Essay: Glaucoma, Diabetes mellitus and Intra ocular pressure

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TITLE: To assess the incidence of glaucoma and Correlation of Diabetes mellitus and Intra ocular pressure in the population of Western India.

ABSTRACT:
The aim of this study was to assess the relationship between Diabetes mellitus and Glaucoma by checking the association between blood sugar levels (BSL) and corresponding intraocular pressure (IOP) in diabetic and non-diabetic patients. Eighty two non-diabetic and Seventy one diabetic subjects were part of the study. The subjects underwent complete ocular examination. IOP using applanation tonometry, at Fasting and Postprandial was recorded. BSL at Fasting and Postprandial was measured by Glucose oxidase/ Peroxidase method. Postprandial IOP was significantly higher than baseline IOP in diabetic (18.01 ± 3.55 versus 15.07 ±...
3.23 mmHg; p < 0.001) and non-diabetic patients (14.58 ± 3.31 versus 12.06 ± 2.50 mmHg; p < 0.001). Postprandial BSL were significantly higher than baseline measurements in both diabetic (mean increase of 79.18 mg/dL; p < 0.001) and non-diabetic patients (mean increase of 20.48 mg/dL; p < 0.001). Correlative analysis showed a very statistically significant association between post-prandial BSL and post-prandial IOP in diabetic subjects with Pearson’s coefficient at 0.3728 (p<0.0001). For non-diabetic patients Correlative analysis showed a non-significant correlation with Pearson’s coefficient at 0.1739 (p<0.05). We concluded that there is a significant association between BSL and IOP variation, especially in diabetic patients.

INTRODUCTION:
Primary Open Angle Glaucoma (POAG) is a chronic, progressive optic neuropathy characterised by morphological changes at the optic nerve head and retinal nerve fibre layer in the absence of other ocular disease or congenital anomalies (with / without a raised IOP) [1]. It is the third leading cause of preventable blindness in India [2]. Glaucoma can remain asymptomatic until a severe stage, resulting in a high prevalence of undiagnosed glaucoma worldwide. Asia accounts for 60% of the world’s total glaucoma cases [3]. Although glaucoma is a multifactorial disease, elevated intraocular pressure (IOP) remains its major known risk factor [4,5]. Studies have demonstrated a significant role of IOP in progression of glaucoma [6,7]. IOP can be influenced by different systemic factors such as hypertension [8-10], atherosclerotic diseases [8], body mass index [11], and diabetes [8, 12, 13].

Diabetes mellitus is a group of metabolic diseases which is characterized by hyperglycaemia, resulting from defects in insulin secretion, insulin action, or both. Diabetes is one of the world’s greatest health challenges and a leading cause of morbidity worldwide [14]. India is the epicentre of the world’s diabetes epidemic [15]. It is already a world leader, with over 35 million people with diabetes – a number that is predicted to increase to around 80 million by 2030 [16]. Moreover, Asian Indians have an ethnic susceptibility to Type 2 Diabetes [17,18] and a familial aggregation of the disease [19,20].

The chronic hyperglycaemia in diabetes is associated with the long-term damage, dysfunction, and the failure of various organs, especially the eyes, kidneys, nerves, heart, and blood vessels, causing severe systemic complications such as retinopathy, neuropathy and nephropathy [21]. It is associated with complications which negatively influence both the quality of life and the survival of affected individuals [22]. Diabetic retinopathy (DR) is a common and serious condition associated with diabetes [23]. Diabetes also causes changes in corneal biomechanics.

Many studies have suggested an increase in the relative risk of people with diabetes mellitus to present ocular hypertension during the clinical course of the disease favouring the emergence of open angle glaucoma [13, 24]. However some studies failed to show any significant correlation between diabetes mellitus and intraocular pressure [25,26].

