

ABSTRACT

Purpose: This study compared corneal endothelial changes in morphology and corneal thickness by specular microscopy of two groups of type I diabetes with and without diabetic retinopathy and were compared to a normal control.

Subjects and Methods: The study included 45 subjects aged 19-29 years old as follow, 15 eyes of 15 patients of type I diabetes without retinopathy (Group I), 15 eyes of 15 patients of type I diabetes with retinopathy (Group II), and 15 eyes of 15 normal persons matched with age and sex (Group III). Non-contact specular microscope (CEM-530, NIDEK) was used to assess the corneal endothelium for endothelial density, coefficient of variation in cell size, percentage of hexagonal cells, and central thickness of the cornea.

Results: There were a highly significant decrease in endothelial density (P value =0.002), and hexagonal cell percentage (P value =0.001) in diabetics comparing to normal control. Highly significant increased variation in cell size (P value =0.001), and corneal thickness (P value =0.001) were reported in diabetics rather than control. Diabetic retinopathy tends to have no impact on corneal endothelial morphology as endothelial density, variation in cell size, percentage of hexagonal cells, and corneal thickness.

Conclusion: Type I diabetes mellitus was found to affect corneal endothelial morphology as decreased endothelial cell density, hexagonal cell percentage and increased cell size variability impairing the endothelial function leading to increased central corneal thickness.

Keywords: Endothelial cell density (ECD), coefficient of variation in cell size (CV), percentage of hexagonal cells (HEX), and central thickness of the cornea (CCT).



**COMPARATIVE STUDY OF SPECULAR
MICROSCOPY IN TYPE I DIABETES WITH
AND WITHOUT DIABETIC RETINOPATHY
COMPARED TO NORMAL PERSONS**

Thesis

*Submitted for partial fulfillment of Master Degree
in Ophthalmology*

Presented by

Mohamed Hamdi Anwar Mohamed Mohamed
M.B.B.Ch

Supervised by

Prof. Dr. Abd El Rahman Gaber Salman

Professor of ophthalmology

Faculty of Medicine, Ain Shams University

Prof. Dr. Thanaa Helmy Mohamed

Assistant Professor of ophthalmology

Faculty of Medicine, Ain Shams University

Ass. Prof. Yousra Ahmed Thabet Farweez

Assistant Professor of ophthalmology

Faculty of Medicine, Ain Shams University

Faculty of Medicine,
Ain Shams University.

2018



مقارنة الفحص المجهرى البراق لخلايا بطانة القرنية في
مرضى السكري النوع الأول ممن لديهم اعتلال الشبكية
السكري وممن ليس لديهم اعتلال الشبكية السكري مقارنة
بالأشخاص الطبيعية

رسالة

توطئة للحصول علي درجة الماجستير في طب وجراحة العيون
مقدمة من

الطبيب/ محمد حمدي أنور محمد محمد
بكالوريوس الطب و الجراحة

تحت إشراف

أ.د/ عبد الرحمن جابر سالمان

أستاذ طب وجراحة العيون

كلية الطب- جامعة عين شمس

أ.د/ ثناء حلمي محمد

أستاذ طب وجراحة العيون

كلية الطب- جامعة عين شمس

د/ يسرا أحمد ثابت فرويز

أستاذ مساعد طب وجراحة العيون

كلية الطب- جامعة عين شمس

كلية الطب

جامعة عين شمس

٢٠١٨

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

لَسْبَدَانِكَ لَا عِلْمَ لَنَا
إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ
الْعَلِيمُ الْعَظِيمُ

صدق الله العظيم

سورة البقرة الآية: ٣٢



Acknowledgement

*First and foremost thanks to **ALLAH**, the Most Merciful.*

*I wish to express my deep appreciation and sincere gratitude to **Prof. Dr. Abd El Rahman Gaber Salman**, Professor of ophthalmology, Ain Shams University, for his close supervision, valuable instructions, continuous help, patience, advices and guidance.*

*I wish to express my great thanks and gratitude to **Prof. Dr. Thanaa Helmy Mohamed**, Professor of ophthalmology, Ain Shams University, for her kind supervision, indispensable advice and great help.*

*I wish to express my great thanks and gratitude to **Prof. Dr. Yousra Ahmed Thabet Farweez**, Assistant Professor of ophthalmology, Ain shams University, for her kind supervision, indispensable advice and great help in this work.*

Last and not least, I want to thank all my family, my mother, my father, my brother, my sister, my lovely wife and my colleagues, for their valuable help and support.

