EVALUATION OF CENTRAL CORNEAL THICKNESS AND CORNEAL TOPOGRAPHY IN CHILDREN WITH VERNAL KERATOCONJUNCTIVITIS

DR MOHD ALIF BIN W MOHD

DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENT FOR THE DEGREE OF MASTER OF MEDICINE (OPHTHALMOLOGY)

UNIVERSITI SAINS MALAYSIA

2023

DISCLAIMER

I hereby certify that the work in this dissertation is my own except for quotations and summaries which have been duly acknowledged. I declare that I have no financial of interest in the instruments and the computer software in this study.

Dated: 28th Feb 2023

……..

Dr Mohd Alif Bin W Mohd P-UM0151/19

ACKNOWLEDGEMENT

In the name of Allah, the Most Merciful and Beneficent. Alhamdulillah, all praise is to Allah, the Almighty, the greatest of all, on whom ultimately, we depend for sustenance and guidance. I want to thank Him for giving me the opportunity, determination, and strength to complete this manuscript. His continuous grace and mercy were with me throughout my life and even more during the tenure of my writing.

A special mention to my immediate supervisor Professor Dr Shatriah Ismail, Head of Department of Ophthalmology and Visual Sciences at Universiti Sains Malaysia, for her enthusiastic encouragement, useful critiques, and continuous support throughout the process. Without her support and guidance, this dissertation would not have been possible.

I would also like to express my utmost thanks to my co-supervisor, Dr Tengku Norina Tuan Jaffar for providing me with personal anecdotes and encouragement. My appreciation also goes to Dr Mohd Nadzrul Safiq Bin Abd Rahim for his guidance in statistical analysis.

My warmest appreciation to all the professors, lecturers and support staff of the ophthalmology department, clinic and ward of Universiti Sains Malaysia in assisting me to complete this dissertation. I am very grateful to Universiti Sains Malaysia, which has provided me with a platform to learn academically and acquire clinical and research skills.

Finally, I must express my very profound gratitude to my family, especially to my parents, Wan Mohd Wan Hassan, Khariah Mohd Daud, my dearest wife, Liyana Ghazali, and my adorable children, Marwa Humaira and Muhammad Imran for their love, endless support, encouragement, and sacrifices. This master journey accomplishment would not have been possible without them.

Thank you.

TABLE OF CONTENTS

ABSTRAK

Pengenalan

Penyakit alergi mata adalah penyakit kronik yang dikenali dengan gejala pada permukaan mata yang teruk dan juga melibatkan kornea. Kornea boleh terkesan dengan penyakit ini dari pelbagai aspek dan boleh menyebabkan kebutaan jika berlaku pada tahap yang teruk.

Objektif

Objektif kajian ini adalah untuk membandingkan perubahan ketebalan kornea dan topografi kornea dalam kalangan pesakit alergi mata dengan kanak-kanak yang sihat, serta perbezaan antara tahap alergi yang berlainan.

Kaedah kajian

Ini merupakan sebuah kajian perbandingan secara keratan rentas. Seramai 86 orang kanak-kanak yang menghidap penyakit alergi mata dan 86 orang kanak-kanak yang sihat sebagai kawalan. Semua peserta menjalani pemeriksaan mata secara menyeluruh termasuk pemeriksaan ketebalan kornea dengan menggunakan alat *'ultrasound pachymeter'* dan topografi cornea dengan menggunakan *'placido disc corneal analyzer'*.

Keputusan

Terdapat penipisan yang signifikan pada ketebalan kornea di kalangan kanak-kanak dengan alergi mata berbanding dengan kanak-kanak yang sihat ($p < 0.05$). Ketebalan kornea adalah paling nipis di kalangan pesakit alergi mata pada tahap teruk (533.09 ± 10.52 μm) berbanding dengan tahap awal, sederhana (546.79 ± 12.52 μm), dan kanak-kanak yang sihat (546.59 ± 12.17 μm) ($p<0.05$). Hampir semua bacaan topografi kornea termasuk 'simulated keratometry 1 and 2' (sim K1, sim K2), 'apical keratometry', 'apical gradient curvature' (AGC), 'superior-inferior index', 'keratoconus prediction index' (KPI), dan 'percent probability keratoconus' (PPK) menunjukkan bacaan yang lebih tinggi dalam kalangan pesakit alergi mata tahap teruk berbanding pesakit alergi tahap awal, sederhana, dan kanak-kanak yang sihat ($p < 0.05$). Namun, tiada perbezaan signifikan pada bacaan rabun silau dalam kalangan pesakit alergi mata dengan tahap keterukan yang berbeza (tahap teruk 1.31 ± 0.90 diopters (D), tahap awal, sederhana 1.33 ± 1.42 D) ($p = 0.912$).