It has not yet been clearly established as to how diabetes affects the intra-ocular pressure. Studies suggest that diabetes may influence risk of Primary Open Angle Glaucoma (POAG) via hyperglycaemia-related vascular constriction leading to elevated intraocular pressure [27,28] and increased susceptibility to glaucomatous optic nerve damage [29]. According to Sato and Roy, high glucose levels in the aqueous humor of patients with diabetes may increase fibronectin synthesis and accumulation in the trabecular meshwork [30]. The accelerated depletion of trabecular meshwork cells is a characteristic feature of the outflow system in POAG [30]. Pasquale et al. noted the correlation between glycosylated haemoglobin and increased ocular pressure [24,31,32] and speculated that glycosylation of extracellular matrix proteins in the trabecular meshwork could further reduce outflow facility in patients with type 2 diabetes[31]. Therefore, relative obstruction of the outflow of aqueous humor via the trabecular meshwork may be a primary mechanism by which diabetes affects POAG risk.

Age factor has been given a lesser importance in most studies. However with increase in aging population, the trend of diabetes is expected to increase [33]. This in turn will increase the morbidity of population. Therefore an early intervention would be essential to reduce complications. Few studies have been conducted to study glucose variation and its impact on glaucoma. In our study we attempted to determine the relationship between glucose level variation and IOP fluctuation in diabetic and non diabetic patients. The correlation would facilitate screening procedures for early detection of glaucoma and in turn reducing morbidity. It can be developed as a tool for monitoring and recording disease progression.
MATERIALS AND METHODOLOGY:
An ethical approval from Institutional Ethics committee was taken before starting the study. Patients attending Medicine and Ophthalmology OPD of our Medical College & General Hospital were prospectively enrolled after applying the inclusion & exclusion criteria. Over a period of 2 months, 153 participants were enrolled in the study. Complete information of study was provided through a Patient Information Sheet and a Written Informed Consent was taken from each participant.
Inclusion criteria:
- Patients of age ≥ 18 years.
- Patients newly diagnosed as glaucoma.
- Patients fulfilling WHO criteria of clinical diagnosis of diabetes

CRITERIA FOR DIAGNOSIS OF DIABETES MELLITUS
Symptoms of diabetes plus random blood glucose concentration ≥ 200mg/dL
Fasting plasma glucose ≥ 126mg/dL
A1C > 6.5%
Two-hour plasma glucose ≥ 200mg/dL during an oral glucose tolerance test
- Healthy individuals were enrolled on basis of a self-reported history of normal glucose level in the past two years.

Exclusion criteria
- Recent ocular surgery done for causes other than glaucoma and cataract within last 6 months
- Secondary glaucoma
- Medications that would affect the Intraocular pressure (Steroids, antidepressants)
- History of endocrinial diseases.

Patients which were Type1 DM were excluded from study because of likely differences in the pathophysiology, risk of associated complications and duration of disease processes between Type1 DM and Type 2 DM.
All diabetic patients included in the study were on medication throughout the study period.
A detailed history followed by ocular examination including visual acuity, central corneal thickness, and visual field using automated perimetry was taken. Intraocular pressure (IOP) using applanation tonometry, at Fasting and post prandial was recorded. Blood sugar level at Fasting and Post prandial was measured by Glucose oxidase/ Peroxidase method (GOD/POD)
Statistical analysis was done using Student’s t test and Pearson’s correlation coefficient.

