Original Article

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Conjunctival and Corneal Endothelium Profile in a Sample of Healthy Electronic Cigarette Smokers

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Abstract:

Objective: Though e-cigarette is thought of as a healthy alternative way of smoking, the unknown nicotine concentration level and chemical compounds from the aerosol mist and flavourings are potentially harmful and may exert irritation or damage to the ocular surface. Thus, a cross-sectional study was conducted to identify the conjunctival and corneal endothelium profile among healthy e-cigarette smokers, and the relationship between smoking behaviour with the conjunctival and corneal endothelium profile.

Material and Methods: Seventeen healthy e-cigarette smokers and 17 non-smokers were recruited for this study where their palpebral redness, bulbar redness, limbal redness, conjunctival roughness, central corneal thickness, endothelial cell density, and coefficient of variation of endothelium cell area were assessed using slit lamp biomicroscope and specular microscope.

Results: There was a non-significant, higher mean rank observed in the total palpebral redness, total bulbar redness, total limbal redness, total conjunctival roughness, central corneal thickness, endothelial cell density, and coefficient of variation of the endothelium cell area in e-cigarette smokers compared to non-smokers (p-value>0.05). Only smoking frequency and total palpebral redness showed a statistically significant, positive, and fair correlation (r=0.349, p-value=0.043), while no other smoking behaviour showed a significant correlation (p-value<0.05).

Conclusion: The use of e-cigarettes showed no significant impact on the conjunctival and corneal profile among the users, but further research with comprehensive evaluation is required in a larger sample size of more established e-cigarette smoking profiles.

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Introduction

The recent prevalence of electronic cigarettes (e-cigarettes), or vape used among smokers aged 15 years and above in Malaysia, was 4.9% of the total 1.13 million population (95% confidence interval [CI]: 4.10–5.92)[1]. This shows a gradual decrement despite the decreasing prevalence of tobacco smokers from 2011 in Malaysia[2,3] and data were collected using a face-to-face questionnaire. The overall prevalence of current, ever, former, and dual users of e-cigarettes in Malaysia were 3.2% (95% CI)=2.5–4.1. At first, the e-cigarette was promoted as the healthier alternative to tobacco cigarettes, and it was supposed to be the first step towards smoking cessation upon their introduction to the market in the mid-2000s[4]. However, this triggers a large concern since many possible detrimental effects of e-cigarettes are documented[5–9], but some of the relations are still inconclusive.

E-cigarettes produce vapours that imitate traditional cigarette smoke by aerosolizing the e-liquid[10]. The device was designed to deliver e-liquid to the lung, through inhalation of a mixture of air and vapours into the respiratory system[11]. There are various types of e-liquid, some of which contain nicotine, flavorings, and other chemicals. The nicotine concentration levels vary, and they can be adjusted according to the user's demands, hence can lead to nicotine toxicity during inhalation, ingestion, or dermal exposure while passing through consumable cartridges[12]. Moreover, the e-cigarettes also contain a heating device that works to vaporize the e-liquid into an aerosol mist. However, the chemical compounds in the aerosol mist contain harmful or potentially harmful constituents to systemic health namely tobacco-specific nitrosamines (TSNAs), aldehydes, metals, volatile organic compounds (VOCs), phenolic compounds, polycyclic aromatic hydrocarbons (PAHs), flavours, solvent carriers, tobacco alkaloids, and drugs (aminotadalafil and rimonabant)[12].

E-cigarettes, initially marketed as a safer alternative to traditional smoking, have raised concerns regarding their impact on ocular health, particularly cornea and conjunctiva. The chemical compound in the e-cigarette could be detrimental to the health of both the cornea and conjunctiva. Conjunctiva is a thin, translucent membrane of the eye that lines the inside of the eyelid to the sclera, where it provides protection and lubrication to the eye by the production of mucus and tears. The conjunctival mucosa, like every other mucosa in our body, is very sensitive to airborne chemicals, fumes, and irritative gasses. It has been explained that environmental factors such as smoke and chemical fumes can trigger ocular redness due to the vasodilation of blood vessels[13]. Increased conjunctival hyperemia is a clinical sign of a wide range of ocular disease, inflammation, and irritation[14]. In tobacco smoke, various chemical constituents evoke pungent sensations like stinging, burning, and prickling, which often cause severe discomfort by stimulating the conjunctival-free nerve endings to produce such reactions[15]. However, the effect of the vapour from e-cigarette on conjunctival redness is still faintly explored and documented.