Kesimpulan

Pesakit alergi mata pada tahap yang teruk menunjukkan penipisan kornea dan bacaan topografi kornea lebih tinggi yang signifikan berbanding pesakit alergi mata tahap awal, sederhana, dan kanak-kanak yang sihat. Rabun silau antara pesakit alergi mata yang berbeza tahap keterukan tidak menunjukkan sebarang perbezaan yang signifikan.

Kata kunci: Alergi, Ketebalan Kornea, Kanak-kanak, Topografi Kornea

ABSTRACT

Introduction

Vernal keratoconjunctivitis (VKC) is a chronic allergic disease characterised by intense ocular surface symptoms and corneal involvement. We aimed to compare the central corneal thickness (CCT) and corneal topography changes between children with VKC and healthy children, as well as among the different groups of severity of VKC.

Materials and Methods

This study is a comparative, cross-sectional, hospital-based study. We recruited 86 children with VKC and 86 healthy children as controls. All participants underwent complete ocular examinations, including CCT using an ultrasound pachymeter and corneal topography using a placido disc corneal analyser. Data from the right eye were analysed.

Results

There was a statistically significant reduction in mean CCT in children with VKC compared to controls ($p < 0.05$). The mean CCT was observed to be thinnest in the severe-very severe groups of VKC (533.09 ± 10.52 μm) compared to the mild-moderate (546.79 ± 12.52 μm) and control groups (546.59 ± 12.17 μm) ($p < 0.05$). Almost all cornea topographic indices including simulated keratometry 1 and 2 (sim K1, sim K2), apical keratometry, apical

gradient curvature (AGC), superior-inferior index, keratoconus prediction index (KPI), and percent probability keratoconus (PPK) were noted to be significantly higher in severe-very severe VKC compared to mild-moderate VKC and controls ($p < 0.05$). However, there was no significant difference in cylinder value when comparing different groups of severity of VKC (severe-very severe 1.31 ± 0.90 diopters (D), mild-moderate 1.33 ± 1.42 D; $p = 0.91$).

Conclusion

The severe-very severe VKC group had significantly thinner CCT and higher values in corneal topographic indices compared to the mild-moderate VKC group and the controls group. Astigmatism was not statistically different among the different severities of VKC.

Keywords: Allergic, Central Corneal Thickness, Children, Corneal Topography, Vernal Keratoconjunctivitis

CHAPTER 1:

INTRODUCTION

1.1 VERNAL KERATOCONJUNCTIVITIS

Vernal keratoconjunctivitis (VKC) is a chronic, bilateral, allergic disease marked by severe ocular surface symptoms and corneal involvement. VKC is one of the several disorders in the spectrum of allergic conjunctivitis, which also includes perennial allergic conjunctivitis, seasonal allergic conjunctivitis, atopic keratoconjunctivitis, vernal keratoconjunctivitis, and giant papillary conjunctivitis (Katelaris, 2011).

The prevalence of VKC varies depending on the region and climate, with a broad geographic distribution. It is more commonly found in the temperate zones of the Asia, Mediterranean, central and west Africa, the Middle East, the Indian subcontinent, and South America. VKC cases are also reported in Western Europe, Australia, and North America (Kumar, 2009). In Asian countries, the prevalence of VKC is mostly unknown or inaccurate. However, the prevalence of 1.2% VKC in Japan has been reported (Mehta et al., 2022; Miyazaki et al., 2020).

Symptoms of VKC typically present in school-age children, ranging from 6 to 11 years old (Bonini et al., 2000; Leonardi et al., 2006). However, it can occur as early as 5 months and as late as 38 years of age, and it usually resolves after puberty (Ukponmwan, 2003; Kumar, 2009). There is a male predominance (Bonini et al., 2000). The common symptoms include pruritus, hyperemia, chemosis, photophobia, and filamentous and sticky mucous discharge.

Although the exact cause is not fully understood, it is thought to be induced by both the typical allergic reaction of immunoglobulin E (IgE) and more complex cell-mediated immunologic processes. Evidence supporting the role of IgE-mast cell activation in the disease's severity includes the detection of IgE in serum and tear cytology, an increase in the number of mast cells in the conjunctival tissue, observations of symptom aggravation after allergen exposure, and a link with other atopic conditions (Leonardi, 2002).

Evidence indicates that T-helper-2 (Th2) lymphocytes, which are elevated in the conjunctiva of VKC patients, are involved in cell-mediated immunologic processes. The Th2-generated cytokines and interleukins stimulate the production of IgE, leading to mast cell degranulation, histamine release, and the recruitment of other inflammatory cells when exposed to an allergen. VKC is characterized by an overexpression of pro-inflammatory cytokines, chemokines, growth factors, and enzymes, including eosinophils and eosinophil-derived proteins such as major basic protein and cationic protein, neurotoxins, and collagenases such as matrix metallopeptidase (MMP)-9, which contribute to corneal involvement in VKC (Trocme et al., 1989; Messmer et al., 2002; Leonardi et al., 2003, 2009).

