Prevalence and risk factors for short tear-breakup time dry eye disease in diabetics

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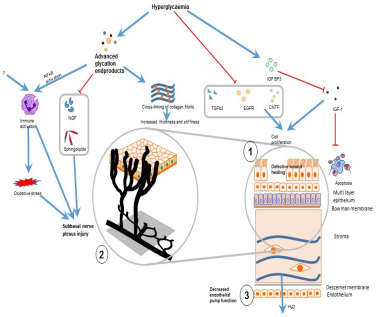
The authors have no relevant financial interests to declare for this study

Introduction

- In Hong Kong, it is estimated that one in ten people have T2DM - a number that is expected to increase with our aging population
- Among the many organs affected by T2DM, the involvement of the cornea is often under-appreciated, yet, it is an important area of focus because severe ocular surface disorder can be sight threatening and thus affecting all aspects of life and productivity
- The ocular and systemic factors affecting tear stability or short tear break up type of dry eye remains to be investigated

Aim

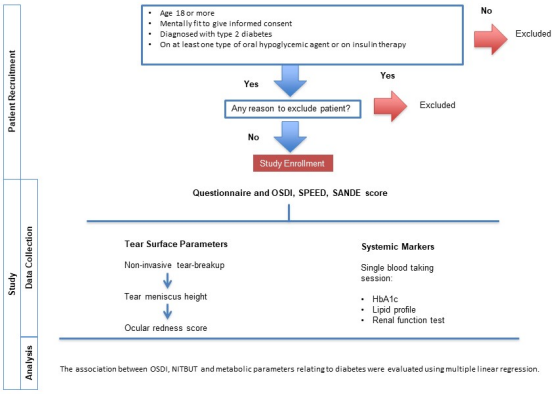
- To evaluate tear film stability and dry eye symptoms in diabetics
- To examine the **association** of systemic risk factors (e.g. long-term glycaemic control) on tear break up times and dry eye symptoms in diabetic patients



Schematic showing pathogenesis of corneal disease in diabetes mellitus. **1**. Defective wound healing in the corneal epithelium, **2**. Abnormalities of sub-basal nerves, and **3**. Loss of corneal endothelial pump function.

Methodology

- A **cross-sectional study was conducted in Hong Kong,** at the Lo Fong Siu Po Eye Centre (Grantham Hospital) from January to March 2017.
- **Eighty consecutive Chinese patients with type 2 diabetes mellitus (T2DM)** were recruited from the diabetes clinic of Queen Mary Hospital.
- Non-invasive tear film assessment was performed using the Oculus Keratograph 5M (Oculus Inc, Germany) to evaluate the non-invasive tear break-up time (NITBUT).
- Ocular symptoms were evaluated using the Ocular Surface Disease Index (OSDI).
- The association between OSDI, NITBUT and metabolic parameters relating to diabetes were evaluated using multiple linear regression.



Results

- Among the 80 patients (mean age 64.95 ± 10.97 years, 44% women), **40% (95% CI: 11-30%) had NIBUT ≤10 seconds**

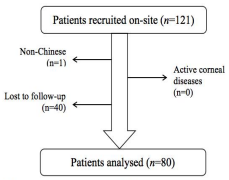


Figure 1. Illustration on exclusion process.

Demographics	n = 80
Age (years)	64 ± 11
Male, no. (%)	46 (57.5)

Clinical parameters	
LDL-C (mmol/L)	1.98 ± 0.68
HDL-C (mmol/L)	1.24 ± 0.36
Triglyceride (mmol/L)	1.57 ± 0.94
Creatinine (umol/L)	104.01 ± 101.97
eGFR (mL/min/1.73m²)	71.89 ± 25.14

Clinical parameters	
DM duration (years)	15.74 ± 9.97
HbA1c (%)	7.43 ± 1.33
Fasting blood glucose (mmol/L)	7.87 ± 2.30
BMI (kg/m²)	25.88 ± 3.98
Total Cholesterol (mmol/L)	3.93 ± 0.80

Eye-specific parameters	n = 80 (means, SD)
OSDI score	17.56 ± 18.50
SANDE score	22.70 ± 25.63
SPEED Score	5.91 ± 5.23
NITBUT (OD) (s)	7.58 ± 2.55
NITBUT (OS) (s)	7.80 ± 2.80

	Symptomatic for dry eye (OSDI ≥13)
NITBUT (s)	Proportions of diabetics (95% CI)
<5	0.20 (0.11, 0.30)
<7.5	0.29 (0.19, 0.39)
<10	0.40 (0.30, 0.51)

Abbreviations: Non-invasive tear break-up time (NITBUT); Ocular Surface Disease Index (OSDI); Confidence interval (CI).