The corneal endothelium envelops the back of the cornea and helps to control the stromal hydration that directly impacts the transparency of the corneal tissue. The endothelial cell density (ECD); which is the number of corneal endothelial cells per square millimeter and coefficient of variation (CoV); which is the mean cell area divided by the standard deviation of the cell area, act as the indicators of corneal stress[16]. Several studies have documented significant changes on endothelial morphology; a decreased number of ECDs and an increased number of CoV among

tobacco smokers[17,18], while some stated otherwise[19]. It is theorized that smoke causes chronic hypoxia which leads to endothelial cell death, leaving the remaining cells to replace the space left by the dead cell. Eventually, this causes an increase in the variation of endothelial cell size and shape[19] which might impair the corneal transparency.

The effect of e-cigarette vapour on conjunctival and corneal endothelium profile is yet unknown, whereby many studies have shown endothelial morphological changes in tobacco smoke. Hence, this study aimed to investigate the difference in conjunctival redness, conjunctival roughness, and corneal endothelium morphology profile between e-cigarette smokers and non-smokers.

Material and Methods

Sample collection

A cross-sectional study was conducted to investigate the degree of conjunctival redness (bulbar conjunctiva redness, palpebral conjunctiva redness, and limbal redness), conjunctival roughness (papillae), central corneal thickness (CCT), endothelium cell density (ECD), and coefficient of variation (CoV) of endothelium cell area among e-cigarette smokers.

For inclusion criteria, male smokers aged 18-40 years old, a minimum of 4-years e-cigarette smoking history at the time of enrolment, or/and had quit tobacco cigarette smoking for at least six months were selected. The control group consisted of age- and gender-matched individuals who do not use e-cigarettes, and live and work in a smoke-free environment. This is defined as having no household members who smoke; office workers must be in a workplace (room) that has been declared smoke-free by management. As for the exclusion criteria, the subjects will be excluded if they are heavy dual smokers who use tobacco and electronic cigarettes at the same time, wear contact lenses or have done so within the past six months, have a current or history of systemic disease, ocular disease, and refractive surgery or ocular surgery such as laser-assisted in situ keratomileusis (LASIK), photorefractive keratectomy (PRK) and phacoemulsification. Subjects who used any medications and topical medications within the last 14 days also were excluded, except those who used artificial tears. The duration of this study was from November 2022 to August 2023 and the location of the data collection was at UiTM Vision Care, UiTM Puncak Alam.

The sample size was calculated using the GPower software (version 3.1.9.7), and based on the calculator, the sample size for this study is 42 with 21 participants in each group with a 0.80 effect size (large effect), alpha of 0.05, and statistical power of 0.80. The statistical power of 0.8 was chosen with reference to a previous study that stated 80% power is enough to detect significant differences between the case and control groups[9].

Approval for this study was obtained from the Faculty Ethics Review Committee (FERC) of the Faculty of Health Science UiTM Puncak Alam (Ref. Number: FERC/FSK/MR/2023/00066).

Procedures

The profiling questionnaire was distributed to the participants to collect information regarding the participants' social demographic, and vaping profile. The questionnaire included in this study has two sections, Section A and Section B. Section A includes a total of ten questions regarding the participants' social demographic information and general health history such as name, gender, age, occupation, highest education level, general health history, ocular health history, and contact lens wear status. Next, Section B includes ten questions regarding smoking behaviour such as type of e-cigarette, duration of smoking, smoking status, e-cigarette brand, total puffs per day, nicotine level used in their e-cigarette, frequency of smoking, and voltage of e-cigarette usage.