There are no established specific diagnostic criteria for VKC, and diagnosis is typically based on common ocular symptoms and clinical signs. On external examination, the lids can appear erythematous and thickened. The tarsal conjunctiva can develop a cobblestone appearance, and, in active disease, mucus can accumulate between the papillae. In the limbal form, the conjunctiva may exhibit a fine papillary reaction. The primary

findings are gelatinous limbal papillae, which are associated with epithelial infiltrates called Horner-Trantas dots. These are focal collections of degenerated eosinophils and epithelial cells.

Clinically, VKC can be divided into several grades based on the disease severity. There are various classifications of VKC severity that had been published, including those by Pucci et al. (2002), Bonini et al. (2007), Sacchetti et al. (2010), Gokhale (2016), and VKC-Collaborative Longitudinal Evaluation of Keratoconus study (VKC-CLEK) system (Leonardi et al., 2018). Most of the grading systems are based on symptoms and signs at the time of review of the patient. According to the latest update by Management of Vernal Keratoconjunctivitis in Asia (MOVIA) Expert Working Group, Bonini classification is the most widely used in Asia (Mehta et al., 2022). However, the grading system by Sacchetti et al. is more recent and simpler that focused on only significant symptoms and signs. This simplified approach can assist even general ophthalmologist in managing the disease.

Table 1: Clinical Grading of Vernal Keratoconjunctivitis by Sacchetti et al. 2010

Grade	Clinical Findings	Treatment
0 = Quiescent	Absence of symptoms	No treatments
1 = Mild	Presence of symptoms with no corneal involvement	Anti-allergic eyedrops occasionally
2 = Moderate	Presence of symptoms associated with photophobia with no corneal involvement	Anti-allergic eyedrops daily
3 = Severe	Presence of symptoms associated with photophobia and mild to moderate SPK	Anti-allergic eyedrops daily associated with pulsed low-dose topical steroid
4 = Very severe	Presence of symptoms associated with photophobia and diffuse SPK or corneal ulcer	Pulsed high-dose topical steroid eventually associated with surgical removal of corneal plaque

SPK =Superficial punctate keratopathy

Chronic ocular surface inflammation and microtrauma due to rubbing of the eyes in VKC can cause changes in the corneal structure and various corneal lesions (Tanaka et al., 2004; Mcmonnies, 2009). Severe VKC can affect the cornea, resulting in punctate epithelial keratitis, epithelial macroerosions, gelatinous limbal hypertrophy, and plaque formation. These can be accompanied by pannus of superficial neovascularization of the peripheral cornea, which makes the limbus appear thickened and opaque.

A shield ulcer, an oval-shaped epithelial defect, usually has its border in the upper half of the visual axis. Subepithelial ring-like scars may result from healed shield ulcers. If the shield ulcers are not treated, a plaque made up of fibrin and mucus may form over the epithelial defect. Shield ulcers that do not form plaques usually heal quickly, resulting in a good visual outcome, while plaques can delay healing and may require surgical intervention. In the peripheral, superficial stroma, gray-white lipid deposits that fluctuate in size create an arcuate infiltrate that is referred to as pseudogerontoxon.

According to Leonardi et al. (2012), corneal confocal microscopy reveals that inflammation involves not only the superficial epithelium but also the corneal nerves and anterior stroma. Vichyanond et al. (2014) suggest that VKC involves a unique corneal neuropathy, as evidenced by corneal nerve abnormalities such as a reduction in density and the number of fibers, higher tortuosity, and inflammatory cell infiltrates. Additionally, corneal thinning, which is a characteristic of VKC, may be caused by corneal stromal cell apoptosis (Kumagai et al., 2006; Smith et al., 2006).

The chronic microtrauma caused by VKC can result in a chronic inflammatory process that damages the cornea, leading to a gradual loss of stromal mass. This can cause corneal thinning and steepening, resulting in acquired astigmatic refractive errors and, in severe cases, keratoconus (Gupta et al., 2018). These changes can be detected using corneal topography. Several studies have reported that children with VKC have a higher incidence of keratoconus and more abnormal corneal topography patterns than those with normal eyes. In their respective studies, Totan et al. (2001), Gautam et al. (2015), and Umale et al. (2019) reported incidences of keratoconus in VKC of 26.8%, 11.3%, and 11.2%.

Despite the severe blinding complications that VKC can cause in children, routine clinical practice does not typically include the measurement of central corneal thickness (CCT) and corneal topography. This study aims to establish baseline data on CCT and corneal topography in children with VKC and compare the results to those of healthy children. Furthermore, this study will be the first to compare the parameters among different grades of VKC severity.

1.2 CENTRAL CORNEAL THICKNESS

The central corneal thickness (CCT) refers to the thickness of the cornea at its center, where there is the least amount of dioptric variation. Measuring CCT can facilitate early detection of corneal thinning caused by stromal degeneration in VKC, which can aid in the diagnosis and management of corneal thickness-related complications, as noted by Hakak (2019).

