RETINOPATHY AMONG PREDIABETES: IMPAIRED FASTING GLUCOSE, IMPAIRED GLUCOSE TOLERANCE (IFG, IGT) and Recent type 2DM

THESIS

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ABSTRACT

Objective: The aim of the work is to study retinopathy in prediabetic patient impaired fasting glucose (IFG), impaired glucose (IGT) and recent onset type 2DM.

Research and method: The study was conducted to patients with impaired glucose tolerance, impaired fasting glucose with no history of diagnosed diabetes other than gestational diabetes not persisting after pregnancy , recent onset type 2 diabetes and normal controls. They subjected to history taking and BP measurement

- fasting and 2hrs post prandial glucose.
- Lipid profile
- HbA1C

Results: Retinopahty consistent with diabetic retinopathy was detected in 6.7% of the prediabetic 4% patients of IFG, 6% patients of IGT and 10% patients of recent type 2DM. Systolic blood pressure and HbAlc were higher at baseline in the diabetic participants who had retinopathy than those with the diabetic participants without retinopathy.

Conclusions: Retinopathy characteristic of diabetes is present in persons with elevated fasting glucose, impaired glucose tolerance with no known history of diabetes and recent type 2DM. The prevalence of retinopathy is significantly higher in persons who develop diabetes, even within years of diagnosis.

Keyword: Impaired fasting glucose (IFG), impaired glucose tolerance (IGT), retinopathy, Type 2 diabetes.

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List of Abbreviations

BMI	**:**	**Body mass index**
CIR	**:**	**Corrected insulin response**
DCCT	**:**	**Diabetes control and complications trail**
DPP	**:**	**Diabetes prevention program**
DPPOS	**:**	**Diabetes prevention program outcomes study**
DR	**:**	**Diabetic retinopathy**
ETDRS	**:**	**Early treatment of diabetic retinopathy study**
GDM	**:**	**Gestational diabetes mellitus**
HDL	**:**	**High-density lipoprotein**
IGT	**:**	**Impaired glucose tolerance**
IRMA	**:**	**Intra-retinal microvascular abnormalities**
LDL	**:**	**Low-density lipoprotein**
NIDDK	**:**	**National institute of diabetes and digestive and kidney diseases**
NPDR	**:**	**Non-proliferative diabetic retinopathy**
OGTT	**:**	**Oral glucose tolerance test**

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INTRODUCTION

Retinopathy is considered the complication most closely associated with and characteristic of diabetes mellitus. Hyperglycaemia below levels diagnostic of diabetes, so called pre-diabetes, is associated with a low prevalence of diabetic retinopathy. However, few longitudinal studies of non-diabetic populations have performed repeated measures of glycaemia and screened for retinopathy to determine its occurrence in the non-diabetic population and the onset of retinopathy in new-onset diabetic patients. The prevalence of retinopathy characteristically seen in diabetes in persons with impaired glucose tolerance and in patients with new-onset diabetes of known duration in the Diabetes Prevention Program (DPP) cohort was found in prediabetics and recent type 2 DM patients ***(Boston et al., 2007)***.

The microvascular complications that accompany diabetes mellitus are sufficiently specific to diabetes that they have been utilized to establish the levels of hyperglycemia, the defining of diabetes, that are diagnostic for the disease (**Expert Committee on the Diagnosis and Classificaton of Diabetes Mellitus**, **2003**). This Expert Committee on the diagnosis and classification & diabetes identified levels of glycemia, both fasting and 2h after an oral glucose test, that were associated with retinopathy in epidemiological studies (**Engelgau**, **1997**).

Fasting and 2-hrs glucose levels 7.0 and 11.1mmol/L, respectively, have been and adopted as diagnostic these holds on the basis of these and other studies, glucose levels less than the diagnostic levels are considered to be either pre-diabetic (fasting 5.6-6.9 mmol/l or 2h , 7.8-11.0 mmol/l) or if lower normal of the micro-vascular complications, retinopathy was

selected owing to large volume 6 cross sectional data available from several studies and the ability to detect lesions objectively with photography. (**American Diabetic Association, 2008**)

The major importance of these diagnostic levels, based on risk for developing retinopathy, is twofold. First, the cut – points selected determine whether an individual is diagnosed as having diabetes or not and whether interventions are applied. Second, appreciating the time course of the development of retinopathy determines when was begin screening for it with regular ophthamological examinations.

