

*Original Article***Visual acuity in an Iranian cohort of patients with type 2 diabetes: the role of nephropathy and ischemic heart disease**

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Abstract

BACKGROUND: The aim of this study was to investigate the risk factors of low vision in type 2 diabetic patients and the prevalence of ischemic heart diseases and nephropathy for different visual acuities.

METHODS: In this cross-sectional study, data from 738 type 2 diabetic patients including evidences for nephropathy and ischemic heart disease, demographic characteristics, blood pressure and body mass index were collected, and then patients were divided into 3 groups based on their best corrected visual acuity in the better-seeing eye. Analysis of variance was used to compare basic characteristics according to different levels of visual acuity.

RESULTS: The prevalence of blindness and low vision was 5.5% and 13.3% respectively, and as age, duration of diabetes, systolic blood pressure and body mass index increased, the visual acuity decreased. The prevalence of hypertension and obesity in patients with visual disabilities was significantly higher than in patients with not impaired visions ($p = 0.008$ and $p = 0.02$, respectively). We also found that with greater decline in visual acuity, the prevalence of nephropathy and ischemic heart diseases increased.

CONCLUSIONS: The factors related to retinopathy play a role in affecting the degree of visual impairment in diabetic patients. Therefore, controlling risk factors can be useful in decreasing impairment of vision and blindness.

KEYWORDS: Diabetes Mellitus, Type 2, Visual Acuity, Diabetic Retinopathy, Blindness, Diabetic Nephropathies, Cardiovascular Diseases.

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Diabetes mellitus is one of the most common non-communicable diseases in the world. The WHO has predicted that, "the number of diabetic patients in the world will reach 300 millions by 2025, and more than 75% of these patients will be living in developing countries.^{1"}

Diabetic retinopathy is one of the most common complications of diabetes,² and one of the leading causes of blindness and visual impairment.³⁻⁶

According to statistics from a decade ago,

40 million people were blind and 110 million had low vision.⁷ The American Diabetes Association claims that diabetes is responsible for 8% of legal blindness.⁸

Diabetic retinopathy and resulting blindness are responsible for a major disability in patients, and they lead to a high financial and social burden on the community indicating the importance of increased efforts in this field.

Diabetic retinopathy is the principal cause of one-third of all cases of blindness,⁹ and also, according to some trials, a factor which is asso-

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ciated to increased prevalence of cardiovascular diseases.¹⁰⁻¹² These trials supposed that the pathogenesis of diabetic retinopathy and cardiovascular diseases are both microvascular.

On the other hand, microalbuminuria which is another microvascular complication of diabetes has a connection with both, the development and progression of retinopathy.¹³

Taking into account the possibility that retinopathy, nephropathy and cardiovascular diseases may have similar pathogenesis in diabetic patients, and considering the role of retinopathy on vision acuity,¹⁴⁻¹⁶ it can be assumed that the prevalence of chronic complications of diabetes is different for different visual acuities, and risk factors related to diabetic retinopathy are possibly connected to visual impairment in diabetic patients. Since there are limited data on this field in Iran, and considering the fact that these data are essential for setting up of Iranian blindness prevention program, and also the clear effect of early screening and suitable intervention on reducing incidence of blindness and low vision related to diabetic retinopathy,^{17,18} this study was performed in an Iranian population of type 2 diabetic patients at the Isfahan Endocrine and Metabolism Research Center with the aim of investigating our assumptions, and collecting as much information as possible concerning the prevalence of blindness and low vision and their related risk factors in our diabetic patients.

Methods

This cross-sectional study was conducted in April 2009, at the Endocrine and Metabolism Research Center of Isfahan University of Medical Sciences which covers 40% of diabetic patients of Isfahan. Study protocol was approved by the ethics committee of the center (Project No. 87015). The study complied with the current version of the Declaration of Helsinki.

For this study we used routinely collected and registered data from patients registered at this center. These data were initially collected by an endocrinologist and subsequently via next follow-up visits to physicians at the cen-

ter, and then the standard check lists that were filled out by these persons entered into the central computer system of the center.

This information included: demographic characteristics, past history, family history, blood pressure, lipid profile, blood urea nitrogen (BUN), creatinin, HbA1c (glycosylated hemoglobin), urine albumin, the results of eye exams and of cardiovascular follow-ups.

Lipid profile, BUN, creatinin, BP and body weight were usually monitored monthly and the ophthalmic, cardiovascular and renal condition of patients at least yearly.

All lab tests were performed by the laboratory at the Endocrine and Metabolism Research Center.

HbA1c was measured by spectrophotometer (DS5) and urine albumin by the sopt collection method. Creatinin was measured by the photometric method and albumin by the immunoturbidimetric method on a DB 3000 appliance.