According to Sadoughi et al. (2015), ultrasound pachymetry is considered the gold standard for measuring CCT. However, due to recent technological advances, CCT can now be measured using a variety of other methods, including scanning slit topography, confocal microscopy, specular microscopy, and spectral oscillation.

Ultrasound pachymetry involves placing the probe of the instrument onto the centrally located, anesthetized portion of the cornea to measure CCT. The average CCT measurement in micrometers is obtained by calculating the mean of five consecutive readings.

1.3 CORNEAL TOPOGRAPHY

Corneal topography is a tool that utilizes computer assistance to generate a three-dimensional map of the cornea's surface. The principle is basically by measuring the curvature of the anterior surface of the cornea. It can identify any irregularities in the corneal surface curvature that may occur in children with VKC, as noted by Dantas et al. (2005).

The technique involves utilizing a placido disc to evaluate the reflection of a series of concentric black and white rings from the cornea's convex anterior surface. However, newer technology has been developed that incorporates scanning slit methods to evaluate elevation data, as well as distortion-free Scheimpflug photography techniques.

The subject is positioned in front of the device and facing an illuminated pattern of rings. The device collects a sequence of data points and generates a color-coded visual representation of the corneal shape on a computer screen. This technique enables the device to provide both qualitative and quantitative measurements of the cornea's morphology, as reported by Klyce et al. (1984). The three-dimensional color-coded map of the cornea surface can be interpreted into several particular patterns. In the case of keratoconus, the typical abnormal corneal topography pattern is an asymmetrical bowtie with inferior steepening and skewed radial axes (Umale et al., 2018).

This study will be using Corneal Analyzer CA 800 (Topcon, Europe) which is a placido disc base corneal topographer. The device generates a variety of quantitative measurements as shown in Figures 1 and 2, including simulated keratometry (Sim K 1 and 2), which calculates the average keratometry powers of the steepest and flattest meridians in the paracentral zone of the cornea. It is considered abnormal when the value is above 48 diopters (D).

Additionally, this device will collect several other parameters with abnormal values suggestive of astigmatism and possible keratoconus. The parameters with the values of possible keratoconus are apical keratometry (AK) which represents the value of the instantaneous curvature in the corneal apex greater than 50 D, cylinder or astigmatism which is the difference between sim K1 and sim K2 of more than 1.5 D, apical gradient curvature (AG/C) which is the average difference per length unit of the corneal power in relation to the apical power greater than 2 D/mm.

Other parameters that will be measured by the device are superior-inferior index is the difference in terms of average power between the superior area and inferior area with a value of more than 2 D, keratoconus prediction index (KPI) of more than 20%, and percent probability of keratoconus (PPK) which is determined by measuring the Cone Location and Magnitude Index (CLMI) with the value of greater than 0.45 or 45% (Mahmoud et al., 2008; Cavas-Martínez et al., 2016; Shetty et al., 2017; Moshirfar et al., 2019).

