Prevalence and Predictors of Diabetic Retinopathy Among Elderly type II diabetics

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Abstract: Background and objectives: Diabetic retinopathy (DR) is the most frequent microvascular complication of Diabetes Mellitus (DM), resulting in blindness for over 10,000 people with DM every year. This research is designed to study the prevalence DR in elderly type II diabetic patients (≥65 years) and the association between DR and some demographic, clinical and biochemical risk factors. **Methods:** A cross-sectional study including 800 patients aging ≥65 years. Signs of diabetic retinopathy were evaluated by ophthalmologist in Farwaniya ophthalmology clinic, Al-Farwaniya governorate, Kuwait, using direct/indirect ophthalmoscopy and/or slit-lamp fundus biomicroscopy. Medical examination and records were used to determine the duration of diabetes mellitus (DM), mode of treatment and the presence or absence of both hypertension and family history of DM. Fasting blood samples were taken to assess fasting blood glucose, lipid profile and glycated haemoglobin ($HbA1_C$). **Results:** 22.5% of the studied diabetic patients had DR. Most of DR patients (71.1%), suffered from non-proliferative diabetic retinopathy (NPDR), while advanced vision threatening proliferative diabetic retinopathy is low (2.2%). Univariate analysis revealed highly significant association between age, smoking, duration of diabetes, use of insulin for treatment, microalbuminuria, Glycated haemoglobin ($HbA1_C$) and the development of DR ($p<0.05$). Gender, level of education, BMI, hypertension, family history of DM, CH, TG, LDL, and HDL, had no significant association ($p>0.05$). Multiple logistic regression analysis revealed a risk to develop DR nearly four times more in patients suffered from DM for (10–<20 years) than reference group (newly diagnosed), OR=4.12 (95% CI=2.84-6.83), while the risk increased six times in the subgroup who had DM for twenty years or more, OR=6.43 (95% CI=3.45-9.26). Those who needed insulin treatment had seven times higher risk to develop DR than those on diet only, OR=7.24 (95% C1=5.78-9.52). (HbA1C) was found to be a strong predictor of DR, OR=8.36, (95% CI=5.75-11.67). The risk to develop DR is nearly eight times more in patients suffered from poor glycaemic control. **Conclusion:** All elderly diabetics particularly those with long history, who need insulin for treatment or with poor glycaemic control, should have regular follow up, through ophthalmic examination at regular intervals.
[Gaafar M. and Khattab A. **Prevalence and Predictors of Diabetic Retinopathy Among Elderly type II diabetics**. *J Am Sci* 2013;9(4):639-646]. (ISSN: 1545-1003). http://www.americanscience.org. 71

Key Words: Diabetic retinopathy, risk factors, elderly diabetics, type II Diabetes Mellitus.

1. Introduction

Diabetes Mellitus (DM) is a major worldwide public health problem. There is no available curative treatment for this costly disease. It is costly in terms of loss of quality of life [(1)], loss of life [(2)] and economic burden on the community, family of the diabetic patient as well as on the health sector [(3)].

Type II (Non insulin dependent) diabetics over the age of 55 comprise most of the diabetic patients and are at considerable risk for the development of both macrovascular and microvascular complications. These patients can be treated with diet modification alone, or in combination with oral hypoglycaemic agents, but in some cases insulin therapy is required [(4, 5)].

Diabetic retinopathy (DR) is a vascular disorder affecting the microvasculature of the retina. It is the most frequent microvascular complication of DM, resulting in blindness for over 10,000 people with DM every year [(6)] and is the leading cause of legal blindness (visual acuity of less than 6/60 or visual field restriction to 20° or less in the better eye) [(7)]. The prevalence of DR at the time of diagnosis varies from 5–35%. If eyes are looked after properly with regular checkups and treatments, the risk to develop DR can be reduced by about 90% [(8)].

The risk of development of DR depends on duration of diabetes and increase in age. If patient has diabetes for 10 years and more, there are about 80 percent chances for development of DR [(9)]. World Health Organization (WHO) estimated that one third diabetics will have DR and from these patients one third would suffer from sight-threatening complications [(10)].

DR can be treated effectively if it is detected early, and blindness can be prevented in the majority of cases by good glycaemic control and timely laser treatment [(11)]. Therefore, a correct reliable evaluation of the prevalence and severity of DR is important for public health planning and treatment services in the individuals with type II diabetes.