Finally I would present all my appreciations to my patients without them; this work could not have been completed.

CONTENTS

Subjects	Page
• List of Abbreviations	I
• List of Tables	II
• List of Figures	IV
• Introduction	1
• Aim of the Work.....	2
• Review of literature:	
Chapter 1: Structure and Function of the Cornea.....	3
Chapter 2: Assessment of Endothelial Structure and Function	12
Chapter 3: Diabetes Mellitus.....	20
• Patients And Methods.....	27
• Results.....	34
• Discussion.....	45
• Summary and Conclusion.....	48
• References	49
• Arabic Summary	-

LIST OF ABBREVIATIONS

ATP	: Adenosine Tri Phosphate
BCVA	: Best Corrected Visual Acuity
BM	: Bowman's layer
CCT	: Central Corneal Thickness
CL	: Contact Lens
CSME	: Clinically significant macular edema
CV%	: Coefficient of Variation
DALK	: Deep Anterior Lamellar Keratoplasty
DL	: Dua's Layer
DM	: Diabetes Mellitus
ECD	: Endothelial Cell Density
FFA	: Fundus Fluorescein angiography
Hco₃⁻	: Bicarbonate ion
HEX%	: Percentage of Hexagonal cells
IDDM	: Insulin Dependent Diabetes Mellitus
IOP	: Intra Ocular pressure
IRMA	: Intra-Retinal Micro Vascular Abnormalities
K⁺	: Potassium ion
Max	: Maximum cell size
Min	: Minimum cell size
Na⁺	: Sodium ion
NIDDM	: Non-Insulin Dependent Diabetes Mellitus
NPDR	: Non- Proliferative Diabetic Retinopathy
NVD	: Neovascularization of Disk
NVE	: Neovascularization Elsewhere
PDR	: Proliferative Diabetic Retinopathy
PMMA	: Polymethyl Methacrylate
PRK	: Photo Refractive Keratectomy
SD	: Standard Deviation
UCVA	: Uncorrected Visual Acuity
WHO	: World Health Organization

LIST OF TABLE

<i>Tab. No.</i>	<i>Subject</i>	<i>Page</i>
Table (1)	Contact vs non-contact Specular microscopes.	13
Table (2)	Endothelial cell density in different ages.	16
Table (3)	Description of personal data among group I cases	34
Table (4)	Description of disease duration and side of examined eye among group I cases.	34
Table (5)	Description of clinical data among group I cases	34
Table (6)	Description of personal data among group II cases	35
Table (7)	Description of disease duration and side of examined eye among group II cases.	35
Table (8)	Description of clinical data among group II cases	35
Table (9)	Description of personal data among study group III.	36
Table (10)	Description of side of examined eye among group III.	36
Table (11)	Description of clinical data among group III.	36
Table (12)	Comparison between the three study groups as regard personal data.	37
Table (13)	Comparison between the three study groups as regard side of examined eye.	38
Table (14)	Comparison between the three study groups as regard clinical findings.	38
Table (15)	Comparison between group I and group II as regard diabetes duration.	40
Table (16)	Comparison between group I and group II as regard clinical findings.	41
Table (17)	Complete group I data.	43
Table (18)	Complete group II data.	43
Table (19)	Complete group III data.	44

