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ASSOCIATION OF TYPE – II DIABETES WITH INTRA OCULAR PRESSURE: A CORRELATIVE STUDY

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ABSTRACT

Diabetes mellitus increases the susceptibility of the retinal ganglion cells to additional stresses which relate to OAG, such as elevated IOP. The present study aims at comparing IOP in patients of Type II diabetic patients with normal subjects; and correlate IOP among Type II diabetic patients in reference to their Age, Gender, BMI, Family History, Duration of Type II diabetes. This was a comparative cross sectional analytical study based on prospective observational study. The study was based primary data collected directly from the subjects. The study design involved 360 subjects, who shall be categorized into two groups, ie., experimental group comprised of Diagnosed Type II Diabetic patients and a healthy controlled group, non diabetic (n=150), which were compared with Group A on similar parameters. Tools used under the study include: Tonometry with Applanation tonometer, Gonioscopy, Ophthalmoscopy, Visual acuity, Slit lamp examination and Corneal Pachymetry. The Covariate Method include interview schedule/questionnaire. It comprised address, age, gender, duration of Type II Diabetes Mellitus, dwelling, past history, occupation, family history, personal history, drug history and ocular pathology. Height and weight was measured using light clothes and body-mass index was calculated as weight divided by squared height in meters. Blood pressure (BP) measurements were taken using the validated oscillometric device. Three measurements were taken at one-minute intervals. The mean of the two latest BP measurements was considered as the clinical BP. The software namely 'SPSS' was used for statistical purpose, computing required measures wherever applicable. The results show that Economic conditions of diabetic and non diabetic subjects are found significantly associated with their IOP. Height of diabetic patients is correlated with IOP of their right eye. The mean score of IOP among diabetic patients is more than non diabetic subjects. IOP right eye is highly and significantly correlated with IOP of left eyes.

KEYWORDS: Gonioscopy, Ophthalmoscopy, Visual acuity.

INTRODUCTION AND RELATED LITERATURE

Diabetes is known to cause microvascular damage and it may affect the vascular auto regulation of the retina and the optic nerve. The development of glaucomatous optic nerve damage, based on the visual field loss and/or the optic disc findings, is more likely to be associated with high intraocular pressure.[1] Besides an increased intra-ocular pressure (IOP), a disturbed microcirculation at the level of the optic nerve head, as well as a primary neurodegenerative component, are thought to contribute to glaucomatous optic neuropathy.[2] In addition to altering the vascular tissues, diabetes mellitus brings about a compromise on the glial and neuronal functions and the metabolism in the retina, which can make the retinal neurons including the retinal ganglion cells, more susceptible to glaucomatous damage.[3] Furthermore, diabetes mellitus increases the susceptibility of the retinal ganglion cells to additional stresses which relate to OAG, such as elevated IOP.[4] It seems reasonable to consider that poor glycaemic control in subjects with diabetes mellitus, with prolonged insult to the retina, would be associated with higher risk of OAG. Davies et al[5] (1984) reported that the glucose levels in the aqueous humor of patients with diabetes were significantly higher (3.2 mM vs. 7.8 mM) as compared to the glucose levels in persons without diabetes. Although the reason for the increased incidence of open-angle glaucoma in persons with diabetes has not been elucidated, it is likely that the diabetes associated changes in the trabecular extra-cellular matrix may contribute to a decreased aqueous outflow. A high glucose level induces fibronectin overexpression in the trabecular meshwork cells and may contribute to excess fibronectin accumulation in the trabecular meshwork. High glucose–induced fibronectin upregulation may be a common biochemical link that on the one hand, contributes to the development of thickened vascular basement membranes in diabetic microangiopathy and on the other hand, alters the structural content, compromises resiliency, reduces cellularity, blocks the aqueous outflow in the trabecular meshwork and leads to the development of POAG in persons with diabetes.[6]