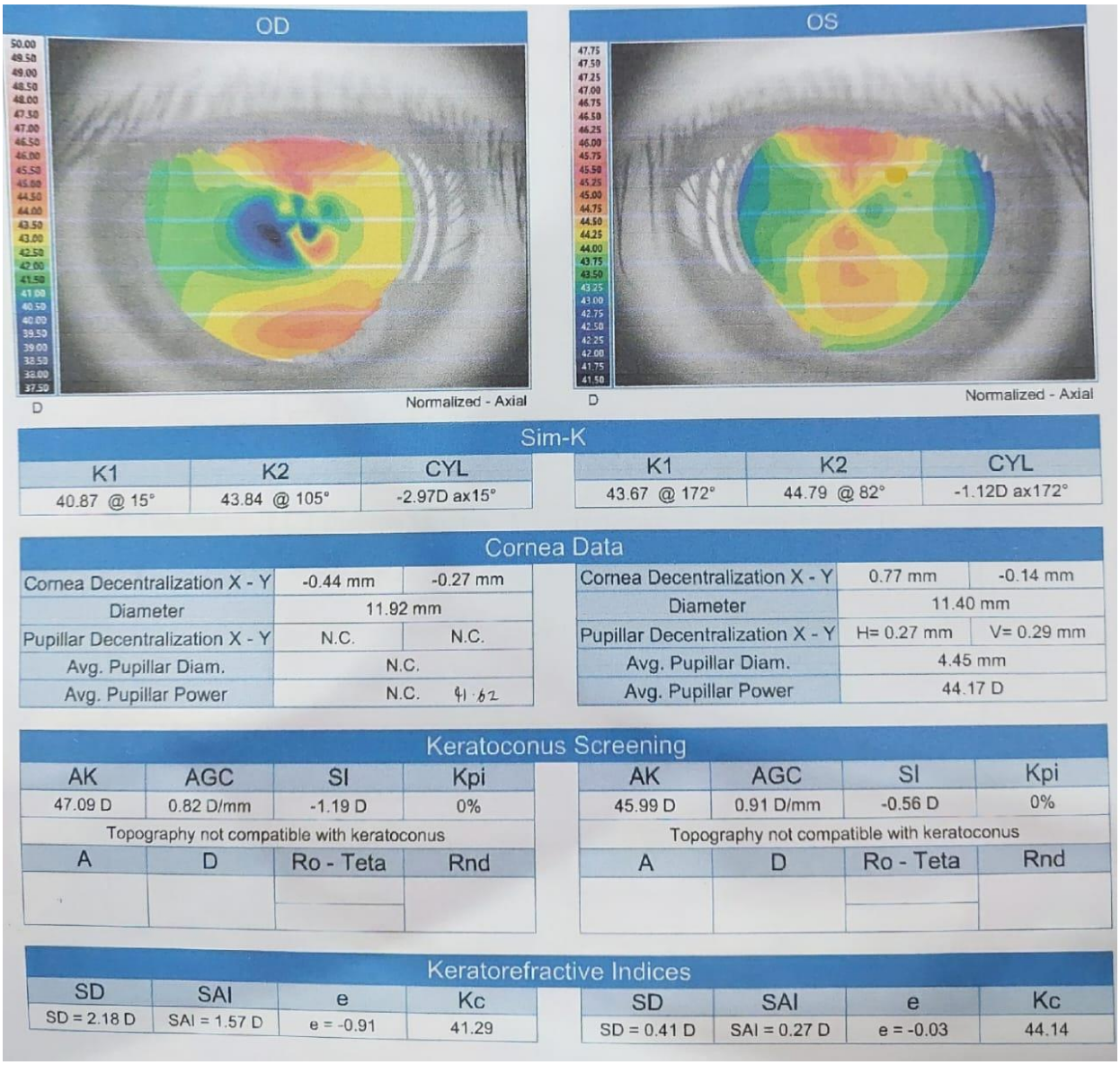

Figure 1: Example of corneal topography indices in mild to moderate VKC.

Parameters show in the figure include sim K1, sim K2, cylinder, apical keratometry, apical gradient curvature, superior inferior index, and keratoconus prediction index. Percent probability of keratoconus is not shown in the figure. Both eyes show superior and inferior symmetrical pattern with no signs of keratoconus based on the parameters.

