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Prevalence of Retinopathy Detected by Fundoscopy among Newly Diagnosed Type 2 Diabetic Patients Visiting a Local Hospital in Lahore

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ABSTRACT

The cross-sectional study was conducted on 200 newly diagnosed diabetic patients to assess the prevalence of diabetic retinopathy and to evaluate its relationship with potential risk factors of diabetes on their first visit to a local hospital. Among the newly diagnosed diabetic subjects 33% (n=66) were with retinopathy. Out of which 30% (n=18) were male and 70% (n=48) were female. High density lipoprotein (HDL), both systolic and diastolic blood pressure, cholesterol level and serum insulin were significantly higher ($p< 0.05$) in proliferative group of diabetic retinopathy, while triglyceride level, HbA1c (%), and low density lipoprotein (LDL) were non-significantly higher ($p> 0.05$) in diabetic retinopathy groups. To conclude high prevalence of diabetic retinopathy was observed among newly diagnosed diabetic patients.

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Authors' Contributions
TF conceived and designed the project. MZ executed experimental work. SS and TF compiled the results and wrote the article. SN and FM analyzed the data.

Key words
Fundoscopy, Retinopathy, Proliferative, BDR, Type 2 diabetes.

INTRODUCTION

An increase in the incidence and prevalence of diabetes mellitus and its complications have been observed in recent decades (Kollias and Ulbig, 2010). In Pakistan according to the National Health Survey the prevalence of impaired glucose tolerance (IGT) and diabetes among the population age >25 years, is 22.4% (Shera *et al*., 2010). Diabetic patients are also susceptible to acute and chronic complications such as retinopathy (Wild *et al*., 2004). Diabetic retinopathy (DR) is a microangiopathy of the retina, in which the visual acuity is lost when the area of the sharpest vision on the retina is affected severely by the pre or intraretinal hemorrhages, macular edema, retinal tractional and detachment, or due to loss of capillaries of the peripheral loop network (Kollias and Ulbig, 2010). In the USA, an estimated 40% (8% for vision-threatening retinopathy) of people with type 2 diabetes and 86% (42%) with type 1 diabetes have DR (Kempen *et al*., 2004; Roy *et al*., 2004). The low prevalence rates of DR have been reported in some developing countries *e.g.,* India (17%) (Rema *et al*., 2005; Raman *et al*., 2009). In South East Asia, data from Singapore showed that 34% of Asian Malay adults with diabetes had signs of retinopathy and 10% had vision threating retinopathy (Wong *et al*., 2008). In Pakistan the overall DR prevalence is 15.3% (Shaikh *et al*., 2008). Background diabetic retinopathy is named appropriately because it sits in the background, not itself a danger to vision, but is instead a warning sign that serious damage may be starting (Watkins, 2003). In non-proliferative DR, the outward ballooning of the capillary wall occurs which is also known as micro aneurysms. They are detected by opthalomoscopy. The pre-proliferative stage, which is characterized by worsening of retinal ischemia, lead to formation of new vessels (neo-vascularization). It is characterized by the presence of one of the following: Multiple large dark blot hemorrhages, multiple (more than 5) cotton wool spots appearing as dead white patches with vague margins and representing micro-infarcts in the nerve fiber layer, Venous bleeding, looping, duplication and intraretinal micro-vascular abnormalities (IRMA).In proliferative diabetic retinopathy (PDR), the diffusion of the capillary bed becomes more severe and spread across the retinal-area. There are several risk factors, which are responsible for the occurrence and progression of diabetic retinopathy. The basic risk factors are hypertension, duration of disease and quality of glycemic control, hyperlipidemia, HbA1c level, and surgery for premature cataracts in diabetic patients (Wong and Mitchell, 2007; Kollias and Ulbig, 2010). Insulin is an important anabolic hormone which stimulates the proliferation of vascular endothelium, so insulin resistance is also an important risk factor for its proliferation. Type 2 diabetes usually remains asymptomatic before the onset of frank diabetes and its clinical diagnosis. The current study aimed to evaluate the prevalence of DR at the time of clinical diagnosis of diabetes mellitus because microvascular complications are directly related to the duration of diabetes mellitus, and

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early detection of retinopathy is an important preventative strategy for the visual impairment in diabetic patients on their visit first to a diabetic centre. In the UK Asian diabetes study researchers showed that after controlling for retinopathy risk factors people with a south Asian origin were more likely to have diabetic retinopathy than were white people (Raymond *et al*., 2009).