In the study of Arora and Prasad[7] (1989), 60 diabetics were examined for intraocular pressure, scleral rigidity and facility of outflow. The intraocular pressure was found higher than in the general population except in patients with proliferative retinopathy. There was no marked difference in scleral rigidity in diabetics. The facility of outflow was lower in diabetic patients. Diabetes mellitus within the last four decades emerged as a major cause of blindness and visual disability not only in developed countries but also in developing countries. Diabetes, besides it other ocular manifestations also affected the intraocular pressure. Diabetics were more prone to have primary open angle glaucoma. The presence of glaucoma in diabetic patients seem to offer some protection from the development of proliferative retinopathy. However, it was not yet clearly established as to how diabetes affects intraocular pressure. The study was undertaken to review the possible relationship between ocular tension and diabetes. A total of 120 patients were included in the study. Out of these, 60 (120 eyes) were diabetics and rest were normal non diabetic persons forming a control group. All the patients were thoroughly examined. Besides careful tonometry, estimation of scleral rigidity and estimation of facility of aqueous outflow was done. Simultaneous blood sugar levels were also recorded. On the basis of ophthalmoscopy, patients were divided as diabetics with retinopathy and diabetics without retinopathy. The patients with retinopathy were further categorised into stage I, II, III (Background retinopathy) and IV (Proliferative retinopathy). The tonometery was done by a standard certified Schiotz tonometer. The same tonometer was used throughout the study. The coefficient of scleral rigidity was calculated by the table according to modified Firdenwald monogram. In the study, two paired readings of intraocular pressure were taken at 5.5gm and 10 gm. The value common to both readings in the table was the ocular rigidity for the eye. Tonography affords one of the most convenient methods for the estimation of outflow facility. It was performed by placing the Schiotz tonometer on the eye for a period of 4 minutes and recording the progressive indentations of the cornea by the plunger. The incidence of diabetic retinopathy was 43.33%. The mean Intraocular pressure in maturity onset diabetes is 19.26 mm which was higher than the normal mean intraocular pressure reported in the general population i.e. 16.1mm of Hg (Becker - Shaffer). In juvenile diabetics the mean intraocular pressure though lower (17.93mm Hg) than the mean LO.P in maturity onset diabetes, was higher, than normal average mean IOP. The finding indicated the higher mean IOP in diabetics as compared to the non-diabetic population. The mean IOP of diabetic eyes without retinopathy was 18.17 mm Hg while eyes with retinopathy was 19.99 mm Hg. The significant finding was the lower intraocular pressure (15.98 mm Hg) in proliferative retinopathy. The scleral rigidity in the majority of cases was within the range of 0.0200 to 0.02. It was in accordance with the normal scleral rigidity. In the study it was observed that scleral rigidity increased with the increase in age, in maturity onset as well as juvenile diabetes. Diabetes does not appear to affect it. The facility of aqueous outflow in normal persons was 0.28 ± 0.05 microlitre/min/mm Hg. In glaucoma it was reported to be 0.16 ± 0.01 microlitre/min/mm Hg. The value of outflow facility was 0.26 microlitre.min/ mm Hg in maturity onset and 0.24 microlitre/min/mm Hg in., maturity onset and 0.24 microlitre/min/mm Hg in juvenile onset diabetes. Thus the facility of aqueous outflow was low in diabetic patients as compared to the normal population. There was no significant difference in facility of outflow in diabetics with retinopathy and diabetics without retinopathy. However, when compared with non proliferative (Grade I, II, III) with proliferative retinopathy (Grade IV) there was a marked difference. The facility of outflow was lower in non-proliferative retinopathy while it was higher or similar to that of the non diabetic population in proliferative retinopathy.

Anandha et.al.[8] (2011) analyzed the relationship between intraocular pressure and type 2 diabetes mellitus and to investigate the effects of chronic hyperglycaemia on the intraocular pressure (IOP). The study prospectively measured the IOP by Schiotz tonometry in 100 normal subjects (Group I) and in 150 subjects with type 2 diabetes (Group II). None of the subjects with diabetes had diabetic retinopathy, secondary glaucoma or a family history of glaucoma nor did they undergo any ocular or laser therapy. The glycosylated haemoglobin (HbA1c) levels of the subjects with diabetes were determined and based on that, they were divided into 3 subgroups as group IIa with HbA1c levels of < 7% (n = 62); group IIb with HbA1c levels of 7 to 8.0% (n = 48); and group IIc with HbA1c levels of > 8.0% (n = 40) All the data were expressed as means Â± standard deviations. The study observed that the IOP values were higher in the subjects with diabetes (mean = 20.4 Â± 3.44) than in the age and sex matched control groups. The mean IOP in the groups IIa, IIb and IIc were 17.32 Â± 2.70, 17.81 Â± 2.76mm Hg, and 18.04 Â± 2.58 mm Hg respectively. The difference in the IOP between the groups IIb and IIc was found to be statistically significant (P = .001). The intra-ocular pressure was increased in the subjects with diabetes as compared to the controls and especially those subjects with a poor glycaemic control were more prone to develop an increased intra-ocular pressure.

OBJECTIVES

- To Compare IOP in patients of Type II diabetic patients with normal subjects.
- To correlate IOP among Type II diabetic patients in reference to their Age, Gender, BMI, Family History, Duration of Type II diabetes.

MATERIAL AND METHOD

This was a comparative cross sectional analytical study based on prospective observational study. The study was based primary data collected directly from the subjects. Written informed consent was obtained from all participants. Such data have proven helpful in understanding the association of IOP with diabetic and normal subjects. The present study was conducted in the Post graduate Department of Physiology in collaboration with the postgraduate department of ophthalmology in Government Medical College, Srinagar. For the purpose, Institutional Ethical Clearance was obtained through proper channel. The study was supposed to be completed within the period of 18 months. However, due to COVID pandemic, it took more than two years to complete the study. The study design involved 360 subjects, who shall be categorized into two groups, namely:

Group A: This was an experimental group comprised of Diagnosed Type II Diabetic patients. This study group was obtained from Outpatient Department(OPD) at Shri Maharaja Hari Singh (SMHS) Hospital, Srinagar (n=180). Patients who satisfied any one of the inclusion criteria were selected.