Using slit lamp biomicroscope Righton NS-2D Zoom Slit Lamp digital unit, the components being assessed were bulbar and palpebral conjunctiva redness, limbal redness,

and conjunctival roughness (papillae). The white light with diffuser and parallelepiped illumination was selected to determine and grade the papillae, bulbar and palpebral conjunctiva, and limbal redness. The Efron grading scale was used for the grading, from a scale of 0 to 4 with a 0.5 unit scaling[20]. The perceived conjunctival redness was subjectively averaged from all four quadrants: the nasal, temporal, superior, and inferior quadrant redness score. Meanwhile, the palpebral roughness was the evaluation of the superior palpebral conjunctiva upon eyelid eversion. The minimum total score was 0 and the maximum total score was 4. The indications for each category are as follows;

0 is normal (no signs of the condition/no roughness),

>1 is trace (minimal signs, barely noticeable/slight roughness, barely perceptible),

>2 is mild (slight signs, more noticeable but not severe /mild roughness, noticeable but not prominent),

>3 is moderate (clear and definite signs, moderate severity/moderate roughness, clearly evident),

4 is severe (prominent and intense signs, severe condition/severe roughness, very pronounced and easily visible).

The grading was made by two examiners on one subject's eye with no prior discussion before the assessment to avoid the element of bias.

Next, the endothelial morphology, which includes central corneal thickness (CCT), endothelial cell density (ECD), and coefficient of variation (COV) of the endothelium cell area was assessed using the specular microscope. The computer-assisted morphometry analysis of the specular microscope analyzed the endothelial cells' size, shape, number, and density which helped to measure the thickness of the subjects' endothelial cells. Once the subject had been properly set up, the joystick was moved to align the patient's cornea and then the instrument automatically captured the image of the endothelial surface and analyzed the cell counts on the central and six peripheral points (2, 4, 6, 8, 10 and 12 o'clock) of the corneal endothelium. The endothelial cell morphology analysis includes the number of analyzed cells (µm), average cell area (square micrometers, µm2), maximum and minimum cell area (µm2), endothelial cell density (cells/mm2), standard deviation of the cell area (µm2), coefficient of variation of the cell area (%), polymegathism (distribution by areas) and pleomorphism (percentage of hexagonal cells). An average of three readings for CCT, ECD, and CoV from one eye only is taken for further analysis.

Data analysis

This study used Statistical Package for Social Sciences (SPSS) software version 27.0 for analysis. The Mann-Whitney non-parametric test was used to compare the ocular redness (bulbar, palpebral, and limbal), papillae, CCT, ECD, and COV of the endothelium cell area status between the e-cigarette group and non-smoker group. Then, the Spearman and Kendall's tau-b correlations were used to identify the correlation between smoking behaviour and ocular redness (bulbar, palpebral, and limbal), papillae, CCT, ECD and COV of the endothelium cell area.

Results

Demographic characteristics of respondents

The total participants in this study were 34 people with 17 people (50%) e-cigarette smokers and 17 people (50%) non-smokers. A smaller number of participants were recruited due to the constraint of getting exclusive e-cigarette smokers within the data collection timeframe. With 34 people, an effect size of 0.8, and an alpha level of 0.05, the achieved power is approximately 0.62 (or 62%), slightly below the desired power. However, the assumption of homogeneity of variances was met across all groups (p-value>0.05).

The average age of the participants was 23.09 years old (S.D.=3.61) in both groups, with the majority coming from age 21-25 years old (82.35%). Among the e-cigarette smokers, the majority of them were current daily smokers

(64.7%), and used disposable e-cigarettes (82.4%). The majority of e-cigarette smokers smoke every day (76.5%) and 52.9% of e-cigarette users were uncertain about their e-cigarette voltage. The average duration of smoking was 6.12 years (S.D.=2.93), the average total puff in a day was 314.41 puffs (S.D.=331.91) and the average nicotine level was 34.71 mg (S.D.=16.38 mg). Table 1 shows the overall demographic data and smoking behaviour of the respondents.

Conjunctival and corneal endothelium morphology profile among smokers and non-smokers

A descriptive analysis of the conjunctival and corneal endothelium profile for electronic cigarette smokers and non-smokers is provided in Table 2. The table includes the minimum, 25th percentile (Q1), median, 75th percentile (Q3), and maximum value of all indicated variables.

