A STUDY ON CHANGES IN RETINAL SENSITIVITY AMONG DIABETIC PATIENTS

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Background & Objectives: There is an increasing problem burden of diabetes with increasing age; adult diabetics are also at risk of vision threatening retinopathies. The absolute number of the over 60 population in India will increase from 76 million in 2000 to 137 million by 2021. Diabetic Retinopathy is the most common ocular manifestation of diabetes. Patients with diabetic retinopathy have a sensitivity loss in the mid-peripheral visual field detected by white-on-white Perimetry; this loss has been correlated with the retinal area of non-perfusion in proliferative diabetic retinopathy (PDR). **Methods:** The present cross sectional observational study comprising of 84 cases was conducted in the Department of Physiology, Pt. Jawaharlal Nehru Memorial Medical College Raipur in collaboration with the Upgraded Department of Ophthalmology, Dr. B.R.A.M. Hospital, Raipur (C.G.) from August 2014 to July 2015. Study subject were selected by simple random sampling, those fulfilling inclusion criteria. In the study, individuals was comprised in two different group i.e. Type 2 diabetic patients (Case) and normal healthy (Control) of age 30 years or older. All patients underwent complete clinical examination. 42 eyes were examined in each group one eye per patient was assessed in all subjects. Eye examination includes Best-corrected visual acuity, refraction, intraocular pressure, Slit lamp examination & Humphrey Visual Field Automated Perimetry 30-2 test were performed. **Results:** Out of 42 diabetics or cases 26(61.91%) were male while 16 patients (38.09%) were female. In diabetic cases 3 males and 6 females belong to 30-40 year age group. Mean age of diabetic was 50.69± 10.69 years in which male was 53.69 ± 10.69 years and female was 45.81 ± 9.01 years. 11 (26.19%) males and 8 (19.05%) females had diabetes of less than or equal to 5 years. Maximum cases 19(45%) had diabetes of less than or equal to 5 years. 64.28% diabetic cases while 43.24% control had decreased vision means visual acuity < 6/6. The mean Intraocular Pressure in diabetic males was 17 mm of Hg. The mean Intraocular Pressure in diabetic females 16 mm of Hg. In 42 diabetic cases, lens opacity present in 29 (69 %) cases while in control group it was present in 23(55%) eyes. Retinal sensitivity was statistically lower in diabetic case as compare to control. **Conclusion:** The primordial, primary as well as secondary preventive measure by periodic ophthalmic examination helpful in early diagnosis and appropriate management of diabetic Retinopathy cases.

Key Words: Diabetic retinopathy, Retinal sensitivity, Perimetry, Visual field defect.

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Introduction:

There is an increasing problem burden of diabetes with increasing age; adult diabetics are also at risk of vision threatening retinopathies. The absolute number of the over 60 population in India will increase from 76 million in 2000 to 137 million by 2021. [1,2,3,4,5]

Diabetic Retinopathy is the most common ocular manifestation of diabetes. DR is a progressive disease which is silent until late stage, at which time it may be too late to prevent or reverse vision loss. To prevent visual loss occurring from diabetic retinopathy, a periodic Fundus examination follow-up:- every year, till there is no diabetic retinopathy, every six month, in nonproliferative diabetic retinopathy and every two month, in proliferative diabetic retinopathy is very important for a timely intervention. **Slit-lamp bio microscopy** through a dilated pupil and standard seven-field stereoscopic 30° fundus photography are the current **"gold standards"** in the evaluation of diabetic retinopathy. However, they suffer the disadvantage of being time consuming, require dilatation of pupil, and can be offered only by a specially trained ophthalmologist.[6]

Patients with diabetic retinopathy have a sensitivity loss in the midperipheral visual field detected by **white-on-white Perimetry**; this loss has been correlated with the retinal area of nonperfusion in proliferative diabetic retinopathy (PDR).[7] The sensitivity loss was closely associated

with microangiopathy and was greater in the midperipheral area than in the paracentral area. Short-wavelength automated Perimetry has been shown to offer improved sensitivity for the detection of clinically significant macular edema (CSME) and localized visual field defects following laser photocoagulation.[8] Isabel Pinilla et al. has evaluated role of frequency-doubling Perimetry (FDT) to identify patients at risk of developing diabetic retinopathy in insulin-dependent diabetes mellitus patients prospectively. Their results suggest that the FDT can detect retinal dysfunction in diabetic patient prior to the onset of significant vascular complication**.**

With the above background the present study was conducted to assess the change in retinal sensitivity among diabetic patients.