Group 2: This was a healthy controlled group, non diabetic (n=150), which were compared with Group A on similar parameters.

Inclusive and Exclusive Criteria: Men as well as women comprised the sample. The age group under study were adults Group A as well as for Group B. The inclusion criteria comprised: diagnosed Type II diabetic Patients; IOP > 21 mmHg (by Applanation Tonometry among Type II Diabetic subjects); and normal IOP with asymmetry of IOP in both eyes of > 5 mmHg. The exclusion criteria included: closed angle on gonioscopy; drug induced (corticosteroids); myopia; hypertension; any Ocular Surgery and other intra ocular pathology.

Techniques Used: Tools used under the study include: Tonometry with Applanation tonometer, Gonioscopy, Ophthalmoscopy, Visual acuity, Slit lamp examination, Corneal Pachymetry.

Covariate Methods Each participant underwent through an interview schedule/questionnaire. It comprised address, age, gender, duration of Type II Diabetes Mellitus, dwelling, past history, occupation, family history, personal history, drug history and ocular pathology. Height and weight was measured using light clothes and body-mass index was calculated as weight divided by squared height in meters. Blood pressure (BP) measurements were taken using the validated oscillometric device. Three measurements were taken at one-minute intervals. The mean of the two latest BP measurements was considered as the clinical BP.

Data Analysis: Under the study, the various parameters were evaluated in relation to diabetic and normal subjects. Content analysis using quantitative as well as qualitative approach was done to understand the research study. Data was scrutinised and analysed keeping objectives in view. The statistical analysis of data was done wherever applicable. Appropriate statistical techniques were employed in order to understand the problem under consideration and to draw the right inferences out of it. The software packages namely 'SPSS' was used for the purpose, computing required measures wherever applicable.

Interpretation

Table 1 shows the quantitative analysis of age. After adding all the ages of subjects, the mean of age was 45.66. Likewise, the age of subjects were divided into quartiles, which indicated the score of 31 under 25th percentile; score of 45 under 50th percentile and score of 60 under 75th percentile. The deviation taken by the data from the mean was 17.25.

The mean scores for the height were 5.44. Moreover, the height of subjects divided into quartiles indicated the score of 5.20 under 25th percentile; score of 5.40 under 50th percentile and score of 5.70 under 75th percentile. The deviation taken by the data from the mean was 0.34.

The mean scores for the weight were 67.45. The weight of subjects divided into quartiles indicated the score of 61 under 25th percentile; score of 68 under 50th percentile and score of 75 under 75th percentile. The deviation taken by the data from the mean was 9.

The mean scores for the BMI were 25.72. The BMI of subjects divided into quartiles indicated the score of 22.80 under 25th percentile; score of 24.20 under 50th percentile and score of 26 under 75th percentile. The deviation taken by the data from the mean was 13.75.

The mean scores for the duration of diabetes were 7.46. Besides, duration of diabetes of subjects divided into quartiles indicated the score of 5.00 under 25th percentile; score of 7.00 under 50th percentile and score of 10.00 under 75th percentile. The deviation taken by the data from the mean was 3.83.

The mean scores for the IOP of right eye were 17.87. Besides, IOP right eye of subjects divided into quartiles that indicated the score of 15 under 25th percentile; score of 18 under 50th percentile and score of 18 under 75th percentile. The deviation taken by the data from the mean was 5.67.

The mean scores for the IOP of left eye were 18.08. In addition, IOP left eye of subjects divided into quartiles that indicated the score of 15 under 25th percentile; score of 17 under 50th percentile and score of 20 under 75th percentile. The deviation taken by the data from the mean was 6.63.

Table 2 depicts the differences in the mean scores of age of diabetic and non-diabetic subjects. Diabetic subjects depict higher mean scores (M=57.05, SD= 11.34, N=

180) than non-diabetic subjects (M=34.29, SD= 14.43, N = 180). Furthermore, there are highly significant differences in the mean scores of diabetic and non-diabetic subjects, f (1,358) = 276.98, p=0.00.

Table 3 depicts the differences in the mean scores of height of diabetic and non-diabetic subjects through ANOVA. Non-diabetic subjects depict higher mean scores (M=5.47, SD= 0.31, N= 180) than diabetic subjects (M=5.47, SD= 0.31, N = 180). Moreover, significant differences were found in the mean scores of diabetic and non-diabetic subjects, f (1,358) = 3.59, p=0.05.

Table 4 depicts the differences in the mean scores of weight of diabetic and non-diabetic subjects through ANOVA. It was observed that Diabetic subjects depict higher mean scores (M=68.38, SD= 8.49, N= 180) than non-diabetic subjects (M=66.52, SD= 9.41, N = 180). In addition, significant differences were depicted in the mean scores of diabetic and non-diabetic subjects, f (1,358) = 3.88, p=0.05.

