THE INFLUENCE OF BLOOD GLUCOSE LEVEL ON TEAR BREAK UP TIME AMONG YOUNG ADULTS WITH DIABETES

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ABSTRACT

Background: It has been reported that diabetics are more likely to develop tear film dysfunction compared to non-diabetics. Even so, there has been very little research reported on the correlation between blood glucose level and quality of tears. **Objective:** The purpose of the study was to investigate the influence of blood glucose level on TBUT among young adults with diabetes. **Methods:** A cross-sectional study consisting of 37 diabetic patients within the age range of 19-39 years was carried out at International Islamic University Malaysia (IIUM) Optometry Clinic, Kuantan, Pahang, Malaysia. The subjects were tested for random blood glucose level (RBS) and undergone tear break up time (TBUT) test. Nonparametric test was used namely Spearman correlation to determine the association between RBS and TBUT. **Results:** TBUT median (interquartile range) value was 7.5 (11.55) seconds. Meanwhile, the negative association was found between (RBS) and TBUT in diabetics (r = -0.126). However, the correlation was not statistically significant (p>0.05). Tear film break up time was not associated with the random blood glucose level. **Conclusion:** Tear film break up time seems to be not affected by blood glucose level.

Keywords: *diabetics, glucose, tear film, stability, break up time*

INTRODUCTION

Over the years, the prevalence of diabetes has risen steeply across the globe. The global prevalence of diabetes mellitus (DM) among adults over 18 years of age has risen from 4.7% in 1980 to 8.5% in 2014. On the top of that, is expected that the prevalence of this disease will be doubled by the year 2030 (Roglig, 2016). Meanwhile, the prevalence of DM in Malaysia is also rising at an alarming rate of 9.9%, estimated to be increased to 12.3% by 2025, subsequently making it one of the worst affected countries in Asia (Whiting et al, 2011).

DM can lead to several ocular complications such as diabetic retinopathy, glaucoma, cataract, and ocular surface disease (Threatt et al, 2013). With the increasing number in diabetic population, people are beginning to be more concern on the effects of diabetes on the anterior instead of just the posterior part of the eye. Hence, anterior eye examination is suggested as part of routine test in clinical practice, particularly in diabetics. In severely high blood glucose level, the autonomic neuropathy is affected which causes declining of tears quality. This is due to increasing amount of glucose in tears which disturbs their normal chemical composition (Misra et al., 2014). Therefore, the current study investigated the correlation between blood glucose level and tear film stability.

MATERIALS AND METHODS

Subjects

This study was conducted from September to December 2016 at the Department of Optometry and Visual Science, IIUM Kuantan. Sample size was calculated using PS Software as suggested by the previous studies of Dogru, Katakami, and Inoue (2001) and Akinci, Cetinkaya, and Aycan (2007). The sample size calculated was 30 subjects, however, the authors managed to recruit 37 diabetic patients from the Hospital Kemaman, Hospital Tengku Ampuan Afzan (HTAA), and health centres nearby districts of Kemaman and Kuantan.

The inclusion criteria of the study were being diabetic and have follow ups visits to hospitals. Whereas, the patients suffering from any other ocular disease (cataract, strabismus) and history of taking regular ocular eye drops / antihistamines or medication prone to contracting dry eye were excluded from this study. The study protocol was approved by the local ethical clearance committees and conducted following the ethical guidelines of the Declaration of Helsinki. This research adhered to the ethical guidelines from IIUM Research Ethics Committee (IREC) and National Medical Research Registry (NMRR). All subjects were given informed consent to participate in the study.

