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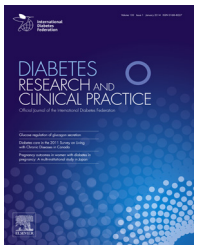

Serum levels of immunoglobulins in an adult population and their relationship with type 2 diabetes

Xiaoyan Guo [a,1], Ge Meng [a,1], Fangfang Liu [a], Qing Zhang [b], Li Liu [b], Hongmei Wu [a], Huanmin Du [a], Hongbin Shi [b], Yang Xia [a], Xing Liu [a], Chunlei Li [a], Xue Bao [a], Qian Su [a], Yeqing Gu [a], Liyun Fang [a], Fei Yu [a], Huijun Yang [a], Bin Yu [a], Shaomei Sun [b], Xing Wang [b], Ming Zhou [b], Qiyu Jia [b], Xin Chen [a], Guowei Huang [a], Kun Song [b], Kaijun Niu [a,b,*]

[a] Nutritional Epidemiology Institute and School of Public Health, Tianjin Medical University, Tianjin, China
[b] Health Management Centre, Tianjin Medical University General Hospital, Tianjin, China

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ABSTRACT

Objective: Some studies have found patients with diabetes had an impaired humoral immune response. Immunoglobulins provide key information on the humoral immune status. But few population-based studies comprehensively estimated the serum immunoglobulins concentration in type 2 diabetes (T2D). So we design a cross-sectional study to investigate the relationships between immunoglobulin levels and prevalence of T2D in a large-scale adult population.

Methods: A cross-sectional assessment was performed in 10,691 participants living in Tianjin, China. Type 2 diabetes was defined in accordance with the criteria of the world health organization, and serum levels of immunoglobulins were determined by the immunonephelometric technique. Adjusted logistic models were used to assess relationships between the quintiles of immunoglobulins concentration and the prevalence of T2D.

Results: In this study, the prevalence of T2D was 11.7%, and the means (standard deviation) of immunoglobulins (IgG, IgE, IgM, IgA) were 1192.3 (241.1) mg/dL, 92.3 (234.6) IU/mL, 104.8 (55.8) mg/dL, 234.1 (96.2) mg/dL, respectively. The adjusted odds ratio (95% confidence interval) of T2D for the highest immunoglobulins (IgG, IgE, IgM, IgA) quintile, when compared to the lowest quintile were 0.64 (0.52, 0.78), 1.00 (0.81, 1.22), 0.77 (0.62, 0.95) and 1.57 (1.29, 1.92), respectively.

Conclusions: Decreased IgG and IgM, and increased IgA levels were independently related to the prevalence of T2D among the adult population. Our findings indicate that the immunoglobulins might useful predictive factors for T2D in the general adult population. Further studies are needed to explore the causality and exact mechanisms of immunoglobulins in T2D.

* *Corresponding author at*: Nutritional Epidemiology Institute and School of Public Health, Tianjin Medical University, 22 Qixiangtai Road, Heping District, Tianjin 300070, China. Tel.: +86 22 83336613; fax: +86 2283336613.
E-mail addresses: nkj0809@gmail.com, niukaijun@tmu.edu.cn (K. Niu).
[1] Co-first author with equal contribution.

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1. Introduction

Diabetes is a multi-factorial group of disorders associated with an abnormality in glucose metabolism. It is characterized by metabolic abnormalities and long term complications involving the eyes, kidneys, nerves, vasculature, and periodontium [1]. Diabetes is a worldwide public health issue. The incidence and prevalence of diabetes (primarily type 2 diabetes (T2D)) has risen sharply since 1990 [2]. It has been estimated that the global prevalence of diabetes will be 7.7% (552 million people) by 2030 [3]. The increasing burden of T2D demonstrates an immediate need to elucidate the mechanisms underlying its pathophysiology of in order to implement preventative strategies.

The exact mechanisms leading to diabetes, however, remain unknown. Prior studies have focused on the relationship between the immune system and T2D [4]. Components of the immune system are disturbed in diabetes [5]. The immunological changes include altered numbers and activation states of various leukocyte populations and changes in specific cytokines and chemokines, such as interleukin (IL)-1β, tumor necrosis factor (TNF)-a and IL-6 [6–9]. In addition, patients with diabetes often exhibit increased susceptibility to infections like periodontal diseases [10,11].