Table 5 depicts the differences in the mean scores of BMI of diabetic and non-diabetic subjects through ANOVA. Diabetic subjects depict higher mean scores (M=26.06, SD= 15.60, N= 180) than non-diabetic subjects (M=24.85, SD= 11.58, N = 180). Furthermore, there is non-significant differences in the mean scores of diabetic and non-diabetic subjects, f (1,358) = 1.45, p=0.22.

Table 6 portrays the differences in the mean scores of IOP Right Eye of diabetic and non-diabetic subjects through ANOVA. It was found that diabetic subjects depict higher mean scores (M=25.82, SD= 6.50, N= 180) than non-diabetic subjects (M=16.93, SD= 4.52, N= 180). In context to this, highly significant differences were seen in the mean scores of diabetic and non-diabetic subjects, f (1,358) = 10.24, p=0.00.

Table 7 reveals the differences in the mean scores of IOP Left Eye of diabetic and non-diabetic subjects through ANOVA. Diabetic subjects depict higher mean scores (M=22.96, SD= 8.31, N= 180) than non-diabetic subjects (M=16.21, SD= 3.49, N= 180). With reference to IOP Left Eye of diabetic and non-diabetic subjects, highly significant differences were found in the mean scores of diabetic and non-diabetic subjects, f (1,358) = 31.05, p=0.00.

Table 8 observes correlation of various variables under study. Age is positively and highly significantly correlated with weight of diabetic patients r=(180) = 0.287, p < 0.001. Age has also shown highly significant correlation with IOP left eye of diabetic patients r=(180) = 0.278, p < 0.000. Height is positively and highly significantly correlated with weight of diabetic patients r=(180) = 0.368, p < 0.000 and IOP right eyes of diabetic patients r=(180) = 0.140, p < 0.008. Weight of diabetic patients is positively and significantly correlated with their IOP of right eye, r=(180) = 0.120, p < 0.023. IOP right eyes of diabetic patients is positively and highly significantly correlated with their left eyes, r=(180) = 0.295, p < 0.000.

DISCUSSION

Although diabetes is associated with higher IOP values in most population studies, the underlying mechanisms are still unclear.[9-10] Recent studies have suggested that changes in corneal biomechanics (increased corneal hysteresis) in diabetic eyes would lead to overestimated IOP measurements.[11-13] However, it is not known whether variations in glucose levels could lead to IOP changes in diabetic and non diabetic individuals. As diabetes and glaucoma (or ocular hypertension) coexists in many patients, a better understanding about how variations in glucose levels can affect IOP changes would give additional information to the IOP assessment. The study of Quraishi[14] (1995) reveals that as age increases, intraocular pressure also increases, with an average of 0.28 mmHg per decade. Knowledge of the normal range of intraocular pressure in various age groups will help glaucoma screeners. This study also shows that moderate increase of IOP with age particularly among diabetic patients. Control of IOP is the mainstay of glaucoma therapy.[15-16] The present study shows significant differences in IOP of men and women subjects. While the study of Ejimadu et.al (2018)[17] reveal insignificant differences in IOP in males than females. Several studies have shown conflicting results; while some showed higher IOP in males[18-19] others showed higher values in females[20- 24] and some showed no association.[25-26] This study showed that the patients with diabetes had a significantly higher mean intra ocular pressure (IOP) than the non-diabetic persons and such difference is statistically significant. A significant difference in mean intraocular pressure was observed in patients with diabetes when compared with non-diabetic patients. Vidhya et. Al (2010) also revealed that the patients with diabetes had a significantly higher mean intra ocular pressure (IOP) than the non-diabetic patients and also in his study, there was statistically significant increase in mean intraocular pressure in the diabetic patients than non diabetic patients.[27] The results of present study are also similar with that of the study conducted by Neeetans et al in 1997.[28]