Most developed world countries had accepted the chronological age of 65 years as a definition of 'elderly' or older person; this is widely accepted as it is the age at which one can begin to receive pension benefits [12]. Most studies included only those aged 30-70 years or selected cases, therefore do not reflect the actual burden of the disease carried by old age. The prevalence of DR and its correlates in the elderly population are important to know, because the number of old people is constantly increasing and researches on epidemiology of diabetic retinopathy among the elderly are scanty.

This study aims to:

1) Determine the prevalence of DR in elderly type II diabetic patients (≥65 years).

2) Study the association between DR and some demographic, clinical and biochemical risk factors.

2. Patients and methods:

This cross-sectional study was carried out in Farwaniya ophthalmology clinic, Al-Farwaniya governorate, Kuwait, from January to December 2011. It included all nationals and non-nationals elderly diabetic patients (≥65 years old) attending the clinic. This clinic is serving about nine hundred thousand population (according to the civil identification authority). Type II DM patients comprise the greater proportion of diabetics in this area and identification of visual status is relevant to their care and service provision.

A total sample of 924 diabetic patients was approached by the ophthalmologist; out of them 810 patients (87.7%) agreed to enroll and gave samples. But because of dense cataract or inability to follow the instructions, ten patients were excluded from the study. As a result, a total of only 800 (86.6%) patients were included. The protocol of the study was reviewed and approved by an ethics committee at the study centre.

The fasting blood glucose level for all participants was measured in the morning and a glucose tolerance test using 75 gm of glucose in 300 ml water, was performed in subjects who gave negative history of antidiabetic medications. Diagnosis of diabetes was based on positive past history of hypoglycaemic medication or high fasting blood glucose level (>7.0 mmol/L) or high glucose level observed in the glucose tolerance test (>11.0 mmol/L). All participants' medical records together with history were reviewed to determine the duration, mode of treatment and the presence of systemic hypertension or family history of DM.

Blood pressure (BP) was measured early in the morning and prior to drawing of blood samples using a suitable mercury sphygmomanometer after a 10 minutes rest. BP was measured two times at 5 minutes interval. The WHO definition of hypertension was used in this study: systolic blood pressure 160 mmHg or more and/or a diastolic blood pressure 95 mmHg or more [13], or if the patient is on treatment with antihypertensive drugs. Height was measured without shoes and weight was recorded while wearing indoor clothing. Body Mass Index (BMI) (weight in Kg, divided by height in meters squared) was calculated. The WHO classification for BMI was used to estimate the degree of obesity. [14]

Fasting blood samples were taken to assess: **1)** *Total lipid profile:* {total cholesterol (CH), triglycerides (TC), high density lipoprotein (HDL) and low density lipoprotein (LDL)}, by a capillary tube whole blood method using the cholesterol LDX lipid analyzer. Dyslipidaemia was taken to be present when the total cholesterol was >5.60 mmol/L and/or triglycerides >2.10 mmol/L, and/or LDL>3.40 mmol/L, and/or HDL <0.91 mmol/L; **2)** *Fasting blood glucose:* by glucose oxidase method, clinical chemistry analyzer; **3)** *Glycated haemoglobin ($HbA1_C$):* by Bayer DCA 2000+ analyzer and a value of less than 7% was taken to indicate good glycemic control. First morning urine samples were taken to assess microalbuminuria using semiquantitative dry immuno chemical screening strips (Micral II ® test strips, Roche diagnostic GmbH Mannheim Mannheim Germany). Value more than 20µg/min was pathological. [15]

All participants after measuring their best corrected visual acuity (BCVA) using Landolt's broken rings charts; they were examined by direct/indirect ophthalmoscopy and/or slit-lamp fundus biomicroscopy with 90 D Volk lens. The pupils were dilated with 0.5% tropicamide and 2.5% phenylephrine. Fluorescein angiography was performed for vision threatening retinopathy and maculopathy. Diabetic retinopathy was graded as NPDR (Non-proliferative diabetic retinopathy), NPDR+CSME (Clinical significant macular edema), PDR (Proliferative diabetic retinopathy) +CSME and advanced PDR. [16]

A diagnosis of DR was made only where a participant had a minimum of one microaneurysm in any field, as well as exhibiting hemorrhages (dot, blot, or flame shaped), and maculopathy (with or without CSME).