Table 3 shows average palpebral redness, bulbar redness, limbal redness, papillae, central corneal thickness, endothelium cell density, and coefficient of variation of the endothelium cell area, displayed higher mean rank in smokers compared to non-smokers, yet it is not statistically significant (p-value>0.05).

The Spearmen correlation test showed a statistically significant, positive, and fair correlation between total palpebral redness and smoking frequency (r=0.349, p-value=0.043). However, none of the other smoking behavior factors and the dependent variables show a statistically significant (p-value>0.05) correlation. Table 4 shows the correlation between smoking behavior and dependent variables.

Table 1 Smoking behaviour among respondents

Variable	Mean (S.D.)	Frequency (%)
Age (n=34) (years old)	23.09 (3.61)	
21-25		28 (82.35)
26-30		4 (11.76)
35-40		2 (5.88)
Smoking behaviour (n=17)		
Smoking status		
Current daily smoker		11 (64.7)
Current smoker		6 (35.3)
Type of e-cigarette		
Disposable		14 (82.4)
Non-disposable		3 (17.6)
Frequency of smoking		
Everyday		13 (76.5)
Not frequent		4 (23.5)
E-cigarette voltage		
Low		3 (17.6)
Medium		1 (5.9)
High		4 (23.5)
Not sure		9 (52.9)
Duration of smoking (years)	6.12 (2.93)	
Total puff in a day	314.41 (331.91)	
Nicotine level (mg)	34.71 (16.38)	

Table 2 Descriptive analysis for conjunctival and corneal endothelium profile by smoking status

Variable	Minimum	25th percentile (Q1)	Median	75th percentile (Q3)	Maximum
Palpebral redness					
EC smokers	1.00	1.00	1.25	1.63	2.00
Non-smokers	0.00	1.00	1.0	1.25	2.00
Bulbar redness					
EC smokers	1.00	1.00	1.36	1.50	2.00
Non-smokers	0.50	1.00	1.25	1.50	2.00
Limbal redness					
EC smokers	0.00	1.00	1.0	1.36	2.00
Non-smokers	0.00	0.13	1.0	1.50	1.63
Papillae					
EC smokers	0.00	0.50	1.00	1.36	2.00
Non-smokers	0.00	0.00	0.75	1.13	2.00
Central Corneal Thickness, (μm)					
EC Smokers	484.00	522.00	537.00	570.00	591.00
Non-smokers	499.00	511.50	531.00	560.00	589.00
Cell density, (cells/ mm^2)					
EC smokers	2543.00	2599.75	2866.00	2997.50	3150.00
Non-smokers	2237.00	2662.75	2838.50	2829.00	2998.00
Coefficient variation (%)					
EC smokers	26.00	33.25	37.50	42.75	59.00
Non-smokers	28.00	31.00	35.50	41.00	48.00

EC smokers=electronic cigarette smokers

Table 3 Median, mean rank, Man-Whitney U statistic, and p-value comparison between smokers and non-smokers

Variable	E-cigarette smokers Median (IQR) Mean rank	Non-smokers Median (IQR) Mean rank	Man-whitney U statistic	p-value
Palpebral redness	1.25 (0.63) 19.94	1.00 (0.25) 15.06	103.00	0.14
Bulbar redness	1.38 (0.50) 18.79	1.25 (0.50) 16.21	122.50	0.44
Limbal redness	1.00 (0.38) 18.56	1.00 (1.38) 16.44	126.50	0.53
Papillae	1.00 (0.88) 19.62	0.75 (1.13) 15.38	108.50	0.21
Central corneal thickness, (μm)	537.00 (48.00) 18.38	531.00 (49.00) 16.62	129.50	0.61
Cell density, (cells/mm^2)	2866.00 (397.75) 16.50	2838.50 (265.25) 14.36	96.00	0.51
Coefficient variation (%)	37.50 (9.50) 16.19	35.50 (10.00) 14.71	101.00	0.65