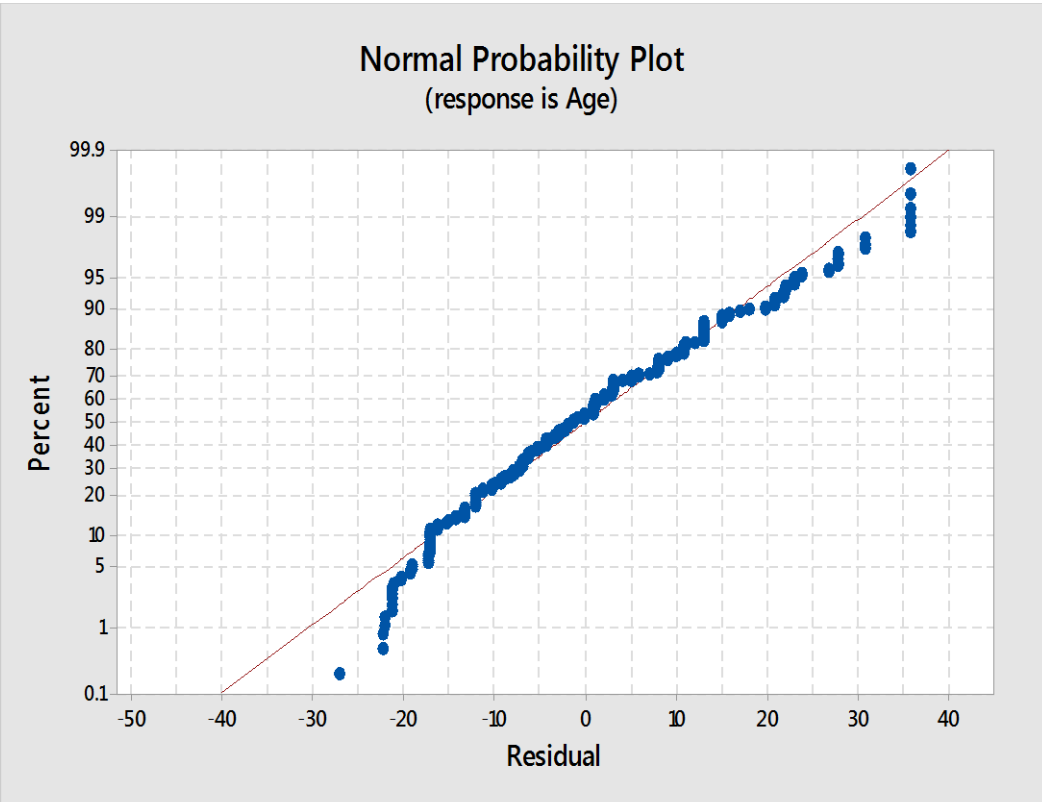
Various studies show mean IOP of patients from the urban area significantly higher than that of those from the rural area. However, present study shows insignificant IOP differences in rural and urban diabetic sample. This study indicates that the SES of patients influences the IOP among diabetic patients in context to their management decisions and the cost of glaucoma therapy. The study of Chakravarti (2018)[29] also observed a strong link between low SES and IOP among diabetic patients. Albuquerque showed in 2013 that there is no relationship between IOP and BMI in obese and non-obese children and in 2012. Geloneck also reported that there is no relationship between IOP and BMI in sitting position, but supine IOP correlated with high BMI. Iqbal et. al[30] showed that there is week relation between IOP and height. Similarly, Lai showed in 2005 that there is inverse relation between height and IOP. Another study carried out in 2013 showed no significance relationship between BMI and IOP, but significance relationship between BMI and age.[31-32]

Table 1: Quantitative Analysis of variables.

Analysis	Age	Height	Weight	BMI	Duration of Diabetes	IOP Right Eye	IOP Left Eye
N	360	360	360	360	360	360	360
Mean	45.669	5.4432	67.458	25.72	7.461	17.878	18.089
Standard Deviation	17.255	0.3406	9.003	13.75	3.833	5.672	6.636
Standard Error of Mean	0.909	0.0180	0.475	0.725	0.286	0.299	0.350
25th Percentile	31.000	5.20	61.000	22.80	5.00	15.00	15.00
50th Percentile	45.000	5.40	68.000	24.20	7.00	18.00	17.00
75th Percentile	60.000	5.70	75.000	26.60	10.00	18.00	20.00

Table 2: One Way ANOVA of Age with Diabetic and Non- Diabetic Subjects.

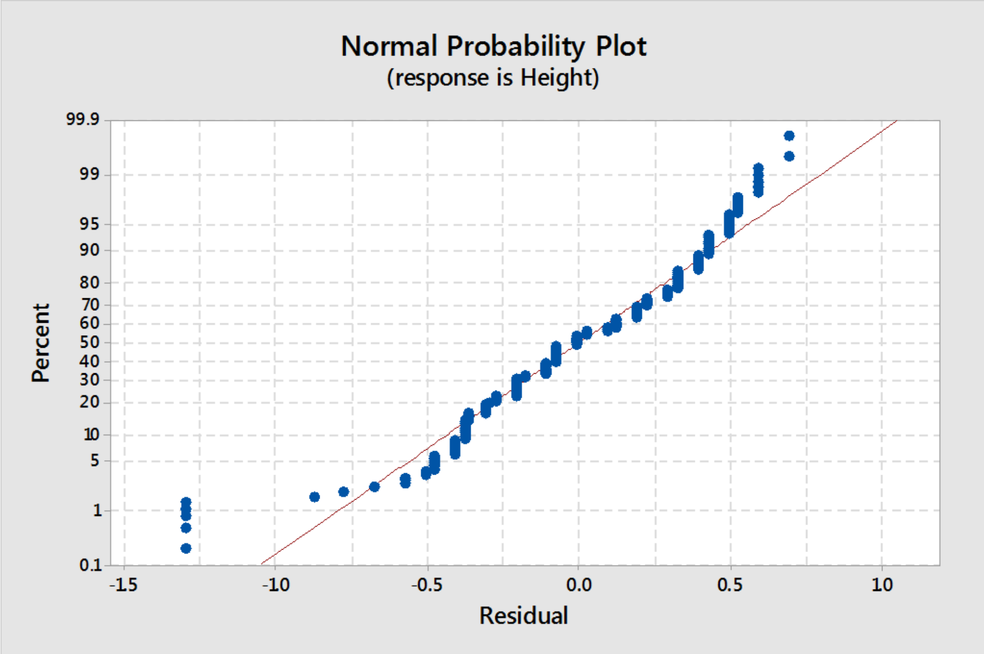
Variable	N	Mean	SD	95 % Confidence Interval for Mean		f-Value	df		p-Value
							Between Groups	Within Groups	
Diabetic	180	57.050	11.340	55.14	58.95	276.98	1	358	0.000
Non-Diabetic	180	34.29	14.43	32.39	36.19				