Eye Examination

Eye examination was performed by an experienced ophthalmologist and included: testing of visual acuity (VA), corrected and uncorrected visual acuities were determined using a Snellen chart and a Canon autorefractometer (R-50m, Japan), best corrected visual acuity (BCVA) was defined as the visual acuity after subjective refraction in the better eye, and also intraocular pressure was measured using Goldman applanation tonometry (Haag-streit AG1A 900, Switzerland).

The pupil of each eye was dilated using tropicamide 1% followed by a dilated fundus examination using a 78-dioptre non-contact fundus viewing lens (Volk). If needed, indirect ophthalmoscopy was performed. All findings were registered in special checklists.

Cardiac Condition Follow-Up

Ischemic heart disease was diagnosed by taking history and an ECG test. If there were electrocardiographic abnormalities as diagnosed by the Minesota-code or symptoms of ischemic heart disease,¹⁹ the patient was referred to a

cardiologist for the exercise tolerance test and other diagnostic and therapeutic procedures.

Patients

Our target population was type 2 diabetic patients of Isfahan. As it has been mentioned before, the center covers 40% of diabetic patients of Isfahan. Between 2008 and 2009, 1300 diabetic patients came to the center for their follow-up visits. Of these patients, 1000 persons had type 2 diabetes and 300 persons had type 1.

For this study we used data collected from 900 conveniently-selected patients with type 2 diabetes who had a complete eye exam during that period. Patients with incomplete records on their ophthalmologic exam or on evidences of nephropathy and ischemic heart disease were excluded from the study

Definitions

The patients were divided into 3 groups based on their best corrected visual acuity (BCVA) in the better seeing eye, using the North American definition.²⁰

Best Corrected Visual Acuity: Not impaired was defined as best corrected visual acuity better than or equal to 20/40 (5/10), low vision as worse than 20/40 but better than 20/200 (2/10-4/10) and blind was defined as 2/200 or worse (1/10 or worse).

Ischemic Heart Disease: The patients who have been put on treatment or undergone surgery like coronary artery bypass graft (CABG) surgery or percutaneous transluminal coronary angioplasty (PTCA) after diagnostic tests

Nephropathy: Urine albumin/creatinin more than 30mg/g²¹

Hypertension: (in diabetic patients) Systolic/diastolic blood pressure \geq 130/80 mmHg²²

Obesity: Body mass index (weight in kg/squared of height in m) \geq 30 kg/m²³

Statistical Analysis

We used t-test to compare continuous

variables, chi-square test to compare categorical variables, and analysis of variance (ANOVA) test to compare basic characteristics according to different levels of visual acuity. In all instances, p values $<$ 0.05 were considered significant. Data analyses were done using the SPSS version 13 (Chicago, USA).

Results

Of the 900 investigated files, 162 were excluded because of incomplete information. The study included data from 738 patients. Of these patients with the mean age of 60.29 \pm 10.3 years, 41 patients (5.5%) were blind (95% Confidence Interval (CI): 2.5-13.2) and 98 patients (13.3%) had low vision, (95% CI: 4.3-32.3).

Tables 1 and 2 show the demographic characteristics for patients divided into 3 groups and results of post hoc tests for continuous variables among 3 groups of patients with different visual acuities, respectively. According to these data, there was a significant difference among 3 groups in terms of mean age, body mass index (BMI), duration of diabetes and systolic blood pressure. Presence of any of the following conditions was associated with corresponding decrease in visual acuity: increasing age, longer duration of diabetes, higher systolic blood pressure, and increased body mass index.

Table 3 shows the prevalence of different levels of visual acuity by the presence of hypertension or obesity. According to this table, when patients in blind and low vision groups are considered together, it is evident that 20.3% of hypertensive patients and 5.5% of non-hypertensive ones have visual disability ($p = 0.008$), and 22.9% of obese patients and 16.2% of non-obese ones have visual impairment ($p = 0.02$).

Table 4 shows the prevalence of ischemic heart diseases (IHD) and nephropathy in 3 groups.

Considering these data, there is a significant difference between the 3 groups in terms of the prevalence of IHD and nephropathy.

