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An evaluation of tear film and ocular surface changes in type 2 diabetes mellitus

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ABSTRACT

Aim

To compare tear film changes and ocular surface abnormalities in diabetics with that in non-diabetics.

Materials & methods

In this prospective case control study 100 eyes of 50 patients with Type 2 diabetes and 100 eyes of 50 normal patients were compared. All the patients were subjected to tear assessment tests- Schimers tests, Tear break up time tests in addition to Corneal sensitivity tests, CCT and CIS.

Conclusion

Our study showed that In Diabetics CCT was 560.14(SD 15.65) and Non diabetics was 534.14(SD 44.50) p value < 0.005.Corneal sensitivity measured by Cochet-Bonnet esthesiometer in diabetics was 26.08+/- 5.14mm and in Non diabetics was 53.58+/-2.06mm(p value <0.001).Tear break up time in diabetics was 6.8 +/-7.01 sec and in non-diabetics was 12.8+/-5.71sec(p value< 0.001).Total secretion by Schimers test was 7.77+/-3.9mm and basal secretion was 13.4+/-5.7mm(p value<0.001) . Conjunctival impression cytology revealed squamous metaplasia in diabetics as 1.25+/-0.63mm and in non-diabetics 0.65+/-0.57mm .Goblet cell density in diabetics was 429.68+/-108.35 cells/mmsq and in non-diabetics was 545.17+/-77.56cells/mmsq. Therefore diabetic patients with poor metabolic control and diabetic retinopathy should be assessed for tear film and ocular surface changes.

Keywords: Corneal sensitivity, Central corneal thickness

INTRODUCTION

Diabetes is one of the leading cause of non-communicable disease in the world. WHO has labeled India as the diabetic capital of the world. It has the highest number of diabetic patients in the world.Uncontrolled diabetes mellitus can lead to various ocular complications such as diabetic retinopathy (DR), cataract, glaucoma, keratopathy, refractive changes, palsy of the oculomotor nerve, and chronic inflammation of the lids. One of the most prevalent but undetected complication in eye

is the dry eye. Diabetic patients often complain of burning or foreign body sensation indicating a clear role of tear film abnormality. These patients are also more prone to decreased corneal sensitivity, superficial punctate keratopathy and persistent epithelial defects, cornealulceration, corneal endothelial damage.

Few studies have been done regarding the tear film abnormalities in diabetics and decrease in tear production has been reported, but the overall data is not conclusive. Moreover, the ocular surface examination is usually missed in diabetics and much importance is given to Diabetic retinopathy in routine practice.

Hence in this present study we investigated the changes of tear film and ocular surface in diabetic patients by corneal sensation, tear break up time (T-BUT) tear secretion test, and Conjunctival impression cytology (CIP), Central corneal thickness, (CCT) We compared the results with those in a control group.

MATERIALS AND METHODS

A Prospective Case Control Study of 100 patients consisting of 50 Type 2 diabetic patients and of 50 non diabetic patients attending Saveetha Medical College & hospital were taken up for study after applying the following inclusion and exclusion criteria ,to study the tear film and ocular surface changes, central corneal thickness in diabetics patients.

Inclusion criteria

All patients of either sex, in 35 to 75 yrs of age groups, diagnosed with Diabetes Mellitus Type 2.

Exclusion criteria

- Contact lens wearers
- Topical medication,
- History of ocular surgery within the previous 3 months,
- Abnormalities in the cornea, conjunctiva, or eyelid,
- And secondary ocular and systemic diseases were excluded from this study.

After obtaining informed consent, detailed history regarding patients name, age, sex, occupation, and presenting symptoms, duration, progression, and associated conditions were recorded. Detailed history regarding diabetes such as the duration, type of treatment, overall control in the past three months (HbA1c values if available), FBS and PPBS levels were recorded. Patients with a fasting blood glucose level of less than 110mg/dl and a glycosylated hemoglobin level of less than 7.8% were regarded as having good metabolic control.

Visual acuity using Snellens chart and near vision by Jagers near vision chart was done. Slit lamp examination to evaluate the tear meniscus< 2mm was considered abnormal and other clinical findings such as lens changes and pupillary abnormalities were also ruled out .Corneal sensation was measured using a Cochet-Bonnet esthesiometer. The tip of the fully extended nylon filament was applied perpendicular to the surface of the central cornea and advanced steadily.