Procedures

All measurements were made in one room with relatively constant temperature. Ambient temperature was $23 \pm 1.0°C$. Three measurements were made from each subject (each eye) and the average of the TBUT values were taken as the mean value. The TBUT was performed using fluorescein, which is instilled into the patient's eye and the patient was asked to blink several times. The stopwatch was started after the last blink and the appearance of dry spots on the corneal surface was observed with the cobalt blue filter. At the first appearance of the dry spots, the stopwatch was stopped and recorded. The time interval between the last blink and the first appearance of the dry spots was recorded in seconds as the TBUT. Random blood glucose level was measured using finger prick test. The finger was pricked, then a drop of blood was placed onto a glucometer strip and the concentration of random blood glucose was recorded in mmol/l.

Statistical Analysis

The statistical analysis was performed by using SPSS Software, Statistical Package for Social Science (version 12.0.1). Correlation between TBUT and blood glucose level was performed using Spearman rank correlation equation due to the non-normal variables. The values were consider significant at 95% confidence of interval (P< 0.05).

RESULTS

A total of thirty-seven diabetic subjects between age ranges of 19 - 39 years the (mean age of 33 ± 4.3 years) with were assessed. The Figure 1 shows that majority (89.2%) of the diabetics who were diagnosed to have DM for 10 years or less in duration. Whereas small numbers (11%) of the subject had DM for more than 10 years, a duration in which possibility of DR to occur.
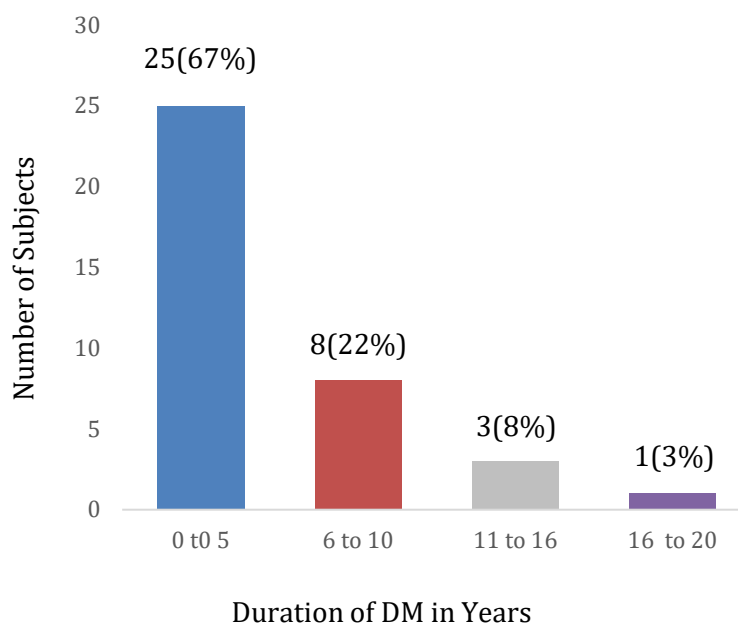

Figure 1 Distribution of subjects according to the duration of DM

The TBUT among the diabetics are within the range between 2.70 - 24.25 seconds with a median (interquartile range) value of 7.5 (11.55) seconds. As shown in the Table 1, that there was no association. Indeed, it was a weak negative correlation between the random blood sugar and the TBUT among diabetics being the r value -0.126. Therefore, it can be deduced that random blood glucose level does not influence the tear film break up time.

Table 1 The cross relations between TBUT and two studied variables (RBS and DM duration)

		RBS	DM duration
TBUT	Correlation coefficient	-0.126	-0.094
	p-value	0.459	0.579

The correlating analysis of the RBS with TBUT reveals that there was no association being the correlation coefficient r = -0.126) was presented. A Spearman correlation test also reported a not significant correlation (p = 0.579), negative correlation (r = -0.094) between duration of diabetes and