Statistical analysis:

The data were analyzed using the Statistical Package for the Social Sciences (SPSS) software (version 17). The association between DR and risk factors was determined using the x^2 test. Statistical significance implies P value <0.05. The degree of risk was determined by Odds ratio (OR) and 95% confidence interval (CI). The multivariate logistic regression analysis was performed; the dependent

variable was: no DR (0), with DR (1). The independent variables (covariates) were: age, smoking, duration of the disease, insulin treatment (INT), microalbuminuria and glycated haemoglobin ($HbA1_C$).

3. Results:

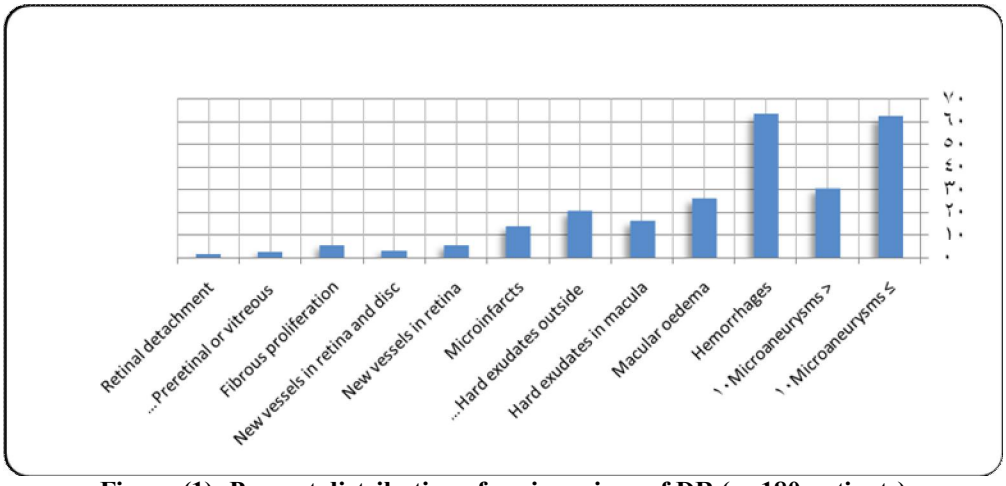

Figure (1): Percent distribution of various signs of DR (n=180 patients)

Signs of diabetic retinopathy (DR) were found in 180 (22.5%) diabetic patients (n=800). Percent distribution of various signs of diabetic retinopathy is shown in **Figure 1**, the most common findings were microaneurysms in 167 patients (92.8%; 62.2% had a number of microaneurysms ≤10 and 30.6% had >10), hemorrhage in 114 patients (63.3 %), macular edema in 47 patients (26.1%), hard exudates in 66 patients (36.7 %; 16.1% in the macula and 20.6% outside the macular area), cotton wool spots (microinfarcts) in 25 patients (13.9 %) and neovascularizations in 16 patients (8.9%).

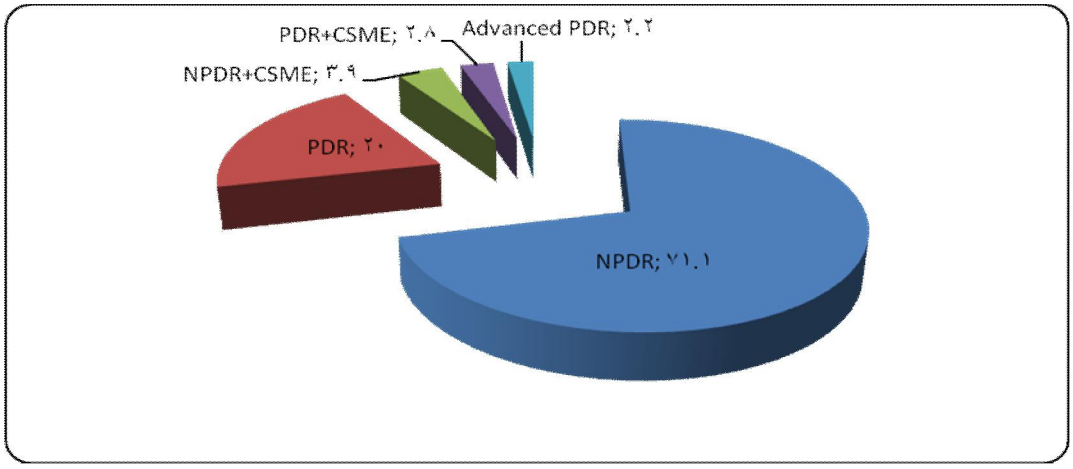

Figure (2): Clinical presentation of 180 DR patients (by percent)

NPDR= Non-proliferative Diabetic retinopathy
PDR= Proliferative Diabetic retinopathy.
CSME= Clinical significant macular edema.