LIST OF FIGURES

<i>Fig. No.</i>	<i>Subject</i>	<i>Page</i>
Fig. (1)	Microscopic layers of the cornea.	3
Fig. (2)	Corneal epithelial layer.	5
Fig. (3)	Dua's Layer.	6
Fig. (4)	Confocal Microscopy of normal endothelium.	8
Fig. (5)	Pleomorphism.	9
Fig. (6)	Polymegathism.	9
Fig. (7)	Mechanism of corneal swelling	10
Fig. (8)	Corneal endothelial pump.	11
Fig. (9)	Optical principle of the specular microscope.	16
Fig. (10)	Endothelial cell density by specular microscopy.	15
Fig. (11)	Factors that compromise the corneal endothelium.	16
Fig. (12)	Corneal guttata.	17
Fig. (13)	Fuchs endothelial dystrophy.	18
Fig. (14)	Endothelium of a 55-year-old woman with a 30-year history of gas-permeable contact lens wear.	19
Fig. (15)	Microaneurysms, dot and blot haemorrhages.	22
Fig. (16)	FFA shows scattered hyperfluorescent spots.	23
Fig. (17)	Intra retinal microvascular abnormality.	24
Fig. (18)	Venous Beading.	24
Fig. (19)	Proliferative diabetic retinopathy with severe NVD.	25
Fig. (20)	Clinically significant Macular Edema.	26
Fig. (21)	CEM-530 NIDEK SPECULAR MICROSCOPE	28
Fig. (22)	Specular photomicrograph of right eye of 24 years old type I diabetic male patient without retinopathy.	29
Fig. (23)	Specular photomicrograph of left eye of 23 years old type I diabetic female patient without retinopathy.	29
Fig. (24)	Specular photomicrograph of left eye of 24 years old type I diabetic male patient with retinopathy.	30
Fig. (25)	Specular photomicrograph of right eye of 27 years old type I diabetic female patient with retinopathy.	30
Fig. (26)	Specular photomicrograph of right eye of 19 years old normal male person.	31
Fig. (27)	Specular photomicrograph of right eye of 19 years old normal male person.	31

List of Figures

<i>Fig. No.</i>	<i>Subject</i>	<i>Page</i>
Fig. (28)	Diagram compares age between group I, group II and group III.	37
Fig. (29)	Diagram compares ECD between group I, group II and group III.	39
Fig. (30)	Diagram compares CV% and Hex% between group I, group II and group III.	39
Fig. (31)	Diagram compares CCT between group I, group II and group III.	40
Fig. (32)	Diagram compares ECD between group I and group II.	41
Fig. (33)	Diagram compares CV% and Hex% between group I and group II.	42
Fig. (34)	Diagram compares CCT between group I and group II.	42

INTRODUCTION

Type I diabetes is an autoimmune destruction of the pancreatic beta cells altering cellular metabolism in the body due to insulin deficiency. Its incidence ranges about 0.2% in children and adolescents. (*Misra et al., 2016*) (*El-Ziny et al., 2014*)

Long standing diabetes affects ocular metabolism and may leads to many complications as cataract, glaucoma, diabetic retinopathy. Early detection of corneal endothelial dysfunction is important particularly as it affects young patients. (*Geloneck et al., 2015*)

Corneal endothelium is formed of non-regenerating hexagonal cells which maintain the corneal transparency and keep stromal hydration level at 78% of water through pumping water from stroma to the aqueous humor. (*Benetz et al., 1999*).

Specular microscopy provides a non-invasive method of morphological analysis of the corneal endothelium which provides an index of the functional status of this layer. (*Sheng and Bullimore, 2007*).

AIM OF THE WORK

Our study aimed to compare changes in corneal endothelium by specular microscopy of two groups of type I diabetes with and without diabetic retinopathy compared to a control group.

STRUCTURE AND FUNCTION OF THE CORNEA

Anatomy

Cornea is a transparent anterior one-sixth of the outer tunic of the eye ball. It is composed of 6 layers from front to back: epithelium, bowman's layer, stroma, dua's layer, descemet's membrane, and endothelium. (**Fig.1**)