- There were **significant inverse Pearson correlations between glycated haemoglobin (HbA1c) and NITBUT** (r=-0.314, P=0.007), and **a positive correlation between HbA1c and OSDI** (r=0.249, P=0.022).
- Stepwise multiple linear regression analysis confirmed HbA1c to be the only significant independent variable for NITBUT (R^2=0.099, P=0.014), and OSDI (R^2=0.062, P=0.044) after controlling for potential confounders.

Table 5. Results of stepwise multiple linear regression analysis of NITBUT and OSDI coefficient among Chinese type II diabetic subjects.

	NITBUT			OSDI		
	β	t	P-value	β	t	P-value
Age	-.196	-1.514	NS	.041	0.33	NS
Gender	-.017	-0.137	NS	.060	0.492	NS
Duration of DM	-.177	-1.354	NS	.017	0.132	NS
BMI	.009	0.076	NS	-.053	-0.431	NS
HbA1c	-0.314	-2.539	*	0.249	2.059	*
Fasting blood glucose	-.006	-0.035	NS	-.043	-0.315	NS
Total Cholesterol	-.034	-0.267	NS	.175	1.434	NS
LDL-C	-.169	-1.373	NS	.208	1.742	NS
HDL-C	.184	1.486	NS	-.093	-0.755	NS
TG	.041	0.325	NS	-.041	-0.332	NS
Creatinine	.011	0.082	NS	-.035	-0.283	NS
eGFR	.135	1.051	NS	.075	0.609	NS

Abbreviations: Non-invasive tear break-up time (NITBUT); Ocular Surface Disease Index (OSDI); Body mass index (BMI); Low-density lipoprotein cholesterol (LDL-C); High- density lipoprotein cholesterol (HDL-C); Triglyceride (TG); Estimated-glomerular filtration rate (eGFR).
* p<0.05; ** p<0.01, *** p<0.001; NS = not significant.

Significant inverse correlation between serum HbA1c level and non-invasive tear break-up time.

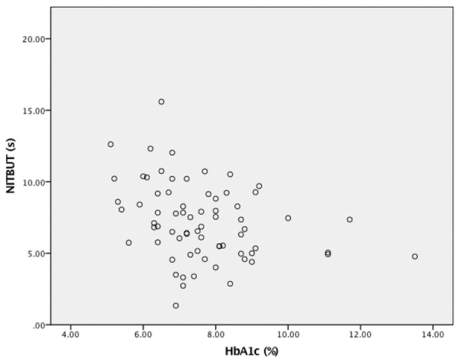


Table 6. The mean values and standard deviations of NITBUT and OSDI by HbA1c quartiles.

	NITBUT		OSDI	
HbA1c Quartiles	mean (s)	SD	mean	SD
1st Quartile	9.22	2.56	15.35	14.07
2nd Quartile	6.44	2.88	12.00	12.00
3rd Quartile	6.74	2.04	19.53	19.32
4th Quartile	6.38	2.09	17.20	17.21

Abbreviations: Non-invasive tear break-up time (NITBUT); Ocular Surface Disease Index (OSDI); Standard deviation (SD).

Summary of Results

- **High prevalence (40%)** of clinically significant tear film instability amongst Chinese T2DM patients in Hong Kong.
- **High level of HbA1c** predicts tear film instability (short tear break up time) and worse dry eye symptoms (high OSDI score).

Conclusions

- **Poor long-term glycaemic control** in T2DM patients **worsens tear film stability and dry eye symptoms**.
- Therefore just like in diabetic retinopathy care, ophthalmologists **should manage diabetic dry eye as a ophthalmic complication of a systemic disease**, with a more holistic approach, including
  - Long-term blood glucose control (HbA1c)
  - Symptomatic/ tear film oriented treatment for dry eye symptoms
- A potential area for research would be whether dry eye severity correlates with diabetic retinopathy grading

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