it has been demonstrated that diabetes may result from a failure of appropriate signaling between insulin-responsive peripheral tissues and insulin secreting beta cells (Bergman *et al.,* 2002; Bergman *et al.,* 2002).

It is well known that diabetic is associated with hyperglycemia on increased glucose concentration. In fact, fasting glucose concentration in diabetic patients or peripatetic is significantly higher than those without diabetic symptoms. On the other hand, Glycated hemoglobin (HbA1C) reflects the mean glycemia over the preceding two to three months. Values are free of day-to-day glucose fluctuations and are unaffected by exercise or recent food ingestion (Bureau, 2010).

It is generally accepted that mast cells are essential components of asthma and allergic responses (heoharides *et al.,* 2006; Bradding *et al.,* 2006). On the other hand, a number of independent studies have indicated that these cells are important in diet-induced obesity and type 2 DM. Mice lacking mast cells or receiving the mast cell inhibitors cromolyn or ketotifen (Zaditor) are fully protected from developing type 2 Diabetic (Liu *et al.,* 2009).

In recent years, some clinical studies have reported, significant association between HbA1C and blood glucose levels or inflammatory or anti-inflammatory markers in obese or diabetic patients (Putz *et al.,* 2004). The researchers have noted that systemic inflammation is one precursor of type II diabetes as recent studies indicate the correlation between such determinants factors of systemic inflammation, as adiponectin *(*Goodarzi *et al.,* 2007*) or CRP (*Shatat *et al.,* 2009*)*. Also the role of markers secreted from mast cells like IgE has been previously reported in patients with chronic diseases or metabolic disorders (Liu *et al.,* 2009).

It was observed that Immunoglobulin E is associated with atopic disease and systemic anaphylaxis. However, its role in host defense, parasitic infection and immune surveillance suggest many other potential functions (Pate *et al.,* 2010). On the other hand, the strong correlation between IgE and inflammatory markers, which had been previously reported to associated with HbA1C in obese subjects or type II diabetic patients, has also reported in some other studies Eizadi *et la.*, 2011). Now the question is whether there is a correlation between HbA1C and IgE as an inflammatory mediator secreted from mast cells in patients with diabetes. Hence, the present study seeks to determine the relationship between these two variables in diabetic patients.

Materials and methods

Subjects

Participants included forty five sedentary adult men with diabetic mellitus (age 41±6 yrs, body weight 95±12 Kg). Given the range of BMI (30.66 ± 2.14 kg/m2) and body fat percentage (31.22 ± 2.53 %), participants were in obese category. In this study, we determined the relationship between serum IgE with HbA1C and insulin resistance in studied patients. After being informed on the nature of the experiment, written informed consent was obtained from all subjects.

Inclusion and exclusion criteria

Inclusion criteria were Type 2 diabetes diagnosis, obesity, failed dietary effort, stable body weight. All diabetic subjects had not participated in regular exercise for the preceding 6 months, nor did all subjects have stable body weight. All subjects were non-smokers. Presence of previous coronary cardiac disease, chronic airway disease, and impaired hepatic dysfunction and presence of any acute disease were determined as exclusion criteria.

Anthropometrical and biochemical measurements

Weight and height of the participants were measured by the same person when the participant had thin clothes on and was wearing no shoes. Body weight was measured in duplicate in the morning following

a 12-h fast. Height was measured on standing while the shoulders were tangent with the wall. Abdominal circumference and hip circumference were measured in the most condensed part using a non-elastic cloth meter. The Body Mass index (BMI) was calculated using the formula body weight/height2 in terms of kg/m². Body fat percentage was determined using body composition monitor (OMRON, Finland). Subjects were asked to attend Hematology Lab between the hours of 8 to 9 am. All blood samples were taken following an overnight 12-hour fast. Blood samples were collected in order to measuring serum IgE, HbA1C, glucose and insulin concentration. Insulin resistance was assessed using the homeostasis model assessment for insulin resistance formula derived from fasting insulin and glucose levels. Serum IgE was determined by ELISA method (Monobind Inc, CA 92630, USA). The Intra-assay coefficient of variation and sensitivity of the method were 5.87% and 1/0 IU/mL, respectively. The blood was centrifuged immediately and serum separated. Glucose was determined by the oxidase method (Pars Azmoun, Tehran, Iran). Serum insulin was determined by ELISA method (Demedite, German). The Intra- assay coefficient of variation and sensitivity of the method were 2.6% and 2.88 µg/L, respectively.

Table 1. The descriptive anthropometric and biochemical features of studied patients.

Variable	Mean	Standard deviation	Range
Age (years)	41	6	37 - 48
Weight (kg)	95	11	87 - 99
Height (cm)	176	9	168 - 182
Body mass index (kg/m²)	30.66	2.14	30 – 32.2
Body Fat (%)	31.22	2.53	29.14 – 33.21
Serum IgE (IU/mL)	127	71	27 - 375
HbA1C (%)	8.9	0.91	7.04 – 10.20
Insulin resistance (HOMA-IR)	5.31	0.78	3.46 – 6.87

Statistical analysis

Statistical analysis was performed with the SPSS software version 15.0. The Kolmogorov-Smirnov test was applied to determine the variables with normal distribution. The relationship between serum IgE with HbA1C and insulin resistance was analyzed by computing Pearson's correlation coefficient. A p-value of less than 0.05 was considered to be statistically significant.