When the subject felt its presence, the length of the filament was recorded in millimeters. A measurement of less than 45 mm was considered as low corneal sensitivity. Tear film BUT, Schirmer test without topical anesthesia (total tear secretion test), and Schirmer test with topical anaesthesia proparacaine 0.5 % (basal tear secretion test) were measured

A BUT value > 10 sec and a tear secretion value of <10mm by Schimers test were regarded as abnormal. Impression cytology was performed as follows.

After topical anesthesia with 0.5% proparacaine hydrochloride strips of cellulose acetate filter paper (6.2 mm diameter) were applied, dull side down, to the lower nasal bulbar conjunctiva adjacent to the corneal limbus. The filter strips were pressed gently with blunt, smooth tipped forceps for 2-3 seconds. They were then gently removed in a peeling motion, avoiding shearing.

A solution containing three parts acetone and one part of a mixture of 1/4 95% methanol and 3/4 95%ethanol was freshly prepared. Immediately after pressing the filter strips onto the slides, the slides were placed horizontally in a glass Petri dish for 3-4 hours in the above solution.

The slides were then fixed in absolute alcohol, stained with periodic acid- Schiff (PAS) and mounted. Degree of squamous metaplasia and goblet cell density was then estimated .Central corneal thickness by Pachymetry with normal range of (510 µm -520µm) was performed in all the patients followed by fundus examination and grading of Diabetic retinopathy by EDTRS classification.

The study was analyzed using SPSS software by Student t test and the analysis of non-parametric values were done by Mann Whitney U test. P value of < 0.005 was considered significant.

RESULTS

There were no significant differences in age or sex between the diabetic and normal control groups. All the patients were in the age group of 35 to 75 yrs of age.23 patients were on regular treatment and had a good glycemic control and 15 patients were on irregular treatment and 12 patients were not on treatment and gave history of poor diet control and lifestyle among the 50 diabetic patients. (Fig 1)