Relatively few studies have measured the occurrence of (diabetic) retinopathy in non-diabetic populations (**Egelgau, 1997 , Yu et al., 1998 and Wong et al., 2003),** and only one study, in Pima Indians, has carefully screened (non-diabetic) populations overtime to ensure that they are in fact non-diabetic (**Nagi**, **1997**). The relationship between subdiabetic levels of glycemia and retinopathy therefore remains unclear.

Aim of the Work :

The aim of the work is to study retinopathy in impaired glucose tolerance (IGT), impaired fasting glucose (IFG) and recent onset type 2DM and try to find correlations between the presence of retinopathy with blood pressure, HBA1C and lipid profile of these patients.

DIABETES MELLITUS

Diabetes Mellitus "DM" is a metabolic disorder characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both. The chronic hyperglycemia of diabetes is associated with long term damage, dysfunction and failure of various organs especially the eyes, kidneys, nerves, heart and blood vessels ***(American Diabetes Association (ADA, 2008)***.

Over 246 million people live with diabetes across the world and 4.4 million of those people live in Egypt. Egypt is currently in the Top 10 countries with the highest number of people with diabetes and will remain so as 7.6 million Egyptians will have the disease by 2025 ***(International Diabetes Federation, 2008)***.

On the other hand, taking USA as one of the developed countries, it is estimated that 23.6 million people, i.e., 7.8% of the U.S. population, have diabetes. Another, 5.2 million people are estimated to have undiagnosed type 2 diabetes It is the sixth leading cause of death (National Institute of diabetes and Digestive and Kidney Diseases ***(NIDDK, 2008)***.

The incidence of both type 1 and type 2 DM has a considerable geographic variations; its is higher in developing countries than in developed countries. DM prevalence also varies among different ethnic populations within a given country. This variability is likely due to genetic, behavioral, and environmental factors ***(Wild et al., 2004)***.

Type 2 DM is the predominant form of diabetes world wide accounting for 90-95% of cases globally. The prevalence of type 2 DM

is expected to rise more rapidly in the future because of increasing obesity and reduced activity levels ***(Kasper et al., 2005)***.

Classification of Diabetes Mellitus:

Improved understanding of the origin and pathogenesis of diabetes has made it possible to revise the classification of diabetes mellitus. This revision contrasts with the previous classification, which was based mainly on therapeutic requirements: insulin-dependent diabetes (IDDM) and non-insulin-dependent diabetes (NIDDM), terms that have been eliminated

Any patient with diabetes may require insulin therapy at some of the disease, -irrespective of the classification. So the recent classification of diabetes depends on the etiology not the pharmacological treatments of the attained types ***(Philip et al., 2001)***.

Etiologic classification of diabetes mellitus:

1- Type 1 diabetes mellitus:

There is B-cell destruction usually which leads to absolute insulin deficiency. It is of two types:

A- Immune mediated.

B- Idiopathic.

2- Type 2 diabetes mellitus:

May range from predominantly insulin resistance with relative insulin deficiency to predominantly secretory defect with insulin resistance.

3- Other specific types:

A- Genetic defects of B-cell function:

Characterized by onset of hyperglycemia at an early age (generally before age 25 years). They are referred to as maturity - onset diabetes of the young (MODY) and are characterized by impaired insulin secretion with minimal or no defect in insulin action. They are inherited in an autosomal dominant pattern. The most common form is associated with mutation on chromosome; 12 in hepatic transcription factor referred to as n hepatocyte nuclear factor (HNF). A second form is associated with mutation in the glucokinase gene on chromosome 7 and insulin promoter factor (IPF)-l. Mutations an mitochondrial DNA have been found to be associated with diabetes mellitus.

1- Chromosome 20 HNF - 4 α (MODY 1).

2- Chromosome 7 glucokinase (MODY 2).

3- Chromosome 12 HNF-1 α (MODY 3).

4- Mitochondrial DNA.

5- Others.

B- Genetic defects in insulin action:

These are unusual causes of diabetes that results from genetically determined abnormalities of insulin action. The metabolic abnormalities associated with mutations of the insulin receptor may range from hyperinsulinemia and modest hyperglycemia to severe diabetes.