Most of DR patients, 128 (71.1%), suffered from non-proliferative diabetic retinopathy (NPDR) without CSME, requiring follow-up for close monitoring of their visual and retinal status. While 52 (28.9%) patients had retinopathy with potentially vision threatening CSME and required immediate intervention. Out of those patients, 36 (20.0%) suffered from PDR, 7 (3.9%) had NPDR+CSME and 5 (2.8%) had PDR+ CSME, all requiring Pan Retinal Laser Photocoagulation (PRP) and/or macular laser treatment to stabilize their vision from further deterioration. Only four (2.2%) patients had advanced PDR and required PPV (Pars plana vitrectomy); two patients due to persistent vitreous

hemorrhage, one due to tractional retinal detachment affecting the macular area and one due to severe cystoid edema with macular traction caused by epiretinal membrane. **(Figure 2)**

Table (1): Socio-demographic characteristics of the studied DM patients (n=800)

Variables	DR Present (n=180)		DR Absent (n=620)		x^2	p-value
	No.	%	No.	%		
Age (Years):						
65-<70	37	20.5	198	31.9	8.88	0.031 (<0.05)
70- <75	41	22.8	172	27.7		
75 -<80	48	26.7	138	22.3		
≥80	54	30.0	112	18.1		
Gender:						
Male	66	36.7	239	38.5	0.14	0.711
Female	114	63.3	381	61.5		
Level of education:						
Illiterate	48	26.7	123	19.8	3.89	0.274
Completed primary school	42	23.3	155	25.0		
Completed secondary school	57	31.7	217	35.0		
University and above	33	18.3	125	20.2		
Smoking:						
Current and ex-smoker	48	26.7	90	14.5	13.58	<0. 001
Non smoker	132	73.3	530	85.5		
BMI:						
Under weight (<18.5)	13	7.2	32	5.2	5.82	0.121
Healthy weight (18.5–24.99)	33	18.3	164	26.4		
Overweight (25–29.99)	80	44.5	264	42.6		
Obese (>30)	54	30.0	160	25.8		

DR: Diabetic Retinopathy, n: number, BMI: Body Mass Index.

Diabetic retinopathy was significantly more frequent in age group ≥80 years (30.0% vs. 18.1%), ($p<0.05$). The presence of DR was significantly associated with the presence of smoking, whether current or ex smoker (26.7% vs. 14.5%), ($p<0.001$). No statistical significant association was found between the prevalence of DR and other covariates, including patient's gender, level of education and BMI ($p>0.05$). (**Table 1**)

Table (2): Clinical characteristics of the studied DM patients (n=800)

Variables	DR Present (n=180)		DR Absent (n=620)		x^2	p-value
	No.	%	No.	%		
Duration of the disease:						
Newly diagnosed	22	12.2	215	34.7	77.83	<0.0001
<10 years	32	17.8	186	30.0		
10–<20 years	54	30.0	123	19.8		
≥20 years	72	40.0	96	15.5		
Anti-diabetic treatment:						
Diet only	53	29.4	280	45.2	40.19	<0.0001
Oral drugs	102	56.7	322	51.9		
Insulin	25	13.9	18	2.9		
Hypertension:						
Present	95	52.8	292	47.1	1.58	0.208
Absent	85	47.2	328	52.9		
Family history of DM:						
Present	104	57.8	332	53.6	0.84	0.359
Absent	76	42.2	288	46.4		

DM: Diabetes Mellitus, n: number, DR: Diabetic Retinopathy.

Highly significant association was found between duration of diabetes and development of DR (p<0.0001). While a similar proportion of both groups was controlled on oral hypoglycemic agents (56.7% vs. 51.9%), a significantly higher proportion of those with DR required insulin (13.9% vs. 2.9%) (p<0.0001), and a correspondingly lower proportion of patients without DR could be managed on diet alone (29.4% vs. 45.2%). Hypertension and family history of DM had no significant association with the development of DR (p>0.05). (**Table 2**)

Table (3): Biochemical characteristics of the studied DM patients (n=800)