Table 1. Basic clinical and demographic characteristics and mean of HbA1c of patients with different visual acuities

	Blind n = 41	Low vision n = 48	Not impaired n = 599	Total n = 738
Male	82.9% n = 34	68.7% n = 68	69.1% n = 420	69.8% n = 522
Female	17.1% n = 7	31.3% n = 31	30.9% n = 188	30.2%* n = 226
Age [†] (Year)	66.15 ± 10.28	65.78 ± 8.62	59.00 ± 10.14	60.29 ± 10.31**
BMI ^{†‡} (kg/m ²)	31.03 ± 5.26	29.37 ± 4.91	29.06 ± 4.48	29.21 ± 4.60***
Duration of diabetes [†] (Year)	20.19 ± 8.02	17.24 ± 7.35	14.11 ± 6.46	14.87 ± 6.88***
HbA1c (%)	7.69 ± 1.86	7.54 ± 2.03	7.67 ± 1.67	7.65 ± 1.73*
Systolic blood pres- sure [†] (mmHg)	128.78 ± 18.26	123.47 ± 16.47	120.35 ± 16.65	121.23 ± 16.83 [§]
Diastolic blood pres- sure [†] (mmHg)	77.80 ± 7.9	75.82 ± 9.41	75.83 ± 9.47	75.94 ± 9.38*

Blind: Best corrected visual acuity (BCVA) 1/10 or worse

Low vision: BCVA worse than 4/10 but better than 2/10

Not impaired: BCVA better than 4/10

[†] Mean ± SD[‡] Body Mass Index

* P > 0.05

** P < 0.001

*** P < 0.05

[§] P < 0.01**Table 2.** Results of post hoc tests for basic clinical and demographic characteristics and mean of HbA1c among 3 groups of patients with different visual acuities

	B* and LV** (P value)	B and NI*** (P value)	LV and NI (P value)
Age (year)	0.980	0.000	0.000
BMI [†] (kg/m ²)	0.153	0.029	0.820
Duration of diabetes (year)	0.060	0.000	0.000
HbA1c (%)	0.893	0.995	0.805
Systolic blood pressure (mmHg)	0.233	0.008	0.231
Diastolic blood pressure (mmHg)	0.523	0.429	1.000

*B: Blind

** LV: Low vision

*** NI: Not impaired

[†] Body Mass Index

Table 3. Prevalence of different levels of visual acuity in type 2 diabetic patients with and without hypertension or obesity

	Blind [§]	Low vision [‡]	Not impaired ^{§§}	Total (n =738)
With hypertension ^{‡‡}	6%	14.3%	79.7%	100%
	n = 40	n = 95	n = 529	n = 664
Without hypertension	1.4%	4.1%	94.6%	100%*
	n = 1	n = 3	n = 70	n = 74
Obese [†]	8.2%	14.7%	77.1%	100%
	n = 24	n = 43	n = 226	n = 293
Non obese	3.8%	12.4%	83.8%	100%**
	n = 17	n = 55	n = 373	n = 445

[§] Blind: Best corrected visual acuity (BCVA) 1/10 or worse

[‡] Low vision: BCVA worse than 4/10 but better than 2/10

^{§§} Not impaired: BCVA better than 4/10

^{‡‡} Hypertension (diabetic patients): Systolic/diastolic blood pressure \geq 130/80 mmHg

[†] Obese: Body mass index \geq 30 kg/m²

* $\chi^2 = 9.687$, $p < 0.01$

** $\chi^2 = 7.695$, $p < 0.05$

The prevalence of nephropathy is significantly higher in the group with blindness than in both groups with not impaired vision ($p = 0.003$) and

those with low vision ($p = 0.01$). Also the prevalence of IHD was significantly lower in patients with not impaired vision than those with visual disabilities.

Table 4. Prevalence of ischemic heart disease and nephropathy in 3 groups of type 2 diabetic patients with different levels of visual acuity

	Blind [§] n = 41	Low vision [‡] n = 98	Not impaired ^{§§} n = 599	Total n = 738
Nephropathy ^{‡‡}	100%	83.7%	82%	83.2%*
	n = 41	n = 82	n =491	n =614
IHD [†]	39%	34.7%	20.5%	23.4%**
	n = 16	n = 34	n =123	n = 173

[§] Blind: Best corrected visual acuity (BCVA) 1/10 or worse

[‡] Low vision: BCVA worse than 4/10 but better than 2/10

^{§§} Not impaired: BCVA better than 4/10

^{‡‡} Nephropathy: Urine albumin/creatinine $>$ 30mg/g

[†] Ischemic heart diseases

* $\chi^2 = 8.751$, $p < 0.05$

** $\chi^2 = 15.283$, $p < 0.001$

Discussion

In this cross-sectional study carried out on 738 registered type 2 diabetic patients, the prevalence of blindness and low vision was 5.5% and 13.3%, respectively. It was observed that the visual acuity decreased with increasing age, duration of diabetes, systolic blood pressure, and body mass index. It was also showed that with greater decline in visual acuity, the prevalence of nephropathy and ischemic heart diseases increased.

