Diabetic Retinopathy: Association with Type and Duration of Diabetes Mellitus, Mode of Treatment and Glycaemic Control

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Abstract

Objective: To assess the association of Diabetic Retinopathy (DR) with type and duration of Diabetes Mellitus, mode of treatment and glycaemic control.
Methods: An observational study was carried out. Patients with the diagnosis of either Type1, insulin dependent diabetes mellitus (IDDM) or Type 2, non-insulin dependent diabetes mellitus (NIDDM) were enrolled into the study through non-probability, convenient sampling method from Jinnah Medical College Hospital Karachi from July 2012 to March 2013. Thorough history and physical examination was done on each patient. Glycaemic control was assessed by glycosylated Hb level (HbAIc). All information so collected was entered into a proforma. Data was analyzed using SPSS version 20.
Results: A total of 108 patients were examined. Out of these, 33 (30.6%) had Type 1 and 75 (69.4%) had Type 2 diabetes. In Type 1 group, 18 (54.5%) were female while in Type 2 group, 37 patients (49.3%) were female.
In Type 1 group, 60.6% (n=20) had DR compared to 37.3% (n=28) in Type 2 group ($p < 0.005$). DR. was seen less frequently in subjects with less than five years duration in both the groups i.e. 12.6% in Type 1, and 15.7% in the Type 2 group. This increased to 100% ($p<0.001$) in Type 1, and 77.7% ($p<0.02$) in the Type 2 group with a duration of over 20 years of diabetes.
In patients on insulin therapy, 60.6% in Type 1 group and 53.1% subjects in Type 2 had DR. In Type 2 group, 25.6% subjects on oral hypoglycaemics and/or diet therapy had DR. None of the subjects in both groups with HbA1c <7% had any evidence of DR.
Conclusion: The frequency of DR. is higher in patients with Type 1, than those with Type 2, in patients receiving insulin therapy and with long duration of diabetes. Higher levels of HbA1c have clear relationship with development of DR.
Keywords: Diabetes mellitus, Diabetic retinopathy, HbA1c (AASH & KMDC 18(2):86;2013).

Introduction

At least 366 million people worldwide have diabetes at present, and this number is increasing as a result of an aging global population, urbanization, a rising prevalence of obesity and sedentary lifestyle[1].

Diabetes has various microvascular and macrovascular complications. Retinopathy, among the microvascular complications, is one of the major causes of morbidity in long standing diabetes. In the developed world Diabetic Retinopathy (DR) remains the leading cause of blindness and vision loss among adults aged less than 40 years[2]. Population based studies suggest that about one third of the diabetic population have signs of DR and approximately one tenth have vision threatening stages of retinopathy such as Diabetic Macular Edema (DME) and Proliferative Diabetic Retinopathy (PDR) [3,4,5].

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pproximately 700,000 persons in the United States have PDR, with an annual incidence of 65,000. A recent estimate of the prevalence of DR in the United States showed a high prevalence of 28.5% among those with diabetes aged 40 years and older[6].

Some factors identified in cross-sectional and longitudinal studies are associated with a higher risk of DR. These include hyperglycaemia, hypertension, dyslipidaemia, duration of diabetes, pregnancy, puberty, and cataract surgery[3]. Despite the importance of glycaemic control in diminishing the progression of DR, intensive glycaemic control appeared to increase mortality among participants in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial which raises concerns over the care of persons with type-2 diabetes who are at high risk of cardiovascular events[7].

Recent evidence from the Atherosclerosis Risk in Communities (ARIC) study suggests that the risk of developing CVD increased twofold, with the presence of DR[8]. Thus, there seems to be an overlap of risk factors between CVD and DR highlighting the need for close collaboration between diabetologists and ophthalmologists.

Recognizing the importance of diabetic retinal imaging, several countries have implemented national screening programs such as the National Plan for Screening in the United Kingdom and the Opthalmological Diabetes Telemedical Network (OPHDIAT) program in France. The OPHDIAT comprises 11 screening centers equipped with non-mydriatic cameras. Fundus photographs are acquired by technicians, with remote interpretation by ophthalmologists who grade the images. In 28 months, 15,307 DR screening examinations were performed, and DRwas detected in 3,350 patients (23.4%)9. The rates of DR screening found to have improved from 50% before to more than 70% after the implementation of OPHDIAT[10-11].