TBUT. A summary of the correlation between both TBUT and RBS; and TBUT and duration diabetes among young adult diabetics were illustrated in Figure 2 and Figure 3 respectively.
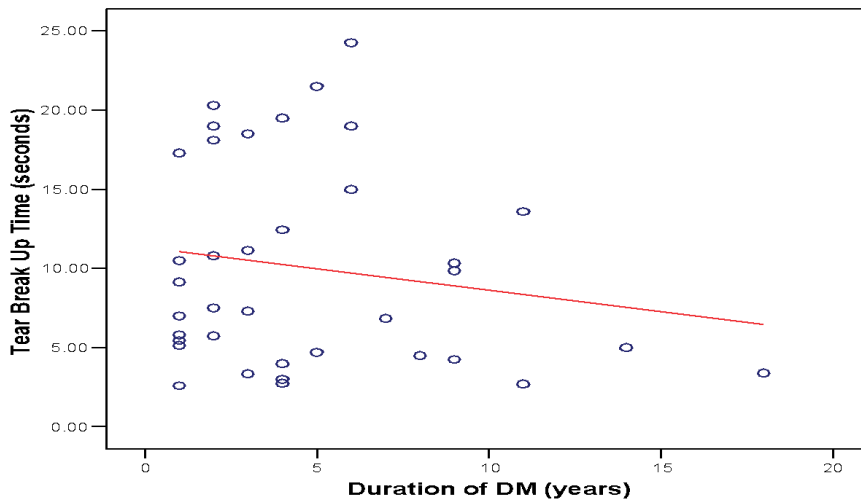

Figure 2 Correlation between TBUT and RBS

Figure 3 Correlation between TBUT and DM Duration

DISCUSSION

Diabetic patients demonstrated poor glycaemic control that can potentially affect the ocular surface integrity. Decrement in tear film stability is often manifested clinically by the low values of TBUT among diabetics compared to non-diabetics (Bal et al, 2014).

The result from this current study suggested that random blood glucose (RBS) may not have an impact on TBUT. This result is in agreement with a previous study by Goebbels (2000) which stated that there is no significant difference in TBUT between insulin dependent diabetics (IDDM) and normal group. However, there are several studies reporting a significant difference in TBUT

among diabetics and non-diabetics. Previous study by Pai Shobha (2014) and his co-researchers reported that the TBUT was reduced in diabetics compared to non-diabetics with a mean of 9.8s and 12.8s respectively. The decrement in the TBUT itself denotes the tear film instability in patients with poor glucose control. Besides, another study also revealed a statistically significant decrement in TBUT of the non-insulin dependent DM (NIDDM) in comparison to control group (Idu and Orge, 2010). Form these various findings, the influence of diabetes on TBUT is still debatable.

We speculate that the RBS did not influence the TBUT which further explained a non-significant association between TBUT and RBS. In this current study, we used RBS which is the most convenient to the subjects, which is the least powerful in diagnosing diabetics. The most accurate indicator method in diagnosing diabetes is Hba1c, followed by fasting blood glucose test and lastly RBS.

Previous study by Stratton et al. (2000) state that HbA1c has a strong predictive value for diabetes complications. However, HbA1c need a blood collection in a laboratory setting which was not available in this current study optometry clinic setting. Besides, an Hba1c or a fasting blood glucose test (FBG) requires the patient to fast one night prior to the eye-check-up, which is rarely practised by a patient in getting their primary eye check-up (first meeting). Hence, we had RBS, an available method for the regular optometry clinic setting. In addition, the RBS reflected on the regular patient faced by most optometry.

The non-significance of the association between RBS and TBUT from this study may have been due to the age disparity because many of previous studies were performed on elderly instead of young adult population (Idu and Orge 2010, Luping and Xinyi 2015, Eissa et al 2016). Previous study on age-related tear function changes among normal subjects revealed significant difference in TBUT between younger and older age group (Ozdemir and Temizdemir, 2010). The authors noticed that the tear film stability declined gradually as the age increases. The factors that lead to the decrement of TBUT with progression of age may vary. Firstly, the tear film might not be distributed evenly in older population due to the lessened lid laxity and disorder of the dynamics of eyelid closure. Secondly, it was suggested that elderly patients are more prone to have disorder of the lid margin morphology in addition to the deterioration of meibomian gland. As a consequence, tear film stability may become more unstable in elderly, leading to evaporative dry eye (Hykin et al 1992, Den et al 2006).