RESULTS:
A total of 153 patients (82 non-diabetic and 71 diabetic) were included. There were 94 female and 59 male patients in the study. Out of females 35 were diabetic and out of male 36 were diabetic.
Selected characteristics of the study are shown in Table 1. Postprandial IOP was significantly higher than baseline IOP in diabetic (18.01 ± 3.55 versus 15.07 ± 3.23 mmHg; p < 0.001 for right eye and 18.60± 3.72versus 15.79± 3.43 mmHg; p < 0.001 for left eye) and non-diabetic patients (14.58 ± 3.31versus 12.06 ± 2.50 mmHg; p < 0.001 for right eye and 14.98± 3.22 versus 12.69± 2.53mmHg; p < 0.001 for left eye).
Postprandial glucose levels were significantly higher than baseline measurements in both diabetic (mean increase of 79.18 mg/dL; p < 0.001) and non-diabetic patients (mean increase of 20.48 mg/dL; p < 0.001).
Correlation between BSL and IOP was done using Pearson’s Test. Correlative analysis showed a very statistically significant association between post-prandial blood sugar levels and post-prandial IOP in diabetic subjects with Pearson’s coefficient at 0.3728 (p<0.0001) for Right Eye and 0.3801 (p<0.0001) for Left Eye. For non-diabetic patients Correlative analysis showed a positive correlation with Pearson’s coefficient at 0.1739 (p<0.05) for the Right Eye and 0.1759 (p<0.05) for the Left Eye. However, it was not as significant as in the case of diabetic patients. This is shown in Table 2 and the scatter diagram is shown in Fig 2.
The correlation between post-prandial BSL and post-prandial IOP were marginally higher in females compared to males. The Pearson’s coefficient between post-prandial blood sugar levels and post-prandial IOP in females was 0.4825 (p<0.0001) for the right eye and 0.4905 (p<0.0001) for the left eye. The Pearson’s coefficient between post-prandial blood sugar levels and post-prandial IOP in males was 0.4658 (p<0.0001) for the right eye and 0.4718 (p<0.0001) for the left eye. This is shown in Table 3 and the scatter diagram in shown in Fig 3.
In our study, of the 71 diabetics evaluated, 2 developed glaucoma.
DISCUSSION:
Although several risk factors for the development of POAG have been evaluated, this is a field of ongoing investigation [48]. Diabetes has been positively correlated with glaucoma in many previous studies [13,24,33,45,46]. Several hypotheses have been established to explain the association between high glucose levels and IOP. Some researchers believe that genetic factors are associated in family history of diabetes [49]. Other researchers are of opinion that a diabetic person may have an autonomic dysfunction which would lead to an IOP increase [50]. However some authors believe that elevated blood glucose results in the induction of an osmotic gradient which leads to fluid shifts into the intraocular space [13].

Anadhi et al correlated glycosylated haemoglobinA1c (HbA1c) levels and IOP [45]. Their study concluded an increase in IOP in diabetic as compared to controls. Our study results are in agreement with their results. Postprandial IOP was significantly higher than baseline IOP in diabetic (mean IOP 18.01 versus 15.07 mmHg for right eye and 18.60 versus 15.79 mmHg for left eye). For ease of measurement in mass population, their study used Schiotz tonometry for IOP measurement. In our study we used applanation tonometry to measure IOP which is a GOLD standard.

Another study by Luis Guilherme et al [46] determined a significant correlation in fasting as well as post prandial variation among diabetics and non diabetics. Our findings are consistent with this study. Their study used peripheral glucose testing to determine blood glucose levels while our study used venous blood sampling. In our study we found a significant positive correlation of glucose variation and IOP in diabetics and non diabetic individuals. The Pearson’s coefficient for fasting blood sugar levels and fasting IOP was 0.3218 (p<0.0001) for Right Eye and 0.3161 (p<0.0001) for Left Eye. The Pearson’s coefficient for post-prandial blood sugar levels and post-prandial IOP was 0.4820 (p<0.0001) for the Right Eye and 0.4659 (p<0.0001) for the Left Eye.

In the Blue Mountain Eye Study[13], the authors attempted to study the relationship between diabetes and open-angle glaucoma and found that glaucoma prevalence was higher in diabetic patients compared to those without diabetes (5.5% versus 2.8%, OR = 2.12). Though our study does not determine the prevalence of glaucoma, it indirectly corroborates the results.

CONCLUSION:
Our study shows a significant positive correlation between blood glucose variation and IOP among diabetics and non diabetics. The post prandial glucose levels were also found to be significantly higher compared to baseline. This evaluation demonstrates the need for ophthalmic evaluation in consideration with blood glucose fluctuation, in diabetic individuals. The study also demonstrates a need for assessment of anti glaucoma medication efficacy in relation with glycemic control of patients.

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