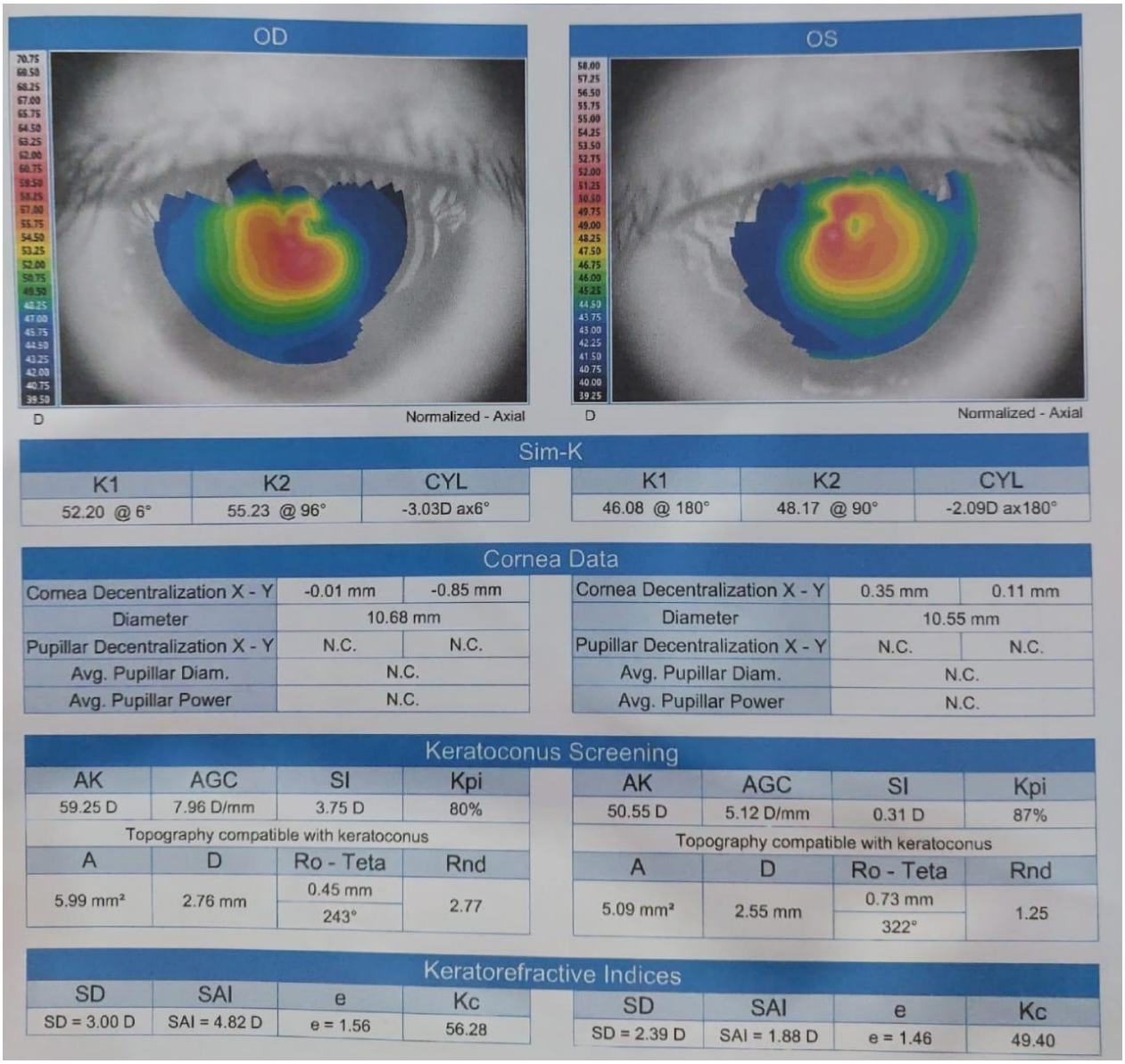

Figure 2: Example of corneal topography indices in severe to very severe VKC

Parameters show in the figure include sim K1, sim K2, cylinder, apical keratometry, apical gradient curvature, superior inferior index, and keratoconus prediction index. Percent probability of keratoconus is not shown in the figure. Both eyes show asymmetrical bowtie pattern with inferior steepening with most of the parameters suggestive of keratoconus.

1.4 STUDY RATIONALE

There is limited study that has been done in evaluating and comparing CCT and corneal topography in children with VKC and healthy children in Malaysia and even in Southeast Asia. We aim to bridge the gap of knowledge with other similar studies that have been done from other regions by conducting this study.

VKC is not a rare disease in our country. As mentioned before, the chronic microtrauma caused by VKC can result in a chronic inflammatory process that damages the cornea, leading to a gradual loss of stromal mass. This can cause corneal thinning and steepening, resulting in acquired astigmatic refractive errors and, in severe cases, keratoconus. Thus, we believe that providing local data with reliable parameters will help in the early detection of those corneal-related changes. We also hope to detect subclinical keratoconus early by taking the corneal topography parameters routinely in VKC.

CCT has been proven to be affected in VKC. However, our study will provide a more comprehensive picture as we also assess the CCT, and corneal topography parameters based on the severity of VKC. This made our study different from other published studies that did comparison among the types of VKC (Gautam et al., 2015; Hakak, 2019).

This study also can be used as a reference in the future for other studies, especially in children with corneal diseases such as corneal ectasia by measuring these two parameters.

1.5 REFERENCE

Bonini, S., Bonini, S., Lambiase, A., Marchi, S., Pasqualetti, P., Zuccaro, O., Rama, P., Magrini, L., Juhas, T., & Bucci, M. G. (2000). Vernal keratoconjunctivitis revisited: a case series of 195 patients with long-term followup. *Ophthalmology*, **107(6)**, 1157–1163.

Cavas-Martínez, F., De la Cruz Sánchez, E., Nieto Martínez, J., Fernández Cañavate, F. J., & Fernández-Pacheco, D. G. (2016). Corneal topography in keratoconus: state of the art. *Eye and vision*, **3**, 5.

Dantas, P. E., Alves, M. R., & Nishiwaki-Dantas, M. C. (2005). Topographic corneal changes in patients with vernal keratoconjunctivitis. *Arquivos brasileiros de oftalmologia*, **68(5)**, 593–598.

Gautam, V., Chaudhary, M., Sharma, A. K., Shrestha, G. S., & Rai, P. G. (2015). Topographic corneal changes in children with vernal keratoconjunctivitis: A report from Kathmandu, Nepal. *Contact lens & anterior eye : the journal of the British Contact Lens Association*, **38(6)**, 461–465.

Gupta, A., & Sravanthi, S. (2018). Corneal topography in vernal keratoconjunctivitis (VKC). *Journal of Evolution of Medical and Dental Sciences*, **7(19)**, 2351-2354.

Hakak, B. (2019). Central corneal thickness in patients with vernal keratoconjunctivitis. *International Journal of Advanced Research*, **7(7)**, 287–290.

Katelaris C. H. (2011). Ocular allergy in the Asia Pacific region. *Asia Pacific allergy*, **1(3)**, 108–114.

Klyce S. D. (1984). Computer-assisted corneal topography. High-resolution graphic presentation and analysis of keratoscopy. *Investigative ophthalmology & visual science*, **25(12)**, 1426–1435.