As mentioned earlier, tear film stability is more likely to reduce in patients with poor long term glycemic control. First, only about 11% of the subjects was diagnosed to have diabetes for more than 10 years. Legal blindness is more frequently reported in diabetics who have had diabetes for 15 years and above (Klein et al., 1983).Vision-threatening retinopathy is rarely reported in the first 3 to 5 years of diabetes (Fong et al., 2004). It was speculated that duration of diabetics in this current study was in early diabetes which was not comparable to majority of previous studies.

In addition, this study is limited in such a way that invasive technique of TBUT require the use of fluorescein, lack of standardization of fluorescein concentration and the possibility of reflex tearing which in turn may influence the result (Kojima et al 2004). Perhaps in the future, another non-invasive technique should be used such as tear thinning time (TTT), which is the time after the complete blink until the first distortion of the keratometer mire (Patel et al 1985). The research compared TTT with TBUT and found that TTT was shorter; assuming that the instillation of fluorescein somehow interferes with the measurement of TBUT.

Moreover, most of the clinical practice nowadays focused more on the posterior part of the eye when dealing with diabetes patient. Taking into considerations that blood glucose level does have an effect on the TBUT, the examination of the anterior ocular health should also be incorporated as well in the routine eye check-up in order to improve patient's lifestyle as well as to preserve the anterior ocular health.

Apart from that, there was none research done on the correlation between blood glucose level and TBUT among young adults in Malaysia. Thus, the findings from this research may help to improve the understanding on the influence of blood glucose level on TBUT.

CONCLUSION

This study shows that random blood glucose level does not have an effect on the tear break up time among young adults in Malaysia. However, it was observed that there is a fair negative correlation pattern despite not statistically significant. When comparing the median TBUT of diabetics in this study, it was found that the TBUT was slightly higher compared to previous study by AlJarousha et al. (2016).

ACKNOWLEDGEMENTS

REFERENCES

Akinci, A, E Cetinkaya, and Z Aycan. 2007. "Dry Eye Syndrome in Diabetic Children." *European Journal of Ophthalmology* 17 (6): 873–78.

Ali, B. M. (2013). Tear proteomics in young Malays with dry eyes. *The International Medical Journal of Malaysia*, 12(2).

Aljarousha, M., Badarudin, N. E., & Azemin, M. Z. C. (2016). Comparison of dry eye parameters between diabetics and non-diabetics in district of Kuantan, Pahang. *The Malaysian Journal of Medical Sciences: MJMS*, 23(3), 72.

Bal, C., Mukherjee, S., & Dan, S. (2014). Effect of Long Term Glycemic Control on Precorneal Tear Film in Diabetic Patients. *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 1(13), 51-53. DOI: 10.9790/0853-131115153

Den, S., Shimizu, K., Ikeda, T., *et al.* (2006). Association between meibomian gland changes and aging, sex, or tear function. *Cornea*, 25(6), 651-655. DOI: 10.1097/01.ico.0000227889.11500.6f

Dogru, M, C Katakami, and M Inoue. 2001. "Tear Function and Ocular Surface Changes in Noninsulin-Dependent Diabetes Mellitus." *Ophthalmology* 108 (3): 586–92. doi:S0161-6420(00)00599-6 [pii].

Eissa, I. M., Khalil, N. M., & El-Gendy, H. A. (2016). A Controlled study on the correlation between tear film volume and tear film stability in diabetic patients. *Journal of ophthalmology*. DOI: 10.1155/2016/5465272

Fong, Donald S., Lloyd Aiello, Thomas W. Gardner, George L. King, George Blankenship, Jerry D. Cavallerano, Iii Fredrick L. Ferris, And Ronald Klein. 2004. "Retinopathy in Diabetes" 27.