The basic aim of this study was to find the DR prevalence and evaluate the potential risk factors including blood pressure, HbA1c, lipid profile serum insulin and insulin resistance in the progression of DR among newly diagnosed type 2 diabetic subjects.

MATERIALS AND METHODS

This cross-sectional study was conducted on 200 newly diagnosed diabetic subjects from January 2010 to June 2010 who visited the Amin-Hayyat Memorial Trust Hospital first time. It is an outpatient diabetic clinic for low income people. Impaired glucose tolerance (IGT) and hyperglycemic state remained undiagnosed for a long period when they first visited the hospital, the retinopathy condition was diagnosed. During the study period 250 subjects were diagnosed as hyperglycemic on the basis of American Diabetic Association criteria as for FBG > 126mg. They were informed verbally to visit the clinic after 12 h fast for detailed checkup. Out of the 250 subjects 200 were responders and 50 were non-responders who refused to eye examination and blood test. All the subjects in the study completed a questionnaire that included information about the subject's age, personal habits (smoking or alcohol consumption), family history of diabetes and socioeconomic status. They all belonged to a low socioeconomic class. Biochemical laboratory tests were performed, included both fasting and random blood glucose levels, lipid profile and HbA1c by using Hitachi 902 biochemical analyzer and insulin resistance was calculated by HOMA IR. A consultant ophthalmologist of the hospital carried out detailed eye examination by using Top con Ophthalmoscope. DR was diagnosed on the basis of presence of lesions like micro-aneurysms, clinically significant macular edema, venous bleading and occasional dot blot hemorrhages. The presence of retinopathy was assessed by fundoscopy after dilating the pupil. DR was clinically graded according to the retinopathy disease severity scale (Wilkinson *et al*., 2003) as: i) No abnormality and no apparent retinopathy (Normal); ii) increased vascular permeability (BDR); iii) Pre-proliferative stage (Aneurism) and iv) Proliferative stage (Neovascularization, Multiple Hemorhages).

Monobind insulin ELISA kit was used for the quantitative determination of insulin in human serum.

Statistical analysis

The mean ± SEM values of demographic and biochemical parameters of each group was calculated. The difference between the groups and with in the groups was done by ANOVA followed by Tukey test. All the statements of significance are based on 0.5 % level of significance. Statistical analysis was done by using SPSS version 13.0 (IL, Chicago).

RESULTS

Out of the total responders 200 diabetic subjects, 40% (n=80) were males and 60% (n=120) were females. The total number of retinopathic subjects were 33% (n=66) and normal subjects were 67% (n=134). Out of the total 33% retinopathic subjects, 20% (n=40) were belonging to BDR group, 7% (n=14) were at preproliferative stage and 6% (n=12) were at the proliferative stage.

The characteristics of the study population are summarized in Table I. No difference in the mean age was observed among the groups. ANOVA followed by Tukey test revealed that both proliferative and BDR groups have significantly higher values of FBG ($p < 0.05$) when compared with normal group while pre-proliferative stage has non-significantly higher values when compared with normal fundoscopic group. Random blood glucose (RBG) was significantly higher in proliferative group when compared with normal ($p < 0.05$). The difference among the pre-proliferative group and BDR group was non-significant ($p > 0.05$). The difference of HbA1c between and within the groups was non-significant ($p > 0.05$). Serum Insulin levels also had a significant difference among the groups ($p < 0.05$). The difference of systolic blood pressure among the normal group and proliferative group was significant ($p < 0.05$) whereas in other groups difference was non-significant. The difference of diastolic blood pressure among the groups was significant ($p < 0.05$). The difference in total cholesterol between pre-proliferative group and proliferative group was significant ($p < 0.05$) while the difference of the BDR group with normal group was non- significant. In triglyceride the differences among the groups were non-significantly higher ($p > 0.05$). HDL had non-significant difference between the groups ($p > 0.05$). The difference of LDL between proliferative group and BDR groups was significant ($p < 0.05$) while the difference between the pre-proliferative group and BDR was non-significant ($p > 0.05$). Significant difference among the groups was observed in the values of fasting serum insulin (Table I). Significant differences were observed for diabetes related parameters according to the presence of DR stage. The significant clinical parameters included random blood glucose, HbA1c, Diastolic blood pressure and lipid profile.