Significance level α = 0.05

Table 3: One Way ANOVA of Height with Diabetic and Non- Diabetic Subjects.

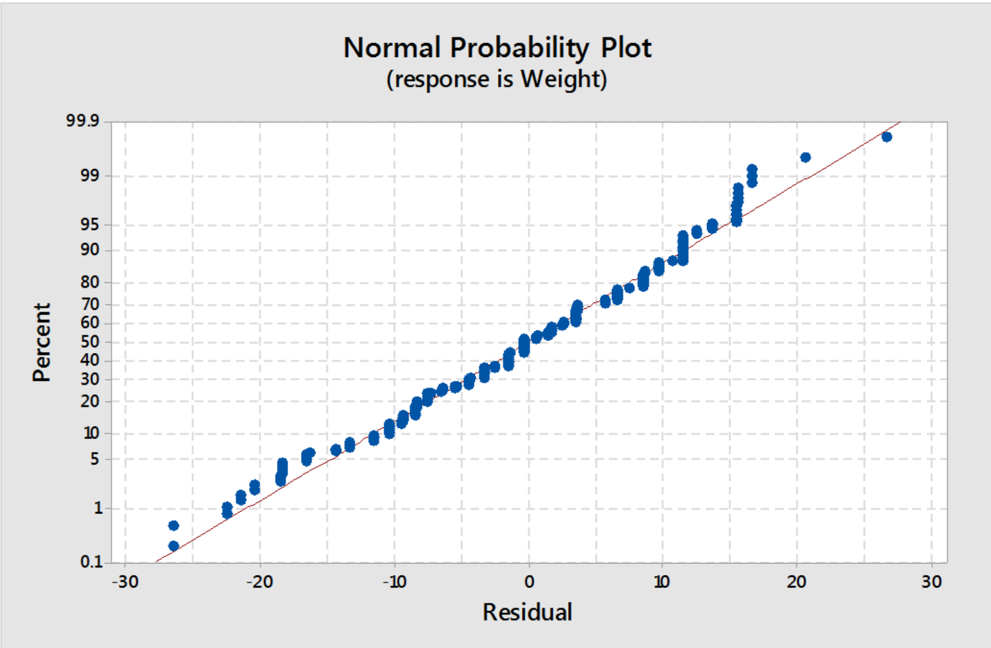
Variable	N	Mean	SD	95 % Confidence Interval for Mean		f-Value	df		p-Value
							Between Groups	Within Groups	
Diabetic	180	5.40	0.36	5.35	5.45	3.59	1	358	0.05
Non-Diabetic	180	5.47	0.31	5.42	5.52				



Significance level α = 0.05

Table 4: One Way ANOVA of Weight with Diabetic and Non- Diabetic Subjects.

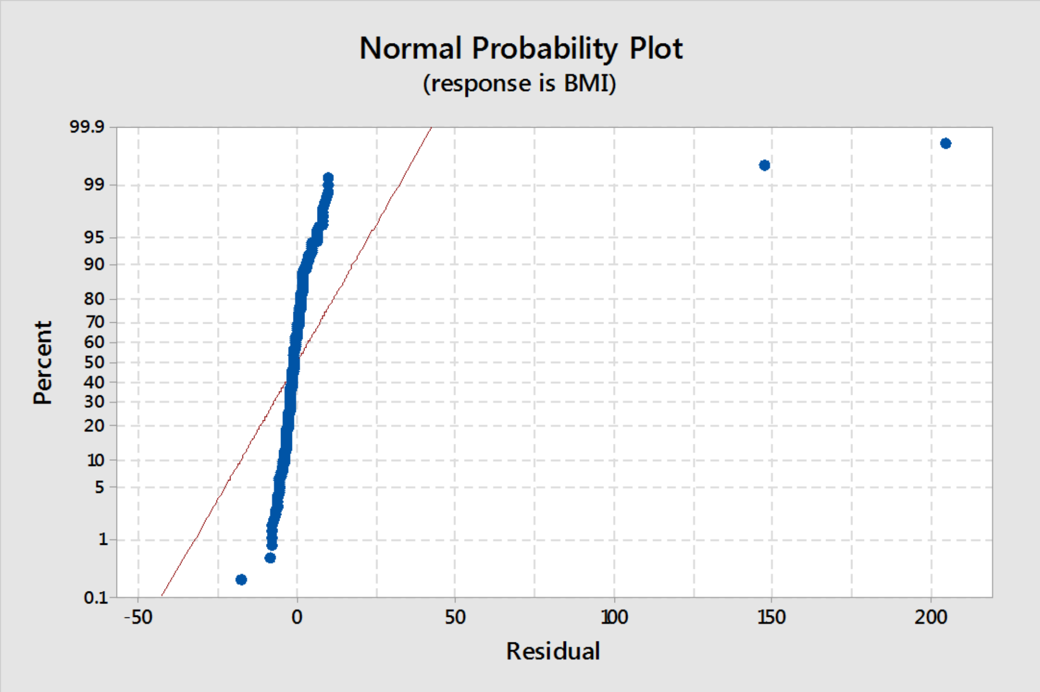
Variable	N	Mean	SD	95 % Confidence Interval for Mean		f-Value	df		p-Value
							Between Groups	Within Groups	
Diabetic	180	68.389	8.49	67.07	69.70	3.88	1	358	0.050
Non-Diabetic	180	66.528	9.41	65.21	67.84				