Goebbels, M. (2000). Tear secretion and tear film function in insulin dependent diabetics. *British Journal of Ophthalmology*, 84(1), 19-21. DOI: 10.1136/bjo.84.1.19

Henricsson, M., Nyström, L., Blohmé, G., *et al.* (2003). The incidence of retinopathy 10 years after diagnosis in young adult people with diabetes. *Diabetes care*, 26(2), 349-354. DOI:10.2337/diacare.26.2.349

Hom, M. & De Land P. (2006). Self-reported dry eyes and diabetic history. *Optometry*. 77(11):554-558. DOI:10.1016/j.optm.2006.08.002

Hykin, P. G., & Bron, A. J. (1992). Age-related morphological changes in lid margin and meibomian gland anatomy. *Cornea*, 11(4), 334-342. DOI: 10.1097/00003226-199207000-00012

Idu, F. & Orge, E. (2010). Tear secretion and tear film stability in Nigerians with non-insulin dependent diabetes mellitus. *African Vision and Eye Health,* North America, 69. DOI: 10.4102/aveh.v69i3.135

Klein, Ronald, Barbara E K Klein, and Scot E Moss. 1983. "Visual Impairment in Diabetes." *Ophthalmology* 91 (1). American Academy of Ophthalmology, Inc: 1–9. doi:10.1016/S0161-6420(84)34337-8.

Kojima, T., Ishida, R., Dogru, M., *et al.* (2004). A new noninvasive tear stability analysis system for the assessment of dry eyes. *Investigative ophthalmology & visual science*, 45(5), 1369-1374. DOI:10.1167/iovs.03-0712

Luping, W. & Xinyi, W. (2015). [Effect of glycosylated hemoglobin on dry eye in patients with type 2 diabetes mellitus]. Journal of Shandong University (otolaryngology and ophthalmology), 29(6): 71-73. [Mandarin].

Mengher, L.S., Bron, A.J., Tonge, S.R. & Gilbert, D.J. (1985). Effect of fluorescein instillation on the pre-corneal tear film stability. *Curr. Eye Res.* 4, 9e12. DOI: 10.3109/02713688508999961

Misra, S.L., Patel, D.V., McGhee, C.N., *et al.* (2014). Peripheral Neuropathy and Tear Film Dysfunction in Type 1 Diabetes Mellitus. *Journal of Diabetes Research.* DOI: 10.1155/2014/848659

Ozdemir, M., & Temizdemir, H. (2010). Age-and gender-related tear function changes in normal population. *Eye*, 24(1), 79-83. DOI: 10.1038/eye.2009.21

Pai Shobha G & Pai Sheila R. (2014). A comparative study of tear film function and tear secretion among diabetics. *International Journal of Bioassays*. 09: 3291-3296. DOI: 10.7439/ijbar.v2i7.39

Patel, S., Murray, D., McKenzie, A., Shearer, D.S. & McGrath, B.D. (1985). Effects of fluorescein on tear breakup time and on tear thinning time. *Am. J. Optom. Physiol. Opt*. 62, 188e190. DOI:10.1097/00006324-198503000-00006

Roglic, Gojka (2016). Global report on diabetes. WHO, Geneva. DOI:10.4103/2468-8827.184853.

Stratton, I. M., Adler, A. I., Neil, H. A. W., *et al.* (2000). Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *Bmj*, 321(7258), 405-412. DOI:10.1136/bmj.321.7258.405

Threatt, J., Williamson, J.F., Huynh, K. & Davis, R.M. (2013). Ocular disease, knowledge and technology applications in patients with diabetis. *Am J Med Sci*.;345:266-270. DOI: 10.1097/maj.0b013e31828aa6fb

Whiting, D. R., Guariguata, L., Weil, C., & Shaw, J. (2011). IDF diabetes atlas: global estimates of the prevalence of diabetes for 2011 and 2030. *Diabetes research and clinical practice*, 94(3), 311-321. DOI: 10.1016/j.diabres.2011.10.029