Results

Anthropometric and metabolic characteristics of the study participants in studied patients are shown in Table 1. The data of Pearson's analysis showed that serum IgE concentration was positively related to HbA1c in diabetic patients (P= 0.000, r = 0.68, Fig 1). In addition, there was a strong, positive, linear relation between serum IgE and insulin resistance (P= 0.000, r = 0.56, Fig 2).

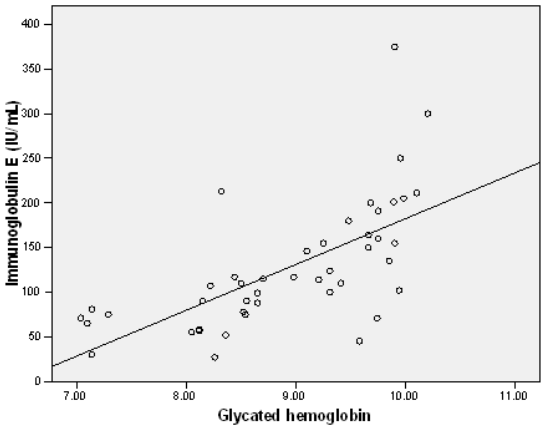

Fig. 1. The correlation pattern between serum IgE and HbA1c in studied patients.

Discussion

Our study finding showed that serum IgE was positively associated with HbA1c in type II diabetic patients. These finding demonstrate that increased serum IgE secreted by mast cells is associated with higher HbA1c or glucose concentration in this patients. Additionally, we observed a positive

significant correlation between serum IgE and insulin resistance in studied patients. Based on high correlation in IgE with insulin resistance and HbA1C, It can be concluded that mast cell–related molecules can be affect pre-diabetes and diabetes mellitus.

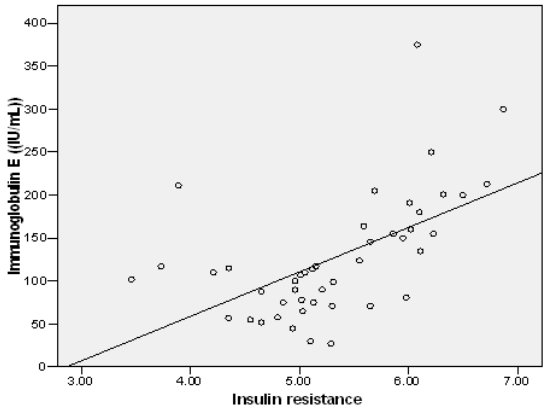

Fig. 2. The correlation pattern between serum IgE and insulin resistance in studied patients.

Scientific information from existing studies indicates that diabetes mellitus has become a problem of great magnitude and a major public health concern. Recent epidemiologic studies have demonstrated that, in some countries, diabetes affects up to 10% of the population aged 20 years and older. This rate may be doubled if those with impaired glucose tolerance (IGT) are also included (Alwan, 1994).

It is important to make a note here that IgE is one of the body's 5 classes (isotypes) of immunoglobulins (antibodies). It has been demonstrated that Circulating IgE levels are predominantly elevated in helminthic parasitic and allergic conditions (Winter *et al.,* 2000). A growing body of literature suggests that immunologic stimulus leading to degranulation of human mast cells is their activation when the IgE molecules on their surfaces bind a relevant antigen (Ishizaka *et al.,* 1984). It has been previously reported that IgE normally accounts for less than 0.001% of total serum immunoglobulin. Its concentration is age dependent and normally remains at levels less than 10 IU/ml in most infants during the first year of life (Anupama *et al.,* 2005).

According to The Diabetes Complications and Control Trial (DCCT), glycosylated hemoglobin (HbA1c) accepted as the gold standard of glycemic control, with levels £7% deemed appropriate for reducing the risk of vascular complications (Rohlfing *et al.,* 2002). Increased HbA1c has been regarded as an independent risk factor for coronary heart disease (CHD) and stroke in subjects with or without diabetes (Selvin[a] *et al.,* 2005; Selvin[b] *et al.,* 2005).

Close relationship between the levels of fasting blood glucose or HbA1c as an average of blood glucose in an interval of 2 to 3 months with serum or plasma levels of inflammatory markers has been reported repeatedly (Putz *et al.,* 2004). However, scientific sources suggest increased IgE levels in inflammatory diseases as well as its close relationship with other inflammatory markers in patients with respiratory diseases and some other diseases that have to do with metabolic disorders (Eizadi *et la.*, 2011). In our study, a significant correlation was observed between IgE with HbA1c and insulin resistance as two precursors of type II diabetes. In fact the findings of this study signify that increased insulin resistance and HbA1c in diabetic patients are associated with higher levels of IgE. Although the mechanisms accounting for the relationship between these variables in patients with diabetes or other inflammatory diseases has not been well identified so far and has been the focus of very few studies.

In accordance with these observations, several small human population studies reported an association between serum IgE levels and CHD. Our findings in line with previous studies, a nested case-control design and logistic regression analysis of 135 patients with CHD and 135 control subjects, serum IgE levels were higher in CHD patients than in control subjects (Erdogan *et al.,* 2003). The study by Wang et al (2011) provided the first evidence that increased plasma levels of mast cell proteases and IgE may serve as important risk factors for type 2 diabetic patients, particularly when hs-CRP or other common diabetes mellitus risk factors are considered (Wang *et al.,* 2011). Based on this data, it was concluded

that IgE may serve as biomarker for human type 2 diabetic.

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