The Wisconsin Epidemiologic study of Diabetic Retinopathy (WESDR) is one of the largest studies documenting the natural history of retinal disease in diabetics which showed that the prevalence of DR increased progressively in patients with both type 1 and type 2 (IDDM and NIDDM) with increasing duration of disease[12]. The duration of diabetes is probably the strongest predictor of progression to DR[13].

Finally, as telehealth and telemedicine programs are implemented worldwide, the role of primary care providers may become even more encompassing, as screening retinal photographs may be obtained directly in the primary care office, and, perhaps in the future, primary care providers may even be trained to evaluate retinal photographs[14].

Severe DR is associated with increased mortality which was demonstrated by Rajala U et al. who showed increased odds ratio for death during 4 years of follow up[15].

Accurate data concerning the prevalence and severity of retinopathy and associated risk factors are of importance in planning a well co-ordinated approach to the public health problem posed by this complication. Identifying who may be at risk of retinopathy is important in advising diabetic care and with early detection it is possible to prevent or slow down the further progress of disease by time honored management. We, therefore, planned to study the salient features of diabetic retinopathy in our population in order to help the physicians to have a better understanding of the disease and its application in the clinical setting.

Patients and Methods

We conducted this study at the diabetic clinic of Jinnah Medical College Hospital - Karachi from July 2012 to March 2013. This was an observational study with non-probability convenience sampling method. We included patients of both genders, over 14 years of age with the diagnosis of either Type 1 or Type 2 diabetes, for duration of more than one year.

We excluded those diabetic patients who had other comorbids like severe anaemia, hypertension, renal disease or any ophthalmological disease other

than diabetic retinopathy which could interfere with the fundoscopic findings or the HbA1c level. Also excluded were the patients who were noncompliant to the prescribed therapy.

Detailed history and physical examination was done on every patient including fundoscopic examination by a trained ophthalmologist. Glycaemic control was assessed by the glycosylated Hb level (HbA1c) which was done in all participants by using plasma adrenomedullin assay technique on ELISA.

The acquired data was entered on an especially designed performa. The results were analyzed on SPSS version [20]. Statistical significance was determined with p-value < 0.05.

Results

A total of 108 patients were included in the study. Out of these patients, 33 had Type I diabetes while 75 had Type 2 diabetes. Among Type 1 patients, more females were seen (54.5%) while in Type 2 group, subjects had equal gender distribution with male to female ratio of 1:1.

Patients with Type 1 were found to be relatively younger with mean age of 42 ± 15.9 years (range 14-60 years) as compared to Type2 where mean age was 69 ± 6.8 years (range 32-74 years). All patients with Type 1 were on insulin therapy since the time of diagnosis. Among Type 2 subjects, 32 patients were receiving insulin therapy while 43 patients were on oral hypoglycaemic agents and/or dietary therapy.

Seventeen (51%) patients of Type 1, IDDM had disease of 10 years duration while among Type 2, relatively more i.e., 42 (56%) subjects had disease of 10 years.

Assessment of glycaemic control was done through HbA1c level. Sixteen (48 %) of Type 1, patients had poor glycaemic control with HbA1c of >10 % (p<0.001). Among Type 2, subjects, 15 (46.9%) patients on insulin therapy had poor glycaemic control in comparison to 9 (20.9%) patients who were on treatment with oral hypoglycaemic agents and/or dietary therapy (p <0.001). Levels of glycaemic control were graded as excellent, good, fair and poor in accordance with established standards published in literature[7](Table 1).

Fundoscopic examination revealed evidence of retinopathy in 20 (60.6%) out of 33 patients with

Table 1. Association of Mode of therapy with glycaemic control

Glycaemic Control	% of patients Type 1group n=33	% of patients Type2 group on insulin therapy. n=32	% of patients Type2 group on oral hypoglycaemic agents n=43
Excellent	6	6.2	11.6
Good	18.2	21.9	41.9
Fair	27.3	25	25.6
Poor	48.1	40.9	20.9

Table 2. Frequency of Diabetic Retinopathy according to Type and Mode of Treatment.

Type of diabetes	Total patients (n)	Retinopathy (n)	%
	Type 1 Diabetes		
Type1	33	20	60.60
	Type 2 Diabetes		
Patients on insulin therapy	32	17	53.10
Patients on Oral hypoglycemic therapy	43	11	25.60
Total patients	108	48	44.40

Type 1, in comparison to 28 (37.3%) out of 75 patients in the Type 2 group. Of the Type 2 patients, 17 (53.1%) were on insulin therapy while 11 (25.6%) were receiving oral hypoglycaemic agents and/or dietary therapy.