Table I.- Demographic and Biochemical characteristic of the study population in control and diabetic retinopathic subjects.

Parameters	Normal (n=134)	BDR (n=40)	Pre.proliferative (n=14)	Proliferative (n=12)	ANOVA P- value
Sex					
Male	60	12	4	4	-
Female	74	28	10	8	-
Age (years)	50.77	50.69 ± 1.21	49.29 ±1.94	51.58 ± 2	0.973
BMI $(kg/m)^2$	27 ± 0.58	26.31± 0.83	27.64 ± 1.97	25.92 ± 3	0.89
FBG (mg/dl)	171.21 ± 4.4	174 ± 10.8	194.1 ± 18.3	231.5 ± 16.8*	0.004
RBG (mg/dl)	233.13 ± 4.8	244.6 ± 8.39	251.4 ± 12.5	303.4 ± 23.1*	0.001
HbA1c level (%)	9.87 ± 0.9	9.95 ± 0.345	11 ± 0.344	11.2 ± 0.42^{NS}	0.925
Chol (mg/dl)	202 ± 3.19	211.7 ± 6.74	234.79 ± 6.57	251.6 ± 11.9*	0.00
TG (mg/dl)	219 ± 7.54	228.2 ±15.2	235.8 ± 13.4	276.9 ± 21.9^{NS}	0.163
HDL (mg/dl)	37.7 ± 0.508	35.69 ± 1.10	34.36 ± 1.35	33.08 ± 1.22*	0.010
LDL (mg/dl)	123.89 ± 2.7	126.56 ± 6.5	138.36 ± 7.95	156.92 ± 8.6	0.008
SystolicB.P (mm of Hg)	129.57 ± 1.1	134.7 ± 3.09	138.29 ± 4.58	142.83 ± 4.3*	0.005
Diastolic B.P (mm of Hg)	86.75 ± 0.83	89.15 ± 1.71	93 ± 2.86	96.75 ± 3.42*	0.002
Insulin (ulU/ml)	21.8 ±1.83	34.35 ± 1.29	37.28 ±1.48	50.16 ± 1.05*	0.000
HOMA-IR	9.22±0.08	14.76±0.71	17.87± 1.27	28.67 ± 2.17	0.001

NS, Non-Significant ($p > 0.05$); *, Significant ($p < 0.05$); FBG, fasting blood glucose; RBG, random blood glucose; BP, blood pressure; Chol, cholesterol; TG, triglyceride; HDL, high density lipoprotein; LDL, low density lipoprotein; Hb, haemoglobin; BMI, body mass index, HOMA-IR, homeostatic model assessment of insulin resistance.

DISCUSSION

It was reported by Farasat *et al*. (2009) that 58% subjects were found undiagnosed of their diabetic status on their first visit to hospital. In this study the diabetic subjects were clinically evaluated by fundoscopy after diagnosis of diabetes. According to our study the prevalence of diabetic retinopathy was very high (33%) as compared to international and national data. According to pilot studies in Pakistan the prevalence of diabetic retinopathy is between 26.1% and 33.3% (Kayani *et al*., 2003). Similarly high prevalence estimates have been reported in other countries (Raymond *et al*., 2009).

In this study the fasting and random plasma glucose was significantly associated with advanced stage of retinopathy *i.e*. Proliferative DR. Hyperglycemia increases production of reactive oxygen species (free radical) leading to the activation of protein kinase C formation of advanced glycation end products contributing to vascular endothelial damage.

These results were similar as compared to other multiple studies in which higher FBG level was associated with diabetic retinopathy. The results of random blood glucose were also similar with findings of Reichard *et al*. (1993). Our finding about HbA1c level revealed that it was significantly associated ($p < 0.05$) with retinopathy stage detected by fundoscopy. These results were similar to other observational studies which reported that the glycated hemoglobin significantly increased with the severity of diabetic retinopathy (Klein *et al*., 1994; Lloyed *et al*., 1995). Significant association of glycated hemoglobin might be attributed due to the prolonged duration of hyperglycemia among these newly diagnosed diabetic subjects. The study population belonged to low socioeconomic status, the hyperglycemia remained undiagnosed and when they approached the clinic persistent hyperglycemic condition damaged the retina resulting in retinopathy.