Variables	DR Present (n=180)		DR Absent (n=620)		x^2	p-value
	No.	%	No.	%		
Total Cholesterol (TC):						
High (>5.60 mmol/L)	49	27.2	148	23.9	0.67	0.412
Within reference range	131	72.8	472	76.1		
Triglycerides (TG):						
High (>2.10 mmol/L)	38	21.1	112	18.1	0.66	0.416
Within reference range	142	78.9	508	81.9		
LDL-C:						
High (>3.4 mmol/L)	25	13.9	62	10.0	1.79	0.180
Within reference range	155	86.1	558	90.0		
HDL-C:						
Low (<0.91 mmol/L)	14	7.8	38	6.1	0.38	0.536
Within reference range	166	92.2	582	93.9		
Microalbuminuria:						
Positive (>20 µg/min)	127	70.6	385	62.1	3.97	0.046
Negative	53	29.4	235	37.9		(<0.05)
$HbA1_C$:						
Poor control (>7%)	142	78.9	155	25.0	119.33	<0.0001
Good control (≤7%)	38	21.1	340	75.0		

LDL-C: Low Density Lipoprotein-C, HDL-C: High Density Lipoprotein-C, HbA1c: Haemoglobin A1c, DR: Diabetic Retinopathy

Dyslipidaemia was present in 70% of DR patients [elevated levels of: serum total cholesterol (27.2%), triglycerides (2.1.1%) and low-density lipoprotein cholesterol (13.9%) and low levels of high-density lipoprotein cholesterol (7.8%)]. While in absence of DR, dyslipidaemia was present in 58.1% of patients [elevated levels of: serum total cholesterol (23.9%), triglycerides (18.1%) and low-density lipoprotein cholesterol (10%) and low levels of high-density lipoprotein cholesterol (6.1%)]. The difference between the two groups was not statistically significant (p>0.05)

The presence of DR was statistically significantly associated with the presence of microalbuminuria (p<0.05). The analysis of glycaemic control of patients using $HbA1_C$ showed that (78.9%) of DR patients had poor glycaemic control, compared to (25.0%) in patients without DR, and the difference is highly significant (p<0.0001). (**Table 3**)

Table (4): Multivariate analysis of predictors for DR among DM patients using stepwise logistic regression

Variable	Adjusted OR	95% CI	p-value
Age	1.55	(0.77-2.14)	>0.05
Smoking	1.88	(0.87-2.53)	>0.05
Duration of the disease:			
10–<20 years	4.12	(2.84-6.83)	<0.0001
≥20 years	6.43	(3.45-9.26)	<0.0001
Insulin treatment	7.24	(5.78-9.52)	<0.0001
Microalbuminuria	2.11	(0.84-3.08)	>0.05
$HbA1_C$	8.36	(5.75-11.67)	<0.0001

OR: Odds Ratio, CI: Confidence Interval.

As to the risk factors associated with the development of DR, multiple logistic regression analysis was performed on a number of predictors that might independently be associated with development of DR. After adjustment of age and gender, a highly significant association was found between duration of diabetes and development of DR. The risk to develop DR is nearly four times more in patients suffered from DM for (10–<20 years) when compared with newly diagnosed cases, OR=4.12 (95% CI=2.84-6.83), while the risk increased to about six times in the subgroup who had DM for twenty years and more, OR=6.43 (95% CI=3.45-9.26).

Glycated haemoglobin ($HbA1_C$) and insulin therapy were found to be strong predictors of DR, OR=8.36 (95% CI=5.75-11.67) & 7.24 (95% CI=5.78-9.52) respectively. The risk to develop DR is nearly eight times more in the patients suffered from poor glycaemic control and seven times in patients using insulin therapy.

Age, smoking and microalbuminuria were significantly associated with retinopathy in univariate analysis ($p<0.05$), but this was weakened somehow when adjusted in multivariate analysis, adjusted OR=1.55 (95% CI=0.77-2.14), 1.88 (95% CI=0.87-2.53) and 2.11 (95% CI=0.84-3.08) respectively. **(Table 4)**

4. Discussion:

This cross-sectional study investigated the prevalence of retinopathy in type II elderly diabetics in Farwaniya ophthalmology clinic, Al-Farwaniya governorate, Kuwait, which is comparatively consistent with other population prevalence and risk factors of DR. It revealed a prevalence of 22.5% of DR among elderly diabetic patients. This is similar to that found in other studies [17, 18]. However, a Denmark study [19] found a prevalence of only 5% and Beaver Dam Eye Study reported a prevalence of 10% [20]. This is may be related to study design whether hospital based or community based.