Kumagai, N., Fukuda, K., Fujitsu, Y., Yamamoto, K., & Nishida, T. (2006). Role of structural cells of the cornea and conjunctiva in the pathogenesis of vernal keratoconjunctivitis. *Progress in retinal and eye research*, **25(2)**, 165–187.

Kumar S. (2009). Vernal keratoconjunctivitis: a major review. *Acta ophthalmologica*, **87(2)**, 133–147.

Leonardi A. (2002). Vernal keratoconjunctivitis: pathogenesis and treatment. *Progress in retinal and eye research*, **21(3)**, 319–339.

Leonardi, A., Brun, P., Abatangelo, G., Plebani, M., & Secchi, A. G. (2003). Tear levels and activity of matrix metalloproteinase (MMP)-1 and MMP-9 in vernal keratoconjunctivitis. *Investigative ophthalmology & visual science*, **44(7)**, 3052–3058.

Leonardi, A., Busca, F., Motterle, L., Cavarzeran, F., Fregona, I. A., Plebani, M., & Secchi, A. G. (2006). Case series of 406 vernal keratoconjunctivitis patients: a demographic and epidemiological study. *Acta ophthalmologica Scandinavica*, **84(3)**, 406–410.

Leonardi, A., Lazzarini, D., Bortolotti, M., Piliego, F., Midena, E., & Fregona, I. (2012). Corneal confocal microscopy in patients with vernal keratoconjunctivitis. *Ophthalmology*, **119(3)**, 509–515.

Leonardi, A., Lazzarini, D., La Gloria Valerio, A., Scalora, T., & Fregona, I. (2018). Corneal staining patterns in vernal keratoconjunctivitis: the new VKC-CLEK scoring scale. *The British journal of ophthalmology*, **102(10)**, 1448–1453.

Leonardi, A., Sathe, S., Bortolotti, M., Beaton, A., & Sack, R. (2009). Cytokines, matrix metalloproteases, angiogenic and growth factors in tears of normal subjects and vernal keratoconjunctivitis patients. *Allergy*, **64(5)**, 710–717.

Mahmoud, A. M., Roberts, C. J., Lembach, R. G., Twa, M. D., Herderick, E. E., McMahon, T. T., & CLEK Study Group (2008). CLMI: the cone location and magnitude index. *Cornea*, **27(4)**, 480–487.

McMonnies C. W. (2009). Mechanisms of rubbing-related corneal trauma in keratoconus. *Cornea*, **28(6)**, 607–615.

Mehta, J. S., Chen, W. L., Cheng, A. C. K., Cung, L. X., Dualan, I. J., Kekunnaya, R., Khaliddin, N., Kim, T. I., Lam, D. K., Leo, S. W., Manurung, F., Tesavibul, N., & Bremond-Gignac, D. (2022). Diagnosis, Management, and Treatment of Vernal Keratoconjunctivitis in Asia: Recommendations From the Management of Vernal Keratoconjunctivitis in Asia Expert Working Group. *Frontiers in medicine*, **9**, 882240.

Messmer, E. M., May, C. A., Stefani, F. H., Welge-Luessen, U., & Kampik, A. (2002). Toxic eosinophil granule protein deposition in corneal ulcerations and scars associated with atopic keratoconjunctivitis. *American journal of ophthalmology*, **134(6)**, 816–821.

Miyazaki, D., Fukagawa, K., Okamoto, S., Fukushima, A., Uchio, E., Ebihara, N., Shoji, J., Namba, K., & Shimizu, Y. (2020). Epidemiological aspects of allergic conjunctivitis. *Allergology international*, **69(4),** 487–495.

Moshirfar, M., Motlagh, M. N., Murri, M. S., Momeni-Moghaddam, H., Ronquillo, Y. C., & Hoopes, P. C. (2019). Galilei corneal tomography for screening of refractive surgery candidates: A review of the literature, part II. *Medical hypothesis, discovery & innovation ophthalmology journal*, **8(3)**, 204–218.

Pucci, N., Novembre, E., Cianferoni, A., Lombardi, E., Bernardini, R., Caputo, R., Campa, L., & Vierucci, A. (2002). Efficacy and safety of cyclosporine eyedrops in vernal keratoconjunctivitis. *Annals of allergy, asthma & immunology*, **89(3)**, 298–303.

Sacchetti, M., Lambiase, A., Mantelli, F., Deligianni, V., Leonardi, A., & Bonini, S. (2010). Tailored approach to the treatment of vernal keratoconjunctivitis. *Ophthalmology*, **117(7)**, 1294–1299.

Sadoughi, M. M., Einollahi, B., Einollahi, N., Rezaei, J., Roshandel, D., & Feizi, S. (2015). Measurement of central corneal thickness using ultrasound pachymetry and Orbscan II in normal eyes. *Journal of ophthalmic & vision research*, **10(1)**, 4–9.