IQR=Interquartile range

Table 4 Correlation between smoking behaviour and dependent variables

		Total palpebral redness	Total bulbar redness	Total limbal redness	Total papillae	Central corneal thickness	Endothelial cell density	Coefficient variation
Age	r^1	0.053	0.110	0.118	0.262	−0.134	−0.352	−0.209
	p-value	0.764	0.536	0.506	0.134	0.450	0.056	0.267
Duration of smoking	r^1	0.239	0.109	0.069	0.193	−0.014	−0.130	0.055
	p-value	0.174	0.540	0.699	0.274	0.935	0.494	0.774
Total puff	r^1	0.159	0.145	0.221	0.088	−0.043	0.063	0.070
	p-value	0.370	0.414	0.210	0.623	0.811	0.739	0.715
Nicotine level	r^2	0.285	0.080	0.108	0.173	0.150	0.148	0.229
	p-value	0.102	0.652	0.543	0.327	0.396	0.435	0.223
E-cigarette type	r^2	0.296	0.208	0.118	0.184	0.107	0.080	0.018
	p-value	0.054	0.163	0.420	0.217	0.445	0.592	0.905
Voltage	r^2	0.221	0.147	0.110	0.221	−0.024	0.036	0.184
	p-value	0.134	0.306	0.434	0.123	0.859	0.804	0.206
Smoking status	r^2	−0.198	−0.137	−0.081	−0.178	−0.011	0.040	−0.098
	p-value	0.190	0.350	0.575	0.226	0.935	0.786	0.508
Smoking frequency	r^2	0.310	0.143	0.095	0.191	0.085	0.151	0.045
	p-value	0.042*	0.336	0.516	0.196	0.542	0.311	0.765

r^1=Spearmen correlation test. r^2=Kendall tau-b correlation test, *p-value<0.05, considered significant

Discussion

This This study found that the range of palpebral and bulbar conjunctival redness of e-cigarette smokers was from 1.00 to 2.00 or categorized as 'traced' to 'mild' grade based on Efron grading scales. As for limbal redness and papillae, the range of score falls between 0.00 to 2.00 or is categorised as a 'normal' to 'mild' score. This is considered as normal, and in parallel with the CCLRU grading system, where normal bulbar redness can range from 1.3 to 2.6 units 21. It is far more important to note the baseline appearance, as a change in bulbar redness score of 0.4 units or more may be significant[21].

Most of the irritant-based sources which include smoke can also induce inflammatory responses that trigger the blood vessel's vasodilation and cause conjunctival redness[14]. In another study by Jaiswal et al., the wildfire smoke exposure to the ocular surface proposed that air pollutants or poor ambient air quality can cause ocular surface damage, which similarly reflects the poor air quality exposed by the e-cigarette smokers[22]. Even if the electronic cigarette chemical concentration level is lesser than tobacco, the toxin from e-cigarette vapour can augment ocular inflammation[23]. To the best of our knowledge, limited studies have determined conjunctival redness among e-cigarette smokers. Nevertheless, the insignificant higher redness found in this study was conclusive and is worthy of attention. Few studies highlighted that using objective methods such as keratograph or digital conjunctival photograph analysis systems can produce high-level data reproducibility and reliability which could be a new improvement in future studies[6].

Previous study has classified the corneal thickness as follows, <510 µm as very thin, <535 µm as thin, 540µm to 560 µm as average, >565µm as thick, and >600 µm as very thick[24]. In this study, the majority of e-cigarette smokers have corneal thickness classified as thin (25th and

50th percentile), and a smaller proportion have corneal thickness at the higher end of the average range (75th percentile). However, this study shows the e-cigarette smokers' CCT is slightly thicker than the non-smokers group, though it is insignificant. Similar to the previous study, a pre- and post-assessment of the epithelium thickness among smokers revealed that there was an insignificant increase in the central corneal epithelium thickness after vaping[25]. The amount of e-liquid consumed may vary among the participants even though a predetermined amount of puffs had been set because the amount of e-liquid that was consumed by experienced vapers and novice vapers varied, seeing that the latter group tended to vape in short and small amounts compared to the experienced vapers[25]. Previous meta-analysis studies have associated smoking with a higher central corneal thickness compared to non-smokers[26] suggesting inflammation and oxidative stress induced by smoking could contribute to the alteration in corneal thickness. However, the study investigated the association with tobacco use only and was not able to eliminate the potential age-related difference which may differ according to tobacco use[26].