Material and Methods:

The present cross sectional observational study comprising of 84 cases was conducted in the Department of Physiology, Pt. Jawaharlal Nehru Memorial Medical College Raipur in collaboration with the Upgraded Department of Ophthalmology, Dr. B.R.A.M. Hospital, Raipur (C.G.) from August 2014 to July 2015. Study subject were selected by simple random sampling, those fulfilling inclusion criteria. In the study, individuals was comprised in two different group i.e. Type 2 diabetic patients (Case) and normal healthy (Control) of age 30 years or older. Objectives & method of the study was explained & an informed consent was taken from the subjects prior to the start of study. Subjects were interviewed about name, age, occupation, education, tobacco & alcohol intake, residence and proformas were filled before eye examination. Detailed clinical history was recorded including presenting complaints past, personal and family history with duration. All patients underwent complete clinical examination including blood pressure, general & systemic examination including neurological examination. 42 eyes were examined in each group one eye per patient was assessed in all subjects. The person with one eye, same eye was examined whereas person with two eyes the better one was selected by ocular examination. Eye examination includes Best-corrected visual acuity, refraction, intraocular pressure, Slit lamp examination & Humphrey Visual Field Automated Perimetry 30-2 test were performed.

Sample size: - Sample size for cross section observational study was calculated

By Comparing Two Independent Proportions

To calculate the optimal sample size the following 4 quantities must be pre-specified:

1. Assuming there is a true underlying difference; how certain do you want to be of detecting this? I.e. **Power**, generally we want power = 90% (should be at least 80%)
2. What **significance level** is difference criterion? The cut off below which we will reject the null hypothesis, generally p=0.05 (5%).
3. The assumed proportion that you wish to detect in group 1, $\mathbf{P_1}$
4. The assumed proportion that you wish to detect in group 2, $\mathbf{P_2}$

[$\mathbf{P_1}$ - $\mathbf{P_2}$ is the smallest difference in proportions that is clinically important]

Then

$$\textbf{Patient per group} = \frac{\mathbf{f}\,(\boldsymbol{\alpha}, \boldsymbol{\beta})\,\{\mathbf{P1}(\mathbf{1}-\mathbf{P1})+\mathbf{P2}(\mathbf{1}-\mathbf{P2})\}}{(\mathbf{P1}-\mathbf{P2})\mathbf{2}}$$

D.K. Nagi, et.al. (1997) conducted a prospective study to determine Diabetic Retinopathy assessed by fundus photography in Pima Indians. In a population-based epidemiological study, 991 Pima Indians with non-insulin-dependent (Type2) diabetes mellitus (NIDDM) and 288 without diabetes adult were examined. Defect in Visual field was present in 375 (37.8%) diabetic subjects and 14 (5.2%) non-diabetic subjects.[10]

Assumptions:

p1 = 0.37 (37.8% retinopathy in diabetics)
p2 = 0.05 (5.2% retinopathy in non diabetics)
90% power, 5% significance [f (α, β) = 10.5]
Then

$$\textbf{Patient per group} = \frac{(\mathbf{10.5})\{\mathbf{0.37}\,(\mathbf{1}-\mathbf{0.37})+\mathbf{0.05}\,(\mathbf{1}-\mathbf{0.05})\}}{(\mathbf{0.37}-\mathbf{0.05})\mathbf{2}} = \mathbf{42}$$

Forty two subjects was selected separately for both group those fulfill inclusion criteria for the study. The one eye with better refraction & visual aquity

was selected for perimetry examination from each subject.

Participants

Group 1: Case group

Persons aged 30 years or older with established diagnosis of Type 2 diabetes mellitus or patient on antidiabetic medication and willing to participate.