Reported prevalence of blindness and low vision is very different in various societies. The prevalence of blindness in type 2 diabetic patients in Yemen was 16%,²⁴ in Taiwan was 1.6%,²⁵ in Denmark was 1.5%²⁶ and in England was 1.16%.²⁷ It has been claimed by the Center for Disease Control that among adults with diabetes, 2.9% suffered from mild vision impairment and 1% had severe visual impairment after correction.²⁸

One reason for the higher prevalence of visual impairment and blindness in our study in comparison with other studies was the nature and the type of groups studied. The Taiwan study was a population-based diabetic retinopathy screening program. The study in England was a population-based study of diabetic patients in a district in the northwest of England. The Denmark study included blind cases registered in a database of diabetic patients, but our study has been carried out at a referral center for diabetic patients, which is affiliated to Isfahan University of Medical Sciences, and the prevalence of each chronic complication may be affected by this referral pattern, because the number of patients with more severe complications is greater, they also make more frequent visits and are more vigilant.

Other possible reasons for high prevalence of low vision and blindness in our study was primarily the long duration of diabetes (more than 15 years in 30.5%) and secondly, high prevalence of hypertension and nephropathy (89.8% and 83% respectively) in our studied population.

Different studies claimed that, the duration of diabetes,²⁹⁻³¹ age,^{29,32} high blood pressure,³³⁻³⁵

and albuminuria,^{14,27} are directly related to the onset and progression of diabetic retinopathy, and diabetic retinopathy is one of the major causes of visual impairment in diabetic patients,^{13,36} so it is reasonable to suppose that risk factors related to it are also related to the status of visual acuity.

The results of our research revealed that our supposition was well-founded, and age, duration of diabetes, body mass index and systolic blood pressure were also related to the severity of visual impairment. In addition, in our study, hypertension and obesity were significantly more prevalent in patients with visual disabilities than in patients with unimpaired visions. Some other trials have also shown that there is a relationship between systolic blood pressure and diabetic retinopathy,³² and have claimed that the severity of retinopathy in type 2 diabetic patients is positively associated with systolic blood pressure²⁸ and body mass index.³⁴

In our study there was no relationship between different levels of visual acuity and sex. In an independent study in Isfahan, Janghorbani et al also reached the conclusion that there was no association between retinopathy and sex,³² which was in agreement with the results of other studies.^{24,33}

We also found a relationship between severity of visual impairment and prevalence of ischemic heart disease and nephropathy.

In the Ossama et al study, there was also a relationship between ischemic heart disease and retinopathy, but after adjustment for risk factors, the relationship was no longer significant.³³ A limited number of studied ischemic heart disease cases (44/500) was mentioned as the possible reason for this finding, but in our study, the number of ischemic heart disease cases was not limited (Table 4); so, it seems that the prevalence of ischemic heart disease does not have an independent relationship with visual acuity. The reason is possibly the difference in pathogenesis of ischemic heart disease and retinopathy; the former is macrovascular in nature and the latter has a microvascular pattern. Nephropathy, which was in direct relationship with visual acuity has also a

microvascular basis.

We are fortunate at our center to have access to some of the most comprehensive data of its kind in the developing world. Based upon information from earlier studies, it is clear that our patients are a representative sample of known diabetics in Isfahan.^{32,37} In addition, a positive aspect of our diagnosis of ischemic heart disease, nephropathy, hypertension and obesity was that it has not been based on a single examination but on continued examinations during follow-ups. However, this study has also some limitations. The study was of course clinic-based rather than population-based. Clinic-based estimates of the prevalence of complications are most likely to be affected by referral patterns, since patients at our clinic are more likely to have complications, and it has been showed by experience that once a complication occurs,

patients are more likely to come regularly for treatment, and this factor affects the estimated prevalence of complications. Considering the above-mentioned reasons, it seems that a population-based study will be needed regarding the matter in the future.

Conclusion

The factors related to retinopathy play a role in affecting the degree of visual impairment in diabetic patients. Considering the fact that the high prevalence of low vision is a serious threat to the health of diabetic patients in Isfahan, control of risk factors can be useful in decreasing impairment of vision and blindness.

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Conflict of Interests

Authors have no conflict of interests.

Authors' Contributions

NH was the principal investigator of the research project, carried out the design, coordinated the study, participated in all of the research stages, and also in manuscript preparation. MF assisted in designing the study and coordinated and assisted in carrying out all the research stages. MG assisted in designing the study and assisted in carrying out the research. SH assisted in designing the study, coordinated in carrying out the research, and participated in manuscript preparation and revision. MA assisted principally in designing the study and participated in manuscript preparation and revision.

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