In similar findings of Stolk et al. [21] no cases of neovascularisation on the disc were detected in this study. Advanced proliferative diabetic retinopathy was observed in only four patients (2.2%) corresponding with the findings of other investigators who share the same experience that severe DR is uncommon in elderly people [17, 21, 22].

This study showed some risk factors like age, smoking, duration of the disease, insulin therapy, microalbuminuria and $HbA1_C$, that are relevant in univariate analysis, whereas gender, level of education, BMI, hypertension, family history, total cholesterol, triglycerides, LDL, HDL are irrelevant. After controlling age and sex in multivariate analysis, we found that longer duration of diabetes mellitus, insulin use and poor blood glucose control (high $HbA1_C$), are the strongest predictors for DR.

The relation between smoking and retinopathy is less well defined than other microvascular complications [23]. Some studies had found an association between smoking and DR [24, 25]. However, smoking is not a risk factor for retinopathy in other studies [26, 27, 28], and this support current findings. This may be explained by the fact that smoking increases this risk for diabetic retinopathy probably via its metabolic effects in combination with increased inflammation and endothelial dysfunction, but this association is strongest in type 1 diabetes. The increased risk for macrovascular complications, coronary heart disease (CHD), stroke, and peripheral vascular disease, is most pronounced in type II diabetes [29].

On the contrary to the studies [30, 31] that found significant association between BMI and DR, current study doesn't found any association and this was supported by other studies [27, 28]. This may be explained by the difference of the study design, where BMI analysed as dichotomous variable might lead to this discrepancy in results.

The present study, like earlier studies found that duration of diabetes was significantly associated with increased prevalence of DR [32-35]. Risk increases four times in diabetics of 10-<20 years duration and six times in diabetics of ≥20 years duration or more than the reference (newly diagnosed) group. This is probably related to the magnitude or prolonged exposure, or both, to hyperglycaemia coupled with other risk factors [36].

A previous population based study found that DR was about the same in elderly patients whether on insulin or oral treatment [33], and this was supported by similar findings in previous studies [15, 23, 26, 30]. On the contrary, in this study the patients on insulin had seven times higher risk to develop DR than reference (diet only) group, those on tablets and/or diet showed non significant increased risk. These results may reflect poor diabetic control, persistent hyperglycaemia and more complications including DR [29]. It is also possible that insulin use itself may have a direct association with retinopathy [16].

In this study no significant association was found between systemic hypertension and increased prevalence of DR which agreed with that found in previous studies by Cahill et al. [20] and McKay et al. [37]. Several studies have shown an association between presence and severity of hypertension and DR [11, 12]. The possible mechanisms by which hypertension affects diabetic retinopathy are haemodynamic (impaired autoregulation and hyperperfusion) and secondly through VEGF (Vascular Endothelial Growth Factor) [38, 39]. This

discrepancy may be related to study design and population sample.

Current study cannot prove that CH, TG, LDL, HDL are associated with DR and this is shown also by other studies [19,26]. On the other hand other studies proved CH as a risk factor and this is explained by the difference in the sample selected where type I diabetics were included [40] whereas [30] a study the population of Cree Indians of James Bay which may be different from our population.

Since both microalbuminuria and DR are the microvascular complications of diabetic patients [23], it is expected to see the two factors correlating with one another. However, this relationship could not be clearly demonstrated in current study, although the data suggests there was such a trend ($p<0.05$), but this was weakened somehow when adjusted in multivariate analysis, adjusted OR=2.11 (95%CI= 0.84-3.08).

HbA1c is a good indicator of diabetic control. Poor blood glucose control indicated by high $HbA1_C$ has been found as a risk factor for DR by other studies [41-44]. It has been reported that for every % point decrease in HbA1c level (e.g. from 9% to 8%), there is a 35% reduction in the risk of microvascular complications [11]. This study had shown that HbA1c level has a positive correlation with the development of DR, the risk to develop DR is nearly eight times more in the patients suffered from poor control, OR=8.36 (95% CI=5.75-11.67).

5. Conclusion:

Longer diabetes Mellitus duration, insulin use and poor glycaemic control increase the risk for development of retinopathy. The significant associations with poor control and duration of diabetes provide further strong evidence for the benefits of optimal glycaemic control.

Diabetic patients whether with or without retinopathy beside receiving proper and regular treatment for diabetes, should have regular follow up, this is more important and should be more frequent in old diabetics particularly those who had diabetes for long duration or who need insulin for treatment, to detect retinopathy in the early stage.

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