Significance level α = 0.05

Table 5: One Way ANOVA of BMI with Diabetic and Non- Diabetic Subjects.

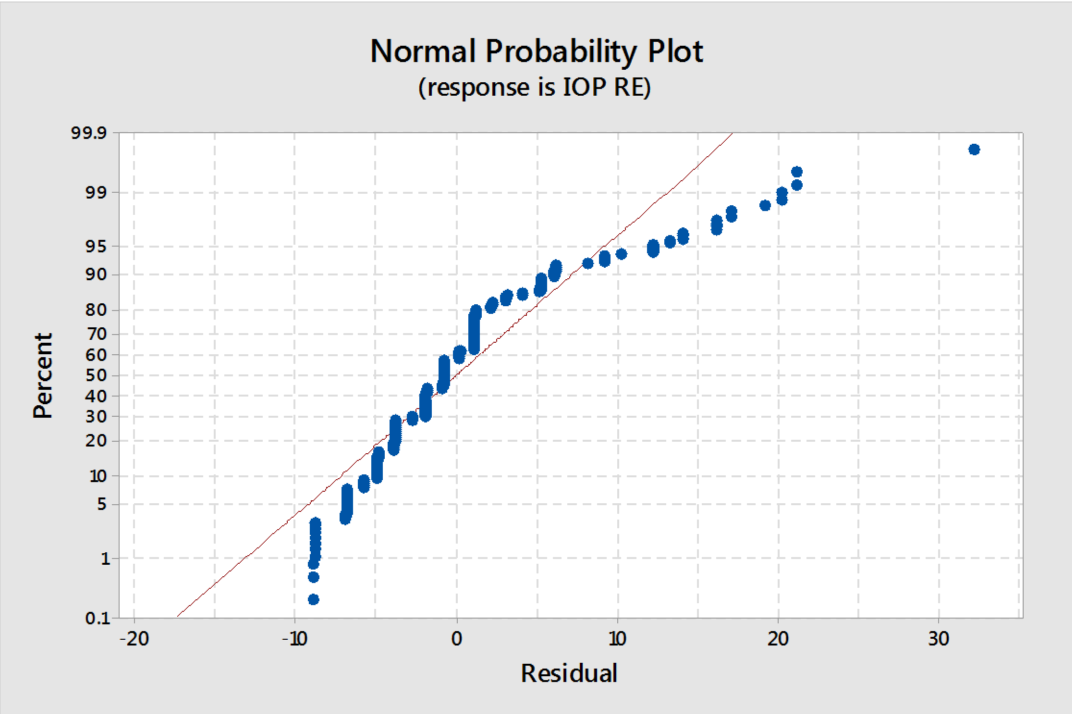
Variable	N	Mean	SD	95 % Confidence Interval for Mean		f-Value	df		p-Value
							Between Groups	Within Groups	
Diabetic	180	26.60	15.60	24.59	28.62	1.45	1	358	0.229
Non-Diabetic	180	24.85	11.58	22.84	26.87				



Significance level α = 0.05

Table 6: One Way ANOVA of IOP Right Eye with Diabetic and Non- Diabetic Subjects.