It was also found that diabetic retinopathy was more frequent in extended duration diabetes irrespective of the type of diabetes. All patients with Type 1 diabetes of over 20 years duration of diabetes had retinopathic changes ($p<0.001$) while this was much lower in Type 2 patients in whom only 77.7% of patients with diabetes for more than twenty years had retinopathy ($p<0.02$).

An important finding was that no subject of Type 1 having HbA1c < 7 % had retinopathy. In contrast, 14 (87.5%) Type 1 patients having HbA1c of more than 10 % suffered from this complication ($p<0.01$). Same results were obtained in both subsets of Type 2 diabetics i.e. 86.6% and 66.7% in insulin treated and oral hypoglycaemic treated subjects respectively with poor glycemic control (HbA1c > 10 %) had some evidence of diabetic retinopathy and none with HbA1c < 7 %. DR was found to be more in Type 2 diabetes when treated with insulin as shown in Table 2.

Discussion

Incidence of DR has increased progressively and is now considered to be the major cause of blindness among the persons of working age group[2]. This increase could be due to the changes in the life style resulting in a rise in the incidence of diabetes mellitus. The prevalence of DR is influenced by type and duration of diabetes, mode of treatment and overall glycaemic control as well as presence of other co-morbids16. Our study revealed that frequency of DR is higher in cases of Type 1, as compared to Type 2, (60% versus 37%). This fact is supported by international data as well. Henricsson et al showed that 64% of Type 1 patients had DR17. In Type 2, we observed that 37.3% of patients had DR ($p< 0.005$) which is in agreement with 36% of Henricsson et al.[17] and slightly higher than 27.5% of Romero- Aroca study18.

Highest preponderance of DR in females i.e., 54.5% was found in the Type 1 group, while equal gender predilection was seen in the Type 2 group in our patients. This is supported by a study done at Bahawalpur which showed similar results irrespective of the type of diabetes [19] and opposed by the data of Naeem MK et al and Pradeepa R et al[20-21].

Another important outcome of the present study was the finding that DR was more frequent in insulin treated patients. In the subset of patients with type II diabetes treated with insulin, 53.1% developed DR as compared to patients on oral hypoglycaemics. Overall, 65(60.1%) patients were receiving insulin therapy in both Type 1 and Type 2. Out of these, 37(56.9%) suffered from DR.

We found that frequency of DR was 12.6% in patients with Type 1, of less than 5 years duration which was similar to the results of Henricsson et al. which showed a frequency of 16% in similar group of patients[17]. International data showed that frequency of DR increased sharply between 5 and 10 years of DM and after 15 years duration, 90.5% of patients had some evidence of DR. In our study, DR was present in all patients with long standing diabetes of over 20 years duration. This is consistent with observations made by Goldstien et al. who showed a prevalence of 100% but higher than 82% in the EURODIAB study[22,23]. In addition Karamanos et al. showed that microvascular complications were lesser in subjects who had better glycaemic control[24].

In Type 2, DR was present in 17.7% patients with less than 5 years duration and reached up to 77.7% in patients having diabetes of over 20 years duration ($p<0.02$). These figures are consistent with 16% and 72% respectively of Henricsson et al. [17].

In 1976, Cahill wrote that the weight of evidence strongly supports the concept that the microvascular complications of diabetes are decreased by reduction of glucose concentrations[25]. Evidence for the link between poor glycaemic con-

trol and greater progression of diabetic retinopathy was provided by many researchers [26-28]. Similar to the study conducted by Monique SR et al. our study showed that poor glycaemic control led to the development of DR in 87.5% patients diagnosed with Type 1, and 86.6% patients in the Type 2 group, which was reflected by high values of HbA1c[16]. The Chennai Urban Rural Epidemiology Study (CURES) conducted by Pradeepa R et al. showed that male gender, duration of diabetes, glycosylated haemoglobin (HbA1c) and insulin therapy were significantly associated with severity of DR. This strong association was also seen in other study groups[21].

The study was done at a suburb of Karachi, where previously this work was not done, and it endorsed the findings of previous studies. The study may help to increase the awareness regarding DR among physicians and diabetologists. However, due to small sample size the results can not be applied over the general population, hence, larger scale studies are required to document the relationship of these risk factors with diabetic retinopathy.

Conclusion

This study has identified that DR is found to be more frequent in patients who had Type 1 diabetes, and were on insulin therapy, irrespective of the type of diabetes. Also a clear relationship was found with prolonged duration of diabetes and poor glycaemic control.

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