Group 2: control group

Person aged 30 years or older nondiabetic and willing to participate

Exclusion Criteria:

- Best corrected visual acuity of less than 6/60 on the Snellen Scale in test eyes
- Refraction more than ±5 D
- Cataracts: nuclear opalescence, nuclear colour and cortical cataract more than grade three. Those with a posterior sub capsular cataract and cataract in the pupillary area even of grade 1 were excluded.
- Known case of previous laser photocoagulation, PDR with sequel (vitreous hemorrhage and tractional retinal detachment), intraocular surgery, and eye disorder that could cause visual field defect (corneal opacity/ media opacity).
- Intra ocular pressure of 22 mmHg or more & glaucoma.
- Vision loss after head injury, or neuro-ophthalmic disorders.
- Blood pressure >140/90 mmHg.
- Sickle cell disease.

Investigations

All subjects who has fulfilled the inclusion/exclusion criteria were enrolled and studied. The subject underwent the investigations using standard apparatus and procedure as following:

- Blood Glucose
- Hba1c Level
- Blood Pressure
- Visual Aquity
- External Eye Examination
- Refraction
- Intraocular Pressure
- Slit Lamp Examination
- Cataract Grading
- Retinal Sensitivity Test

Data was compiled in MS-Excel and checked for its completeness and correctness then it was analysed using suitable software and p-value < 0.05 was considered as statistically significant.

Result:

TABLE.1- SEX WISE DISTRIBUTION OF PATIENTS

	Male	Female	Total
Case	26 (62%)	16 (38%)	42
Control	24 (57%)	18 (43%)	42

In our study a total number of observations taken were 84. Out of which, 42 were diabetic patients i.e. case and 42 were non-diabetic patients i.e. normal adult or control. Out of 42 diabetics or cases 26(61.91%) were male while 16 patients (38.09%) were female. The ratio of diabetic male to female was 1.62:1. Out of 42 non-diabetic or control 24(57.14%) were male while 18 (42.85%) were female. The ratio of male to female was 1.34:1. It was slight male predominant study. **[Table-1]**

TABLE.2 - AGE AND SEX WISE DISTRIBUTION OF CASES AND CONTROL

Age in years	Total	
	Case	Control
30-40 Yr.	9	24
41-50 Yr.	14	5
>50 Yr.	19	13

In diabetic cases 3 males and 6 females belong to 30-40 year age group. 8 males and 6 females belong to 41-50 age group and 15 males and 4 females were more than 50 years of age. Mean age of diabetic was 50.69± 10.69 years in which male was 53.69 ± 10.69 years and female was 45.81 ± 9.01 years. This age difference were statistically

significant (P=0.0184). Out of 42 non-diabetic or control 13 males belong to 30-40 year age group, 2 belong to 41-50 age group and 9 males were more than 50 years of age. Among females 11 belong to 30-40 year age group, 3 belong to 41-50 age group, 4 females were more than 50 years of age. Mean age of control was 42.26± 11.17 years in which male was 43.42± 12.04 years and female was 40.72± 10.04 years. The age difference between case & control were statistically significant (P value = 0.0007). **[Table-2]**

TABLE.3- DISTRIBUTION OF CASES ACCORDING TO DURATION OF DIABETES

Duration in years	**Male**		**Female**		**Total**	
	No.	**%**	**No.**	**%**	**No.**	**%**
0- 5	11	26.19	8	19.05	19	45.24
6—10	9	21.43	5	11.90	14	33.33
11—20	6	14.29	3	7.14	9	21.43
Total	26	61.90	16	38.10	42	100
Mean duration± SD	**8.12 ± 4.52**		**7.25 ± 3.37**		**7.78 ± 4.11**	
T test = 0.6567, df = 38, SE = 1.325, p=0.51[Not significant]						

All the cases (n=42) were divided into three strata according to duration of diabetes. 11 (26.19%) males and 8 (19.05%) females had diabetes of less than or equal to 5 years. Maximum cases 19(45%) had diabetes of less than or equal to 5 years. 9 (21.43%) males and 5 (11.90%) females had diabetes of 6-10 years duration. 6 (14.29%) males and 3 (7.14%) females had diabetes of 10-20 years duration. In our study, average duration of diabetes was 7.78± 4.11years in which male was 8.12±4.52 years and female was 7.25±3.37years. Duration of diabetes in male & female were not statistically significant. **[Table-3]**