The endothelial cell density in both e-cigarette smokers and non-smokers showed normal values given the normal endothelial cell density for adults is 2,000 to 3,000 cells/mm^2 [27]. Both groups have a healthy amount of endothelium cell density since a minimal density of 400–500 cells/mm^2 is required for pumping activity of the endothelium cell can be sustained[28]. However, the coefficient of variation of the endothelium cell area in both e-cigarette smokers and non-smokers shows elevated readings from the normal value (>30%). The coefficient of variation is classified as <30% for uniform endothelial cells, 31–40% for mild polymegethism, 41–50% for moderate polymegethism, and >50% for marked polymegethism[29]. An elevated coefficient of variation is one of the common early signs of the endothelial disease since this reading represents the endothelial cell size variation amount and a marker of endothelial cell remodeling. Previous studies revealed that the mean value of ECD was significantly higher in non-smokers compared to smokers, and the CV was insignificantly higher in smokers compared to non-smokers[17,18]. The reason is that tobacco smoke and other nicotine derivatives lead to apoptosis and necrosis in the endothelial cells due to oxidative damage or hypoxia in the endothelial cell. The variation in the endothelial cell size and shape will increase with cell death because when an endothelium cell dies, the remaining cells will enlarge to cover the space of the dead cells since they cannot divide fast enough to replace the dead cells. However, whether a similar mechanism happened to endothelial cells due to e-cigarette vapour is still unknown due to the limitation of previous studies.

The association of smoking behaviour factors and the variables, which are palpebral redness, bulbar redness, limbal redness, papillae, central corneal thickness, endothelium cell density, and coefficient of variation of the endothelium cell area showed statistically not significant (p-value>0.05). However, the palpebral redness and smoking frequency revealed a statistically significant, positive, and fair correlation which indicates that the palpebral redness increases as the smoking frequency increases. There is still a lack of studies to prove this relationship, however, it might be due to the increase in exposure to the chemicals from the e-cigarette due to increased smoking frequency triggers irritation and inflammation of the palpebral conjunctiva[14].

As there was insignificant difference and correlation in most of the variables tested, the possible factors could be the modest variation of smoking behaviour among smokers. The frequency of smoking in the smokers' group is largely varied with small sample sizes, ranging from seldomly smoke and some smoke every day. Similarly, the number of puffs per day also varied between the smokers where

the minimum was 40 puffs per day and the maximum was 1,200 puffs per day, also, the nicotine level varied with the least was 6 mg and the highest was 50 mg. In addition, other factors could also affect the ocular redness during the day of assessment since environmental factors like air conditioning room, exposure to smoke for the non-smokers, amount of sleep and other factors could indirectly influence the ocular redness among the e-cigarette smokers and non-smokers group. So, the possible factors that could trigger papillae, palpebral redness, bulbar redness, and limbal redness should be thoroughly filtered and eliminated before and during the assessment so that the sensitivity of the result can be increased.

For future research, a larger sample size with exclusive and established e-cigarette smokers is recommended to limit the variations in smoking behaviour for more significant findings. This study is only able to obtain a smaller number of participants due to the time constraint of getting the desired sample size and smoker's criteria with the convenient sampling design. A pre- and post-study design would be beneficial to foresee the immediate changes of ocular surface due to e-cigarette usage. An objective assessment like keratograph or computerized system is preferable to assess the palpebral, bulbar, and limbal redness to ensure data reproducibility and reliability. Lastly, other possible factors that could trigger the redness should be thoroughly filtered so that the quality of the data can be increased.