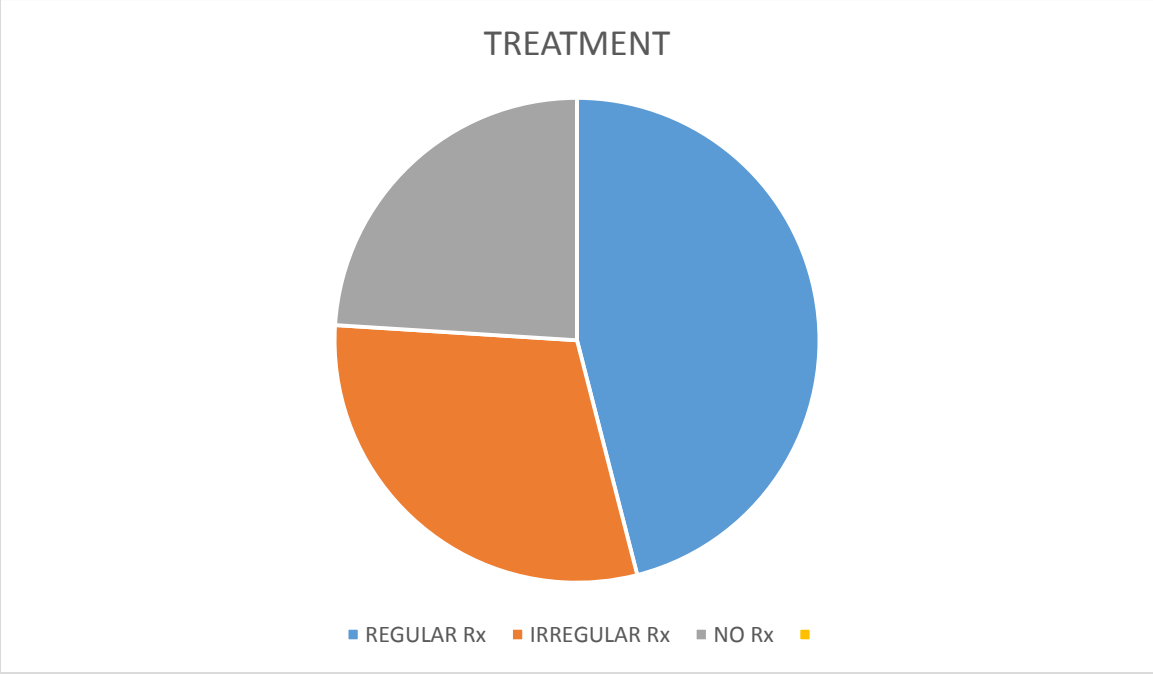

Fig 1

In Diabetics CCT was 560.14(SD 15.65) and Non diabetics was 534.14(SD 44.50) p value < 0.005.Corneal sensitivity measured by Cochet-Bonnet esthesiometer in diabetics was 26.08+/-5.14mmand in Non diabetics was 53.58+/-2.06mm(p value <0.001).Tear break up time in diabetics was 6.8 +/-7.01 sec and in non-diabetics was 12.8+/-5.71sec(p value< 0.001).Total secretion by Schimers test was 7.77+/-3.9mm and basal secretion was 13.4+/-5.7mm(p value<0.001) (Fig 2) .Conjunctival impression cytology revealed squamous metaplasia in diabetics as 1.25+/-0.63mm and in non-diabetics 0.65+/-0.57mm .(fig 3)Goblet cell density in diabetics was 429.68+/-108.35 cells/mmsq and in non-diabetics was 545.17+/-77.56cells/mmsq. (Table1). Fundus examination revealed that 21 patients had no evidence of diabetic retinopathy and 29 patients had diabetic retinopathy.

(Table 1)

DIABETIC	569.14 (SD 15.65)	26.08+/-5.14mm	6.8+/-7.01sec	7.77+/-3.9mm	3.82+/-2.22mm	1.25+/-0.63mm	429.68+/-108.35 Cell/mmsq
NON DIAB	534.14 (SD 45.50)	53.58+/-2.06mm	12.8+/-5.71sec	13.4+/-5.7mm	6.42+/-4.00mm	0.65+/-0.57mm	545.17+/-77.56 cells/ mmsq
P VALUE	<0.005	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