Shetty, R., Rao, H., Khamar, P., Sainani, K., Vunnava, K., Jayadev, C., & Kaweri, L. (2017). Keratoconus screening indices and their diagnostic ability to distinguish normal from ectatic corneas. *American journal of ophthalmology*, **181**, 140–148.

Smith, V. A., Matthews, F. J., Majid, M. A., & Cook, S. D. (2006). Keratoconus: matrix metalloproteinase-2 activation and TIMP modulation. *Biochimica et biophysica acta*, **1762(4)**, 431–439.

Tanaka, M., Dogru, M., Takano, Y., Miyake-Kashima, M., Asano-Kato, N., Fukagawa, K., Tsubota, K., & Fujishima, H. (2004). The relation of conjunctival and corneal findings in severe ocular allergies. *Cornea*, **23(5)**, 464–467.

Totan, Y., Hepşen, I. F., Cekiç, O., Gündüz, A., & Aydin, E. (2001). Incidence of keratoconus in subjects with vernal keratoconjunctivitis: a videokeratographic study. *Ophthalmology*, **108(4)**, 824–827.

Trocme, S. D., Kephart, G. M., Allansmith, M. R., Bourne, W. M., & Gleich, G. J. (1989). Conjunctival deposition of eosinophil granule major basic protein in vernal keratoconjunctivitis and contact lens-associated giant papillary conjunctivitis. *American journal of ophthalmology*, **108(1)**, 57–63.

Ukponmwan C. U. (2003). Vernal keratoconjunctivitis in Nigerians: 109 consecutive cases. *Tropical doctor*, **33(4)**, 242–245.

Umale, R. H., Khan, M. A., Moulick, P. S., Gupta, S., Shankar, S., & Sati, A. (2019). A clinical study to describe the corneal topographic pattern and estimation of the prevalence of keratoconus among diagnosed cases of vernal keratoconjunctivitis. *Medical journal, Armed Forces India*, **75(4)**, 424–428.

Vichyanond, P., Pacharn, P., Pleyer, U., & Leonardi, A. (2014). Vernal keratoconjunctivitis: a severe allergic eye disease with remodeling changes. *Pediatric allergy and immunology : official publication of the European Society of Pediatric Allergy and Immunology*, **25(4)**, 314–322.

CHAPTER 2:

OBJECTIVES

2.1 General Objective

To evaluate central corneal thickness and corneal topography in children with Vernal Keratoconjunctivitis.

2.2 Specific Objectives

1. To compare the mean central corneal thickness between children with VKC and healthy children.
2. To compare the mean corneal topography parameters between children with VKC and healthy children.
3. To compare the mean central corneal thickness in severe-very severe VKC with minimal-moderate VKC.
4. To compare the mean corneal topography parameters in severe-very severe VKC with minimal-moderate VKC.

CHAPTER 3:

MANUSCRIPT

Evaluation of Central Corneal Thickness and Corneal Topography in Children with Vernal Keratoconjunctivitis

Mohd-Alif Wan Mohd[1,2,3], Tengku Norina Tuan Jaffar[3], Ismail Shatriah[1,2]

[1]Department of Ophthalmology and Visual Science, School of Medical Sciences, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia

[2]Hospital Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia

[3]Department of Ophthalmology, Hospital Raja Perempuan Zainab II, 15200 Kota Bharu, Kelantan, Malaysia

Corresponding Author: Shatriah Ismail, Department of Ophthalmology and Visual Sciences, School of Medical Sciences, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia.

Email: shatriah@usm.my

Tel: 60-9-767-6363, Fax: 60-9-765-3370

Abstract

Purpose

Vernal keratoconjunctivitis (VKC) is a chronic allergic disease characterised by intense ocular surface symptoms and corneal involvement. We aimed to compare the central corneal thickness (CCT) and corneal topography changes between children with VKC and healthy children, as well as among the different groups of severity of VKC.

Methods

This study is a comparative cross-sectional hospital-based study. We recruited 86 children with VKC and 86 healthy children as controls. All participants underwent complete ocular examinations, including CCT using an ultrasound pachymeter and corneal topography using a placido disc corneal analyser. Data from the right eye were analysed.

Results

There was a statistically significant reduction in mean CCT in children with VKC compared to controls ($p < 0.05$). The mean CCT was observed to be thinnest in the severe-very severe groups of VKC (533.09 ± 10.52 μm) compared to the mild-moderate (546.79 ± 12.52 μm) and control groups (546.59 ± 12.17 μm) ($p < 0.05$). Almost all cornea topographic indices including simulated keratometry 1 and 2 (sim K1, sim K2), apical keratometry, apical gradient curvature (AGC), superior-inferior index, keratoconus prediction index (KPI), and percent probability keratoconus (PPK) were noted to be significantly higher in severe-very severe VKC compared to mild-moderate VKC and controls ($p < 0.05$). However, there was