Conclusion

This study has demonstrated that there was no significant difference in the palpebral redness, bulbar redness, limbal redness, papillae, central corneal thickness, endothelium cell density, and coefficient of variation of the endothelium cell area between e-cigarette smokers and non-smokers. Higher smoking frequency and increased palpebral redness showed significantly fair and positive relationship. While there might be possibility that differences in the redness profile and the endothelial morphology are indeed not significant between e-cigarette smokers and non-smokers, further research that can tackle down the limitations needs to be done to explore more on the ocular surface profile among the e-cigarette smokers. The findings from this study could be the starting point of reference for future research on the potential implication of e-cigarette usage on the integrity of ocular surfaces.

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Conflict of interest

The authors declare that they have no competing interests.

References

1. Institute for Public Health (IPH), National Institutes of Health (NIH), Ministry of Health Malaysia. National Health and Morbidity Survey (NHMS) 2019: NCDs – Non-Communicable diseases: risk factors and other health problems. [monograph on the Internet]. Putrajaya: Ministry of Health Malaysia; 2019 [cited 2023 Sep]. Available from: https://iku.moh.gov.my/images/IKU/Document/REPORT/NHMS2019/Report_NHMS2019-NCD_v2.pdf.
2. Ab Rahman J, Mohd Yusoff MF, Nik Mohamed MH, Mahadir Naidu B, Lim KH, Tee GH, et al. The prevalence of e-cigarette use among adults in Malaysia. Asia-Pacific J Public Heal 2019;31:9S-21. doi: 10.1177/1010539519834735.