Serum immunoglobulins levels are determined routinely in clinical practice because they provide key information on the humoral immune status. Immunoglobulins production is prototypical function of B cells, and immunoglobulins has important roles in multiple inflammatory diseases including lupus, rheumatoid arthritis and atherosclerosis [12–14], and now T2D is also considered as an inflammatory disease [5]. In mice with diabetes, glucose impaired B-1 cell function and the levels of immunoglobulins changed [15]. However, the lack of definitive evidence for an autoimmune component of T2D has limited interest in defining a role for antibodies in T2D. At present, we have designed a cross-sectional study to investigate the possible relationship between immunoglobulins and T2D.

2. Methods

2.1. Participants

Tianjin chronic low-grade systemic inflammation and health (TCLSIHealth) cohort study is a large prospective dynamic cohort study focusing on the relationship between chronic low-grade systemic inflammation and the health status of a population living in Tianjin, China [16,17]. Tianjin is a city of approximately 15.17 million inhabitants, located in the northeast of the North China Plain, facing the Bohai Sea [18]. Participants were randomly recruited, while taking routine preventive examination (annual physical examination) at Tianjin medical university general hospital-health management center, the largest and most comprehensive physical examination center in Tianjin. Nearly all occupations are covered in this study, and we also included retired individuals living in residential communities. So the sample population used here is representative of the general adult population in Tianjin. The protocol of this study was approved by the institutional review board of Tianjin medical university and all participants gave written informed consent prior to participation in the study. This study conforms to the strengthening the reporting of observational studies in epidemiology (STROBE) guidelines for cross-sectional study.

The TCLSIHealth data from 2010 to 2014 was used in this study. During the research period there were 12,093 participants who had received at least one annual physical examination including serum-immunological tests. We excluded participants who did not have data of IgG, IgE, IgM and/or IgA ($n = 600$), body height and/or body weight measurements ($n = 22$), or those with a history of cardiovascular disease (CVD) ($n = 660$) or cancer ($n = 120$). Owing to these exclusions, the final cross-sectional study population comprised 10,691 participants (mean [SD] age 51.1 ± 10.8 years).

2.2. Assessment of T2D

Fasting blood glucose (FBG) was measured by the glucose oxidase method using reagents from Roche diagnostics on an automatic biochemistry analyzer (Roche Cobas 8000 modular analyzer, Mannheim, Germany). Type 2 diabetes was defined in accordance with the criteria of the world health organization [19]. Participants were considered to have T2D when their FBG accorded with level of ≥7 mmol/L or physician-diagnosed diabetes and/or current use of antidiabetic medications.

2.3. Serum-immunological tests

Serum-immunological tests were measured as a health examination item. Serum levels of immunoglobulins (IgG, IgE, IgM and IgA) were determined by the immunonephelometric technique using the automated IMMAGE 800 immunochemistry system (Beckman Coulter, Brea, CA, USA), and expressed as mg/dL. The detection limit of the assay was: IgG 33.3 mg/dL, IgM 4.2 mg/dL, IgA 6.7 mg/dL, IgE 5 IU/mL; the measurement range was: IgM, 4.2–14,400 mg/dL, IgA 6.7–25,200 mg/dL, IgG 33.3–21,600 mg/dL, IgE 5–30,000 IU/mL. The manufacturer indicates the following reference intervals for healthy adults: IgM 46–304 mg/dL, IgA 82–453 mg/dL, and IgG 751–1560 mg/dL, IgE <165 IU/mL.

2.4. Assessment of other variables

Waist circumference was measured at the umbilical level with participants standing and breathing normally. Blood pressure (BP) was measured twice from the upper left arm using an automatic device (Andon, Tianjin, China) after 5 min of rest in a seated position. The mean of these 2 measurements was taken as the BP value. Blood samples for the analysis of lipids were collected in siliconized vacuum plastic tubes. Total cholesterol (TC) and triglyceride (TG) was measured by enzymatic methods, low density lipoprotein cholesterol (LDL-C) was measured by the polyvinyl sulfuric acid precipitation method, and high-density lipoprotein cholesterol (HDL-C) was measured by the chemical precipitation method using reagents from Roche diagnostics on an automatic biochemistry analyzer (Roche Cobas 8000 modular analyzer, Mannheim, Germany). White blood cell (WBC) counts were measured