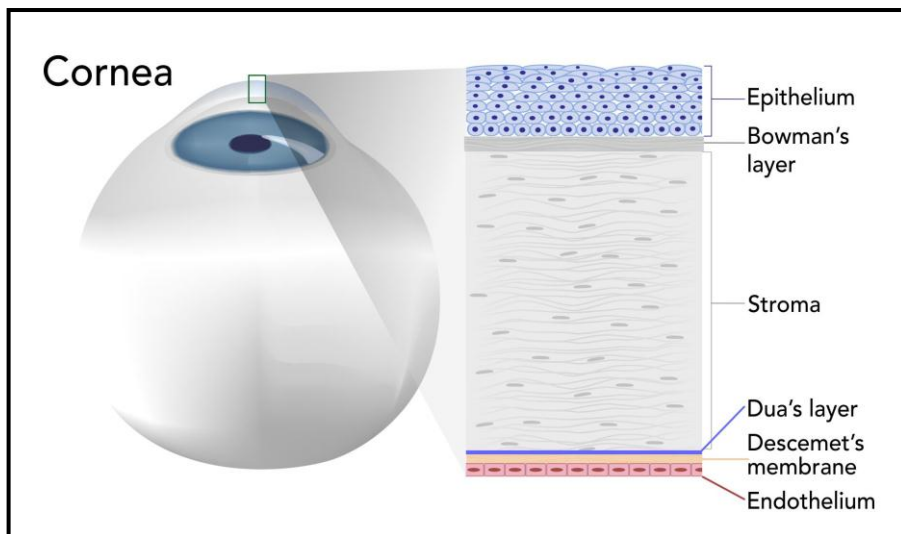


Fig. (1): Microscopic layers of Cornea (*Harminder and Lana, 2013*)

Corneal anatomy :***Epithelium:***

Non-keratinized, Stratified squamous epithelium, 4–6 cell layers thick (40–50µm) which is divided morphologically into three layers: the superficial squamous cell layer, the middle wing cell layer, and the deep basal cell layer. The superficial cells form an average of 2-3 layers of flat cells joined laterally by tight-junctions which restrict entry of tears into the intercellular spaces. The most superficial cells have apical microvilli characterize their cell membranes, which in turn are covered by tear film. The tear film of 7 µm thickness is optically important in smoothing out micro irregularities of the anterior epithelial surface (*Ayad and Mark, 2008*).

Wing cells form 2–3 cell layers; Cells are less flat than the overlying superficial cells, but possess similar tight, lateral, intercellular junctions (*Jay et al., 2011*).

The basal cell layer is composed of a single-cell layer of columnar epithelium. Basal cells are the only corneal epithelial cells capable of mitosis. They are the source of both wing and superficial cells, and possess lateral intercellular junctions characterized by gap junctions and zonulae adherens. The basal cells are attached to the underlying basement membrane by an extensive hemidesmosomes *Fig (2)* (*Jay et al., 2011*).

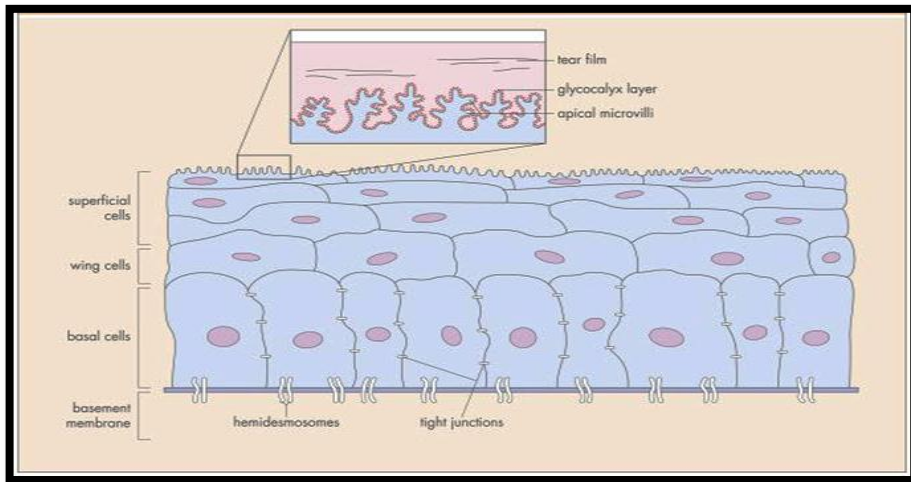


Fig. (2): Corneal epithelial layer (*Myron and Jay, 2014*).

Bowman's membrane (BM):

The uppermost part of the corneal stroma, which is an acellular, unorganized fibrils of collagen types I, III, V, and VI, and is about 8-12 μm thick (*Marshall, Konstas, and Lee, 1993*).

Stroma:

The stroma constitutes more than 90% of the corneal thickness. It is responsible for corneal physical strength, stability of shape, and transparency. The uniform arrangement and continuous slow turnover of collagen fibers in the stroma are essential for corneal transparency (*Jay et al., 2011*).

Collagen constitutes more than 70% of the dry weight of the cornea (*Jay et al., 2011*). The stromal collagen fibrils, which provide the major tensile strength to the