3. Palipudi KM, Mbulo L, Morton J, Bunnell R, Blutcher-Nelson G, Kosen S, et al. Awareness and current use of electronic cigarettes in Indonesia, Malaysia, Qatar, and Greece: Findings from 2011-2013 global adult tobacco surveys. Nicotine Tob Res 2016;18:501-7. doi: 10.1093/ntr/ntv081.
4. US Department of Health and Human Services. E-cigarette use among youth and young adults : a report of the surgeon general, US department of health and human services. Atlata (GA): Centers for Disease Control and Prevention (US); 2016.
5. Martheswaran T, Shmunes MH, Ronquillo YC, Moshirfar M. The impact of vaping on ocular health: a literature review. Int Ophthalmol 2021;41:2925-32. doi: 10.1007/s10792-021-01842-w.
6. Alshammeri S. Evaluation of the effects of electronic cigarettes on the tear film of Smokers using Keratograph and SM Tube. Pakistan J Ophthalmol 2023;39:80-5. doi: 10.36351/pjo.v39i2.1599.
7. Kalayci M, Cetinkaya E, Suren E, Yigit K, Duman F, Erol MK. The effect of electronic cigarette smoking on retinal microcirculation: enlargement of the foveal avascular zone. Photodiagnosis Photodyn Ther 2020;32. doi: 10.1016/j.pdpdt.2020.102068.
8. Makrynioti D, Zagoriti Z, Koutsojannis C, Morgan PB, Lagoumintzis G. Ocular conditions and dry eye due to traditional and new forms of smoking: a review. Contact Lens Anterior Eye 2020;43:277-84. doi: 10.1016/j.clae.2020.02.009.
9. Md Isa NA, Koh PY, Doraj P. The tear function in electronic cigarette smokers. Optom Vis Sci 2019;96:678-85. doi: 10.1097/OPX.0000000000001422.
10. Yamin CK, Bitton A, Bates DW. E-cigarettes: a rapidly growing internet phenomenon. Ann Intern Med 2010;153:607-9.
11. Syx E. The case of the electronic cigarette in the EU. Eur J Health Law 2014;21:161-75. doi: 10.1163/15718093-12341312.
12. Meo SA, Al Asiri SA. Effects of electronic cigarette smoking on human health. Eur Rev Med Pharmacol Sci 2014;18:3315-9.
13. Janson B. Encyclopedia of Ophthalmology. Encycl Ophthalmol 2016;2011-2. doi: 10.1007/978-3-642-35951-4.
14. Singh RB, Liu L, Anchouche S, Yung A, Mittal SK, Blanco T, et al. Ocular redness – i: etiology, pathogenesis, and assessment of conjunctival hyperemia. Ocul Surf 2021;21:134-44. doi: 10.1016/j.jtos.2021.05.003.
15. Solberg Y, Rosner M, Belkin M. The association betwen cigarette smoking and ocular diseases. Surv Ophthalmol 1998;42:535-47. doi: 10.1016/S0039-6257(98)00002-2.
16. Sheng H, Bullimore MA. Factors affecting corneal endothelial morphology. Cornea 2007;26:520-5. doi: 10.1097/ICO.0b013e318033a6da.
17. Golabchi K, Abtahi MA, Salehi A, Jahanbani-Ardakani H, Ghaffari S, Farajzadegan Z. The effects of smoking on corneal endothelial cells: a cross-sectional study on a population from Isfahan, Iran. Cutan Ocul Toxicol 2018;37:9-14. doi: 10.1080/15569527.2017.1317783.
18. Ilhan N, Ilhan O, Coskun M, Daglioglu MC, Ayhan Tuzcu E, Kahraman H, et al. Effects of smoking on central corneal thickness and the corneal endothelial cell layer in otherwise healthy subjects. Eye Contact Lens 2016;42:303-7. doi: 10.1097/ICL.0000000000000212.
19. Sayin N, Kara N, Pekel G, Altinkaynak H. Effects of chronic smoking on central corneal thickness, endothelial cell, and dry eye parameters. Cutan Ocul Toxicol 2014;33:201-5. doi: 10.3109/15569527.2013.832688.
20. Walker MK, Tomiyama ES, Skidmore K V, Assaad JR, Ticak A, Richdale K. A comparison of subjective and objective conjunctival hyperaemia grading with AOS® anterior software. Clin Exp Optom 2022;105:494-9. doi: 10.1080/08164622.2021.1945406.
21. Murphy PJ, Lau JSC, Sim MML, Woods RL. How red is a white eye? Clinical grading of normal conjunctival hyperaemia. Eye 2007;21:633-8. doi:10.1038/sj.eye.6702295.
22. Jaiswal S, Jalbert I, Schmid K, Tein N, Wang S, Golebiowski B. Smoke and the eyes: a review of the harmful effects of wildfire smoke and air pollution on the ocular surface. Environ Pollut 2022;309:119732. doi: 10.1016/j.envpol.2022.119732.
23. Asaari SAH, Iqbal T, Lott PPW, Reddy SC, Ramli N. Electronic cigarette (vaping) induced panuveitis: a case report and literature review. J Clin Images Med Case Reports 2022;3:1-3. doi: 10.52768/2766-7820/2157.
24. Pateras E, Koufala C. Comparison between orbscaniiz, pentacam, ultrasound pachymetry (Tomey SP-100) at different stages of keratoconus. Ophthalmol Res An Int J 2020;13:7-33. doi: 10.9734/or/2020/v13i230163.
25. Munsamy A, Bhanprakash B, Sirkhot A, Mlambo L, Dlamuka S, Mhlongo N, et al. A pre-test post-test assessment of non-invasive keratograph break up time and corneal epithelial

thickness after vaping. Afr Health Sci 2019;19:2926-33. doi: 10.4314/ahs.v19i4.13.

26. Frifelt LEW, Subhi Y, Holm LM, Singh A. Impact of tobacco use on corneal thickness and endothelial health: a systematic review with meta-analyses. Acta Ophthalmol 2022;100:26-34. doi: 10.1111/aos.14897.
27. McCarey BE, Edelhauser HF, Lynn MJ. Review of corneal endothelial specular microscopy for FDA clinical trials of refractive procedures, surgical devices, and new intraocular drugs and solutions. Cornea 2008;27:1-16. doi: 10.1097/ICO.0b013e31815892da.
28. Ewete T, Ani EU, Alabi AS. Normal corneal endothelial cell density in Nigerians. Clin Ophthalmol 2016;10:497-501. doi: 10.2147/OPTH.S97070.
29. Doughty MJ. On the regional variability of averaged cell area estimates for the human corneal endothelium in relation to the extent of polymegethism. Int Ophthalmol 2018;38:2537-46. doi: 10.1007/s10792-017-0765-2.