According to the present study the concentration of serum insulin and insulin resistance were significantly high with the progression and proliferation of diabetic retinopathy. In persistent undiagnosed hyperglycemia diabetes might reduce insulin receptor signaling in the retina leading to neurodegeneration and damage to the retina (Curtis *et al*., 2009). The differences between all the groups were significant as ($p < 0.05$). These results were similar with Gwinip and Elias (1991) who reported increased concentration of serum insulin in the advanced stages of the retinopathy. The blood pressures both systolic and diastolic were significantly high with the advancement of retinopathic stage. Hendrick *et al*. (2002) reported that the increasing blood pressure is associated with increased proliferation in diabetic retinopathy. Other studies done

in different countries in Iran, India and in Denmark also revealed the similar results and concluded that the blood pressure is an important risk factor for the progression and proliferation of diabetic retinopathy (Hov *et al*., 2004; Abdollahi *et al*., 2006; Agarwall *et al*., 2006). In the present study the total cholesterol level was significantly higher with the progressive diabetic retinopathy. The results were in agreement with Wahab *et al*. (2008) who reported that an increased cholesterol level was associated with retinopathy. The mean value of HDL cholesterol decreased during the subsequent stages of retinopathy with a significant difference in the progressive stages of retinopathy ($p<0.05$). These results were in contrast to Kordonouri *et al*. (1996) who reported that the level of HDL was significantly higher in the diabetic retinopathy ($p < 0.05$). In present study the LDL cholesterol concentration increased as the proliferation of retinopathy increased. The difference in the mean values of LDL between the groups was significant ($p < 0.05$). These results were also in agreement with Kostraba *et al*. (1991) who reported an increase in LDL cholesterol with progression of PDR in a multivariate analysis. Two other studies done by Wahab *et al*. (2008) and Hendrick *et al*. (2002) had revealed that LDL cholesterol is an important risk factor the diabetic retinopathy. The mean values of triglycerides in the present study, showed an increasing trend for triglyceride level in subsequent stages of diabetic retinopathy.

There are conflicting reports in the literature regarding the effect of lipid profile on retinopathy. In a study by Lyons *et al*. (2004) observed that severity of retinopathy was associated with increasing triglycerides and inversely associated with HDL cholesterol. It was reported by Keech *et al*. (2006) that intensive glycemic control and combination treatment of dyslipidemia reduced the rate of progression of DR. In another study it was reported that serum lipids may have a strong influence only in the severe forms of diabetic retinopathy that involved the pathogenesis only *via* exudation of lipids through damaged retinal vasculature and breakdown of the blood retinal barrier (Benarous *et al*., 2011). On the contrary Hove *et al*. (2004) in a study conducted in Denmark reported no significant association between DR, triglycerides, HDL and total cholesterol in the diabetic population. In another study, there was no association between DR and lipid profile, however, clinically significant macular edema was found to be associated with serum lipids (Benaraus *et al*., 2011). Although all ethnic groups are susceptible to the established risk factors of DR such as duration of the disease, severity of hyperglycemia, dyslipidemia and hypertension, Significant differences in the prevalence and severity of DR and Diabetic macular edema between different ethnic groups has been reported (Wong *et al*., 2006; Sivaprasad *et al*., 2012). This population represented a low income group without any management of diabetes and medical care. A high %age of HbA1c in these newly diagnosed groups indicates chronic hyperglycemia and other causal factors, including dyslipidemia and consistent hypertension that initiated a cascade of biochemical and physiological changes that lead to the manifestation of microvascular damage and diabetic retinopathy.

CONCLUSION

The results of present study revealed high percentage (33 %) of diabetic retinopathy among newly diagnosed type 2 diabetic patients that underscores the need for fundoscopic examination in newly diagnosed diabetic patients.

Statement of conflict of interest

Authors have declared no conflict of interest.

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