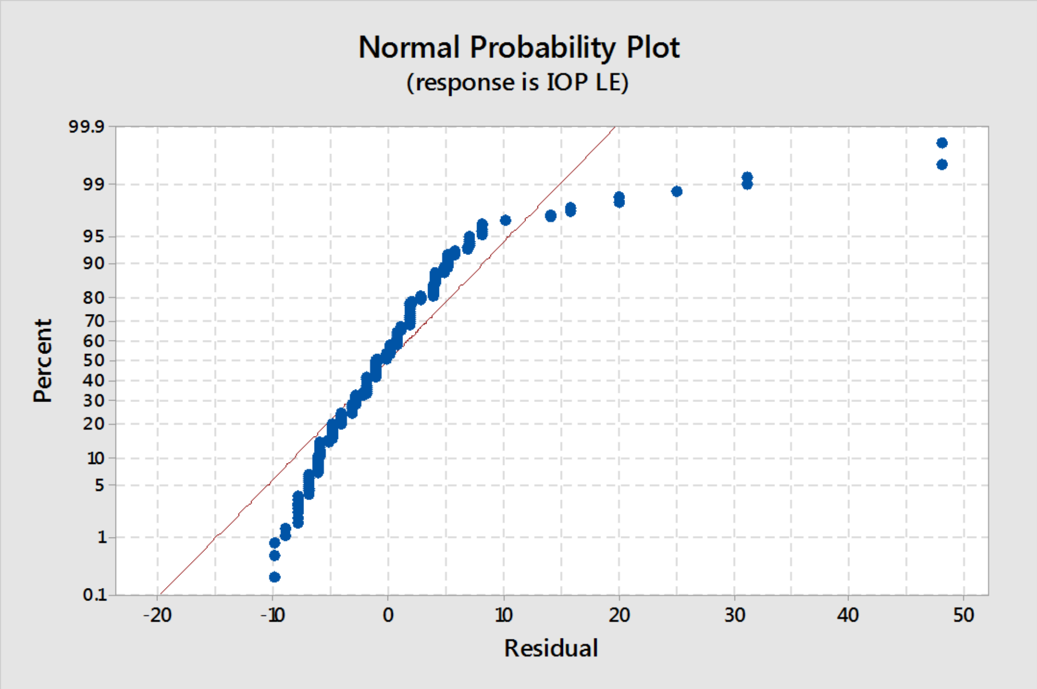
Variable	N	Mean	SD	95 % Confidence Interval for Mean		f-Value	df		p-Value
							Between Groups	Within Groups	
Diabetic	180	24.82	6.50	18.00	19.64	10.24	1	358	0.001
Non-Diabetic	180	16.93	4.52	16.11	17.75				



Significance level α = 0.05

Table 7: One Way ANOVA of IOP Left Eye with Diabetic and Non- Diabetic Subjects.

Variable	N	Mean	SD	95 % Confidence Interval for Mean		f-Value	df		p-Value
							Between Groups	Within Groups	
Diabetic	180	22.96	8.31	19.02	20.89	31.05	1	358	0.000
Non-Diabetic	180	16.21	3.49	15.28	17.15				



Significance level α = 0.05

Table 8: Correlation Analysis of Diabetic Patients.

Correlation (Pearson's)		Age	Height	Weight	BMI	IOP Right Eye	IOP Left Eye	Duration of Diabetes	SES
Age	R	-	0.62	0.287	-0.025	0.104	0.278	0.136	-0.003
	p-value	-	0.239	0.000	0.641	0.049	0.000	0.069	0.955
Height	R	0.062	-	0.368	-0.092	0.140	0.064	-0.065	0.060
	p-value	0.239	-	0.000	0.083	0.008	0.222	0.385	0.254
Weight	R	0.287	0.368	-	0.044	0.120	0.060	0.089	-0.019
	p-value	0.000	0.000	-	0.404	0.023	0.254	0.234	0.725
BMI	R	-0.025	-0.092	0.044	-	0.045	0.036	-0.089	0.022
	p-value	0.641	0.083	0.404	-	0.399	0.498	0.234	0.682
IOP Right Eye	R	0.104	0.140	0.120	0.045	-	0.295	-0.016	0.008
	p-value	0.049	0.008	0.023	0.399	-	0.000	0.830	0.880
IOP Left Eye	R	0.278	0.064	0.060	0.036	0.295	-	-0.085	0.058
	p-value	0.000	0.222	0.254	0.498	0.000	-	0.256	0.273
Duration of Diabetes	R	0.136	-0.065	0.089	-0.089	-0.016	-0.085	-	-0.051
	p-value	0.069	0.385	0.234	0.234	0.830	0.256	-	0.494
SES	R	-0.003	0.060	-0.019	0.022	0.008	0.058	-0.051	-
	P –value	0.955	0.254	0.725	0.682	0.880	0.273	0.494	-

SUMMARY AND CONCLUSION

Economic conditions of diabetic and non diabetic subjects are found significantly associated with their IOP. The mean age of diabetic patients is 57.05 years, which is significantly different from non diabetic subjects. The mean weight of diabetic patients is more than non diabetic subjects. Weight of diabetic and non diabetic subjects is statistically significantly different. Height of diabetic patients is correlated with IOP of their right eye. The mean score of BMI is significantly higher than mean scores of BMI among non diabetic subjects. Duration of diabetes among patients has revealed mean score of 4-8 years. Highly significant differences are observed in BP measurements of diabetic and non diabetic subjects. The mean score of IOP among diabetic patients is more than non diabetic subjects. IOP right eye is highly and significantly correlated with IOP of left eyes. High IOP is a major risk factor for glaucoma, it would be reasonable to speculate that similar associations for both conditions. However, the real association between these IOP-related risk factors and glaucoma still need further investigation.

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