TABLE.4- DISTRIBUTION OF CASE AND CONTROL ACCORDING TO VISUAL AQUITY

Visual Aquity	**Case**	**Control**
Normal (6/6 or 0.00 LogMar)	15 (35.71%)	23 (54.76%)
Decreased (<6/6)	27 (64.28%)	19 (43.24%)
Total	42	42
Chi squared X^2 (df=1) = 6.151, P value = 0.0131[Significant]		

64.28% diabetic cases while 43.24% control had decreased vision means visual acuity < 6/6. In diabetic cases median visual aquity was 0.20 LogMar, ranging from 1.00(6/60) to -0.19(6/5) LogMar, 15 had normal vision (6/6) and 27 had decreased vision (<6/6) while in control group having same number of cases median visual aquity was 0.15 LogMar, ranging from 1.00(6/60) to -0.19(6/5) LogMar, 23 had normal vision and 19 had decreased vision. This means in diabetic, the probability of decreased visual aquity was statistically significant (P value = 0.0131) as compared to control. **[Table-4]**

TABLE. 5- DISTRIBUTION OF CASE AND CONTROL ACCORDING TO MEAN INTRAOCULAR PRESSURE IN MMHG

IOP	Male	Female	Average	P value
Case	17 ±2.7	16.1 ±2.1	16.6 ±2.5	0.25
Control	14.1 ±1.6	13.4 ±1.5	13.8±1.6	0.17
t = 6.0217, df = 82, SE= 0.467, p value < 0.0001[Significant]				

The mean Intraocular Pressure in diabetic males was 17 mm of Hg. The mean Intraocular Pressure in diabetic females 16 mm of Hg. This mean Intraocular Pressure difference between diabetic male and female were not statistically significant. The mean IOP in males of control group were found to be higher (14 mm of Hg) as compared to females (13 mm of Hg), but this difference was not statistically significant. The average IOP was higher (16.64 mm of Hg) in case group as compared to control group (13.83 mm of Hg). These differences were statistically significant (P value < 0.0001). So according to our study intra ocular pressure (IOP) was higher in diabetic case as compare to control in both male and female sex. **[Table-5]**

TABLE.6- DISTRIBUTION OF CASE AND CONTROL ACCORDING TO CATARACT (LOCS-III)

Lens Opacity (grade)	No. of case (n=42)	No of control (n=42)
1	13	11
2	12	9
3	4	3
Total(1+2+3)	29	23
Chi-square- 1.817, D.f- 1, P-value > 0.05 [Not significant]		

In 42 diabetic cases, lens opacity present in 29 (69 %) cases while in control group it was present in 23(55%) eyes. This means the probability of development of cataract was higher in diabetic as compared to non-diabetic. **[Table-6]**

TABLE.7- : DISTRIBUTION OF CASES AND CONTROL ACCORDING TO RETINAL SENSITIVITY

PERIMETRY	CASE			CONTROL		
	M	F	Total	M	F	Total
Normal limit	5	5	10	20	13	33
Borderline / General reduction	6	3	9	2	3	5
Outside normal limit	15	8	23	2	2	4
Total	26	16	42	24	18	42
Sex diff-- Chi square X^2 (df=1) = 0.279 P value = 0.5976[Not significant]						
Group diff.-- Chi square X2 (df=1) = 6.151 P value = 0.0131 [Significant]						

In diabetic cases 23 out of 42 eyes (54.76%) had obvious area of reduced retinal sensitivity on the printout. In males 15 out of 26 eyes (57.69%) and in females 8 out of 16 eyes (50%) were found reduced retinal sensitivity. The difference between diabetic male and female were statistically not significant. In 42 control eyes, 4 eyes (9.52%) had obvious area of reduced retinal sensitivity on the printout. In males 2 of the 24 (8.34%) eyes and in females 2 of the 18 (12%) eyes were found to reduce retinal sensitivity. In our study 54% of diabetic patient suffer from significantly reduced retinal sensitivity as compared to only 9 % in control group. Retinal sensitivity was statistically lower (P value = 0.013) in diabetic case as compare to control. **[Table-7]**

Discussion:

In our observation out of 42 diabetic cases median visual aquity was 0.20 LogMar, ranging from 1.00(6/60) to -0.19(6/5) LogMar, 15 had normal vision (6/6) and 27 had decreased vision (<6/6) while in control group having same number of

cases median visual aquity was 0.15 LogMar, ranging from 1.00(6/60) to -0.19(6/5) LogMar, 23 had normal vision and 19 had decreased vision. This means in the diabetic person the probability of decreased visual aquity was statistically significant (P value = 0.0131) as compared to control.

