

# Detection of Islet Cell Cytoplasmic Antibodies in First Degree Relatives of Type-1 Diabetic Patients

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## ABSTRACT

**Objectives:** To estimate the islet cell cytoplasmic antibodies (ICA) and insulin level in the sera of asymptomatic first degree relatives of patients with type 1 diabetes and compare with normal subjects.

**Design of study:** Cross sectional comparative study

**Data source:** First degree relatives of patient with diagnosed type 1 diabetes attending various hospitals in Lahore.

**Setting:** Department of pathology, postgraduate Medical Institute, Lahore.

**Methodology:** 120 subjects, 60 asymptomatic first degree relatives of type 1 diabetics (Group A) and 60 normal subjects were taken. The blood samples were collected in fasting state. 5 ml blood was collected and serum obtained was used for glucose, insulin and ICA antibodies estimation. Flu: results obtained from both groups were compared. Glucose was measured by Oxidase method, insulin level by ELISA method, and ICA by indirect immune fluorescence method by commercially available kits. The students t test was applied for glucose and insulin level while chi square test was applied for ICA to see the level of significance.

**Conclusions:** Islet cell cytoplasmic antibodies (ICA) are positive in 11 subjects (18.3%) of group A and 02 subjects (3.3%) of group B.

**Key words:** ICA, Type-1 diabetes, first degree relatives

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## INTRODUCTION

Type -1 diabetes develops as a result of the synergistic effects of genetic, immune, and environmental factors that eventually destroy the beta (B)-cells of the pancreas<sup>1,2</sup>. Subjects with a genetic susceptibility have normal B-cell mass at birth. They start losing cells secondary to auto immune destruction that takes place over months to years. This autoimmune process is considered to be triggered by environmental or infectious stimuli. The immunologic markers appear after the triggering event, B-cell mass begins to decline, and insulin secretion becomes progressively impaired.<sup>3, 4</sup> Features of diabetes do not become evident until a vast majority of B cells (80%), are destroyed. Residual functional B cells still exist but are insufficient in number to maintain glucose tolerance. The transformation of glucose intolerance to clinical diabetes is associated with periods of increased insulin requirements as might take place during puberty or infection<sup>5</sup>.

Islet cell antibodies (ICAs) are a composite of several different auto antibodies directed at pancreatic islets cell molecules such as insulin,

glutamic acid decarboxylase (GAD; the biosynthetic enzyme for neurotransmitter GABA), islet ganglioside, and ICAs 512/ IA-2 (homology with tyrosine phosphatases). ICAs can be detected by a fluorescent antibody technique which detects binding of antibodies to islet-cells. Much of this staining reaction is due to antibodies specific for ICA-512 and GAD. Insulin autoantibodies also appear in the circulation but do not contribute to the ICA reaction<sup>6,7</sup>. The most important antibodies are decarboxylase, islet cells cytoplasmic antibodies (ICA), insulin autoantibodies (IAA), and antibodies to glutamic acid decarboxylase anti-GAD<sup>8,9</sup>. Identification and characterization of the autoantibody- auto antigen system in Type 1 DM is of crucial and fundamental importance in prediction and potential immunotherapy.

## METHODOLOGY

The study was performed on 120 subjects, Group A Included 60 subjects of first-degree relatives of patients of Type-1 Diabetes who have suffered at least one episode of Diabetic Ketoacidosis. Group B Included 60 asymptomatic first degree relatives of non Diabetics. The blood sample was collected in fasting state. 5 ml of blood was collected and serum thus obtained was used for glucose, insulin and ICA antibodies estimation.

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## RESULTS

Details of fasting glucose, insulin and ICA antibodies were given in tables 1 - 3.

Table 1: Fasting glucose level in group A and B

Fasting glucose(mg/dl)	Group A	Group B
Mean $\pm$ SD Value	70.27 $\pm$ 15.42	66.1 $\pm$ 14.89
Ranges	46–112	48 - 86

**Statistical Analysis:** A Vs B=P > 0.05 (Non-Significant)

Table 2: Fasting insulin level in group A and B

Fasting Insulin ( $\mu$ U/ml)	Group A	Group B
Mean $\pm$ SD Value	4.21 $\pm$ 0.611	4.97 $\pm$ 0.631
Ranges	0.5–7.0	1.5–8.0

**Statistical Analysis:** A Vs B =P > 0.05 (Non-Significant)

Table 3: Islet cell cytoplasmic autoantibodies (ICA) in group A and B

Groups	+ve Cases	-ve Cases	Total
Group A	11(18.3%)	49(81.7%)	60(100%)
Group B	02(3.3%)	58(96.7%)	60(100%)

**Statistical Analysis:** A Vs B=P < 0.01 (Significant)

Group A=First degree relatives of patients with type 1 diabetes

Group B=Asymptomatic first degree relatives of non-diabetics.

## DISCUSSION

Out of 60 subjects in group A, 11 (18.3%) subjects are positive for Islet cytoplasmic autoantibodies while in group B, only 02 (3.3%) subjects are positive for Islet cytoplasmic auto antibodies. The comparison between group A and B showed significant difference statistically ( $p < 0.01$ ). This study is in favour of the results of Sacks (2001)<sup>8</sup>, Clarke(1991)<sup>11</sup>, Gale and Anderson<sup>6</sup>, Powers<sup>12</sup> and Shranz (1998)<sup>13</sup> who also observed similar changes.

The concept of an autoimmune pathogenesis for IDDM is supported by the observation that patients who die shortly after the onset of the disease often exhibit an infiltrate of mononuclear cells in and around the islets of Langerhans, termed insulinitis. Among the inflammatory cells, CD8<sup>+</sup> T lymphocytes predominate, although some CD4<sup>+</sup> cells are also present. The infiltrating inflammatory cells also elaborate cytokines, for example, IL-1, IL-6, interferon- $\alpha$ , and nitric oxide, which may further contribute to the pathogenesis of B cell injury<sup>14</sup>. An autoimmune origin for IDDM was initially suggested by the demonstration of circulating antibodies against components of the B cells of the islets (Including insulin itself) in most newly diagnosed children with diabetes. Many of these patients develop islet cell antibodies months or years before the production of insulin by the islets decreases and clinical symptoms appears, a clinical state known as "Prediabetes". However, these antibodies are regarded as a

response to the B-cell antigens released during the destruction of B cells by cell-mediated immune mechanisms, rather than the initial cause of B-cell depletion. The detection of antibodies to islet cells and islet antigens (GAD-65, ICA-512, insulin, etc.) in a blood sample is a useful tool for establishing the diagnosis of type 1 diabetes (Martin et al 2001)<sup>15</sup>.

**Conclusions:** Islet cell cytoplasmic antibodies (ICA) are positive in 11 subjects (18.3%) of group A and 02 subjects (3.3%) of group B.

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