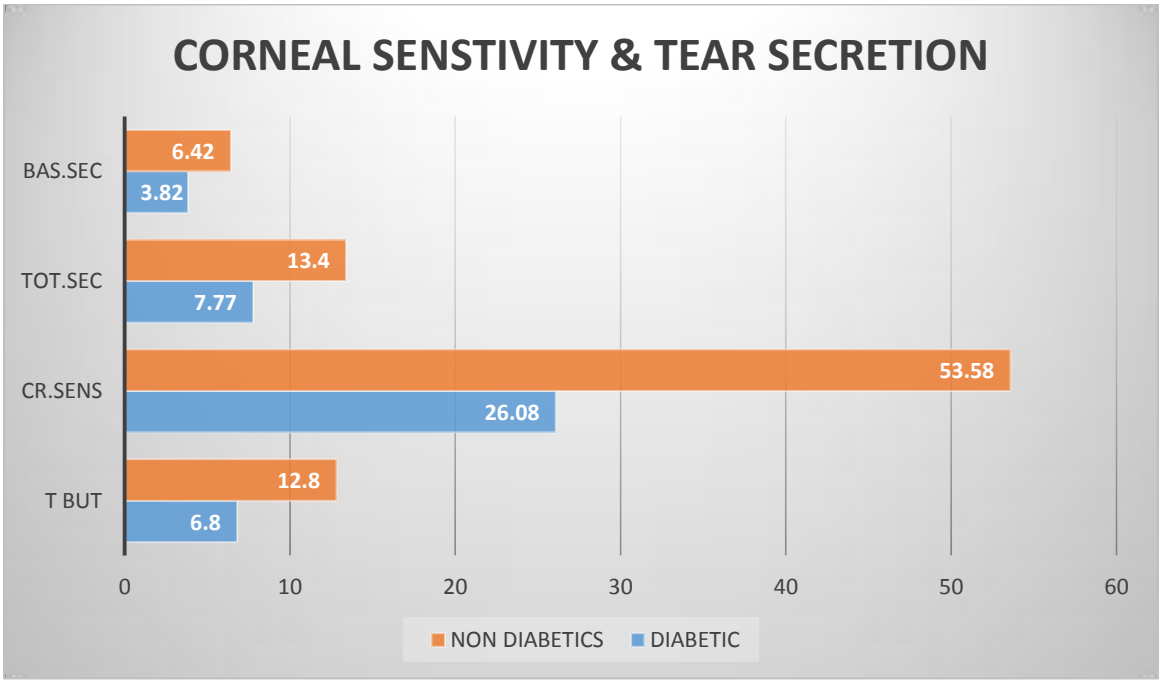

Fig 2

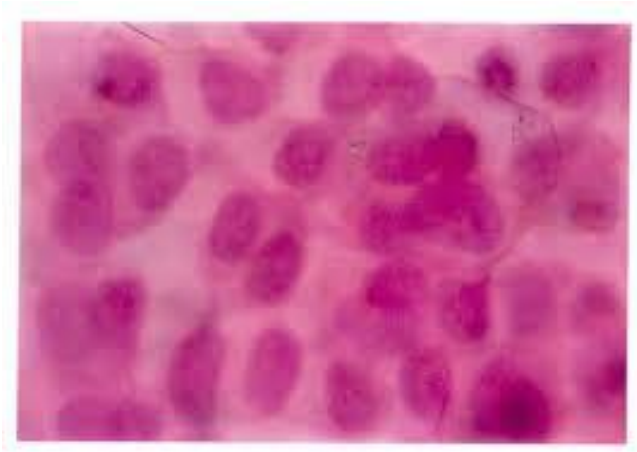

Fig 3 Conjunctival impression cytology showing squamous metaplasia of cells in non-diabetic patients

DISCUSSION

Decreased corneal sensitivity and tear secretion in diabetic patients occurs as manifestations of poor diabetic control, diabetic polyneuropathy which we noticed in our.

The decrease in tear film in total secretion is the first change of tear film when Diabetic retinopathy progresses. Schimers test and T BUT test were useful in detecting these changes. [10, 11].

GoebblesM, Dogru*et al* , Kenji I *et al* ,Ozdemir*et al* observed significantly decreased TBUT in the diabetics as compared to the non-diabetic group .We also obtained similar results in our study. The suggested theory is that amount of the reflextearing is lowered in the diabetics which may be due to diminished corneal and conjunctival sensations or maybe due to neuropathy involving the innervations of the lacrimal gland. [1]

The decrease in tear secretion and disturbed trophic function of tear film such as vitamin A and epithelial growth factors may induce chronic damage of the conjunctiva surface, resulting in conjunctivalmetaplsia. The goblet cells loss is a well-known sign of squamous metaplasia, along with the increase in cellular stratification and keratinization.The loss of neurotrophic effects

evidenced by corneal hyposthesia, fluctuation in glucose level and insufficiency of metabolic control may induce conjunctival squamous metaplasia. [2] The disturbance in trophic functions like vitamin A, vitamin A carrier, and epithelial growth factors present in tear film leads to chronictrophic damage to the conjunctival surface. The ocular surface changes found in the diabetics could partially be the result of a primary ocular surface disease or of metabolic alteration of conjunctival epithelial cells independent of the tear film abnormality. The concurrent involvement of the conjunctival and corneal epithelial surface may be viewed as a primary ocular surface disease. The mechanisms of these ocular surface changes during the course of the diabetes is not clear but tropic effects of trigeminal sensory nerves on the conjunctiva and cornea, may be responsible. [3] Fluctuating glucose levels may induce conjunctival squamous metaplasia in the diabetics leading to tear film instability.

In our study we found that diabetics had increased central corneal thickness when compared to non-diabetics. The probable mechanisimis advance glycation end products which form irreversible cross links with collagen resulting in increased thickness of cornea.

McNamara et al pointed that corneal structures are altered in diabetic patients suggesting that hyperglycemia affects control over corneal hydration, thus varying corneal thickness in diabetic patients. [4] Busted et al interpreted that increase corneal thickness is present during the early stages of the disease and may be one of the most noticeable clinical changes in diabetic patients. Lee et al stated that diabetic patients with a history of more than 10 years showed corneal morphological abnormalities compared to non-diabetics, Specially in terms of variability coefficients in cell size, thus finding a correlation between central corneal thickness and the duration of diabetes. [7, 8]

CONCLUSION

In our study we found that diabetic patients tend to have decreased corneal sensitivity, tear secretion due to diabetic polyneuropathy when compared to non-diabetics. Our study also indicates that squamous metaplasia and decreased goblet cell density occurs in diabetics.

We also found that Diabetics tend to have increased CCT values when compared to non-diabetics due to alteration in corneal physiology. Hence it is found that tear film and ocular surface changes are more common in diabetics and it is important to rule out these abnormalities in order to improve the ocular status of the patient.

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