In support of above findings, **Boel B. (2008)** stated that median visual aquity was -0.45 LogMar, ranging from 0.39(6/18) to -0.19(6/5) LogMar in study of 50 diabetic patients.[11]

Bengtsson B. (2005) resulted that visual acuity was significantly decreased by 0.02 LogMar with increasing severity of retinopathy in examination of 59 diabetic patients with different degree of retinopathy.[12]

In our study the average IOP was higher (16.64 mm of Hg) in case group as compared to control group (13.83 mm of Hg). The mean IOP in diabetic case of males were found to be higher (17 mm of Hg) as compared to the diabetic case of females (16.06 mm of Hg). The mean IOP in males of control group were also found to be higher (14.33 mm of Hg) as compared to females of control group (13.17 mm of Hg). So according to our study intra ocular pressure (IOP) was higher in diabetic case as compare to control in both man and women.

This result was supported by **Jain I S et al. (2013),** who recorded a higher mean intraocular pressure of 17.28 mm of Hg in diabetic eyes as compared to the mean of 14.9 mm of Hg in control eyes in 50 young diabetic and 30 normal controls of comparable age group.[13]

Becker et al. (1966) reported intraocular pressure greater than 20 mm of Hg in 21% and greater than 23 mm of Hg in 8% out of a study of 52 juvenile diabetics.[14]

Safir et al. (1966) reported intraocular pressure of over 22 mm of Hg in 29.7% and between 20-22 mm Hg in 20.3% from a study of 64 patients.[15]

Rajiv Raman et al. (2011) recorded a higher mean intraocular pressure of 14.88± 2.9 mm of Hg from cross-sectional evaluation of 1368 subjects, aged- 40 years, with type 2diabetes.[16]

Ida Dielemanns et al. (1996) reported that the presence of diabetes mellitus was associated with an overall rise in mean IOP of both eyes of 0.31 mmHg from examination of 4178 subjects having ages, 55 years and older.[17]

Anselm H. et al. (2003) resulted that an IOP >21 mmHg in black and in mixed (black and white) participants than in whites. Mean IOP in black participants increased by 2.5 (standard deviation, 3.9) mmHg over 4 years in population-based cohort study of 2996 persons residents of Barbados, West Indies, aged ≥40 years .[16]

Luis G. M. P. et al. (2015) evaluate the relationship between glucose levels and intraocular pressure (IOP) fluctuation in 17 nondiabetic and 20 diabetic subjects in two distinct situations: first, fasting for at least 8 hours and, second, postprandial measurements. Result showed that Postprandial IOP was significantly higher than baseline IOP in diabetic (17.8±0.80 mmHg) and non-diabetic patients (15.9±0.77 mmHg). There was a significant association between glucose levels variation and IOP change in both diabetic patients (R^2=0.540: P<0.001) and non-diabetic individuals (R^2=0.291: P<0.025). There is also a significant association between the baseline glucose levels and IOP change in diabetic group (R^2=0.445: P<0.001). So they concluded that there is a significant association between blood glucose levels and IOP variation, especially in diabetic patients.[18]

In our study out of 42 diabetic cases, lens opacity present in 29 (69 %) cases while in control group it was present in 23 (54.77 %) eyes. This means the probability of development of cataract was higher in diabetic as compared to non-diabetic.

So the above result was supported by **Li Li et al. (2014)** who showed that the risk of any cataract (AC) in Type-2 Diabetic patients was higher than that in non-diabetic subjects (Odd Ratio = 1.97, 95% Confidence Interval: 1.45-2.67, P value < 0.001) from meta analysis of 20837 subjects.[19]

Eydis Olafsdottir et al (2012) evaluate the prevalence and risk factors of lens opacities in 275 type 2 diabetes mellitus and 256 control population. The prevalence of significant cortical, posterior subcapsular and nuclear cataract was 65.5%, 42.5% and 48.0%, respectively, in the type 2 diabetes population. In the diabetic population, all types of cataract were likewise strongly associated with age (p < 0.0001), posterior subcapsular cataract with HbA1c (p = 0.0032), nuclear cataract with b 1993; 77: 726-730

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