INVESTIGATING LENS ELASTICITY AND ITS CORRELATION WITH REFRACTIVE ERRORS AND BIOMETRIC PARAMETERS ACROSS AGE GROUPS USING ULTRASONIC ELASTOGRAPHY SHEAR WAVE

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ABSTRACT: The lens in human eyes possesses elastic properties that facilitate shape change to focus light onto the retina, with ultrasound elastography shear wave being a common imaging technique to assess tissue elasticity. This study aimed to determine the correlation between lens elasticity and various factors across different age ranges, including refractive error and biometric properties (axial length and lens thickness). The study included responses from 84 individuals aged 19 to 65, with eligibility determined through tests assessing refractive errors and visual acuity. Axial length and lens thickness were measured after selecting the best eye for testing, followed by scanning with ultrasound elastography using shear wave technology. The data analysis revealed a significant correlation between participants' age and lens elasticity ($r = 0.83$, $P = 0.00$), an insignificant correlation between elasticity and refractive error ($r = 0.247$), weak correlations with axial length ($r = 0.006$), lens thickness ($r = 0.27$, $P = 0.14$), and a negative correlation between axial length and lens thickness ($r = 0.233$, $P = 0.033$). The results indicated that the alterations do not appreciably influence lens elasticity changes with age, but the variations in refractive error or ocular morphology.

KEYWORDS: *Lens; axial length; lens thickness; ultrasound elastography; refractive error*

1.0 INTRODUCTION

The human eye is a complex biological and optical system that has been extremely well developed to fulfil the visual requirements of the subject. The cornea and lens combine their refractive properties to provide the focusing ability of the human eye [1]. For the duration of an organism's life, the lens forms a distinct cellular structure and protein complements, and they stop undergoing cell division and changeover upon completing the maturation and differentiation stages. Instead, the lens is maintained throughout the entirety of the individual's life in a state of functional and structural integrity [2].

The lens is a unique tissue comprising layers of relatively dense fibre cells containing crystallins and highly stable proteins. More than 90% of the dry weight of the lens is composed of crystallins [3], which maintain its transparency and high refractive index. As a result, light can be focused on the retina [4-5]. A thin and translucent membrane creates the lens capsule, which encloses the crystalline lens within the eye [6-8]. The critical responsibilities of the capsule are related to its physical and mechanical duties in sustaining the lens shape and accommodation processes [7]. Accommodation changes the eye's dioptric power [9-10].

Formally, diopter is the term of a lens optical power standard measurement equivalent to the reciprocal of the focal length expressed in metres. To accommodate for near distance, the eye undergoes gradual modifications to the lens's shape, thickness, and refractive surface [11-13].

The degree of this process diminishes with age in the adult human eye, reaching a minimum by middle age. This phenomenon is referred to as presbyopia, which develops when a decline in the eye's focusing range that is physiologically typical and associated with ageing reaches a point [14-15].

Evaluation of the elastic properties of tissues utilises various methods resulting from the invention of X-ray imaging in the late 19th century, which provides a good instrument for diagnosis, screening, and treating therapeutic conditions. The medical imaging discipline has produced a wide variety of sophisticated methods. These instruments can measure and visualise various physical properties, from absorption coefficients to twist relaxations [16-17]. Thus, various non - non-destructive imaging techniques have been used for tissue evaluations in the field of ophthalmology, such as Brillouin microscopy [18-19], Optical Coherence Tomography [20-22], Magnetic Resonance Elastography[23-24], and ultrasound elastography[25-27].

Refractive error is a prevalent eye problem that affects several individuals worldwide. This condition arises when the geometry of the eye inhibits light from focussing correctly on the retina, thereby leading to impaired vision. There are numerous varieties of refraction errors, such as myopia (near-sightedness), hyperopia (farsightedness), and astigmatism [27-34]. The lens's biometric parameters can affect the degree of refractive error. The axial length and thickness of the lens are two of the most important biometric parameters, both having the potential to influence the degree to which light is bent or refracted while travelling through the lens. Lenses in younger people tend to be thinner and more elastic, making it simpler to switch focus from near to far. In general, biometric assessments of the lens are significant factors that should be considered during diagnosing and treating refractive problems [27, 35-39]

However, there is data paucity regarding the relationship between biometric parameters and refractive error, especially among different age groups. Previous studies have focused on specific age groups, such as geriatric patients/elderly subjects or younger populations, whereas research encompassing these various ages is limited. Hence, the present study aims to determine the correlation between lens elasticity and various factors across different age ranges, including refractive error, axial length, and lens thickness.

However, there is a lack of sufficient data on the relationship between biometric parameters and refractive error, particularly across different age groups.

2.0 METHODOLOGY

2.1 Study design

The study is a cross-sectional investigation conducted at the ophthalmology and radiology departments of Hospital Sultan Abdul

Aziz Shah, University Putra Malaysia (UPM), Serdang, Selangor. It commenced in April 2022 and targeted individuals aged 19 to 65 visiting the ophthalmology clinic. The University of Putra Malaysia's Ethics Committee for Research Involving Human Subjects (JKEUPM) approved this study on March 7th, 2022 (Ref No. JKEUPM-2022-052).

2.2 Sample Size and Sampling Method

G-Power is recommended to determine the sample size quantitatively. Considering a low positive correlation coefficient of 0.15 from a previous study, with a statistical power of 80% and a precision error 0.05, the estimated minimum sample size required is 84 participants. Nevertheless, participants were selected according to the following inclusion criteria.

2.3 Inclusion and exclusion criteria

The inclusion criteria entailed participants visiting Hospital Sultan Abdul Aziz Shah and providing informed and written consent to participate in this study. Individuals must be between 19 and 65 years old and have the best possible corrected visual acuity of 6/9. A single eye with the clearest vision will be selected while monocularly identifying the best visual acuity. In terms of exclusion criteria, those presented with corrective eye surgery for any refractive defect ('Lasik', 'Laser', 'PRK'), Patients with amblyopia, any previous eye surgery, previous trauma to the lens, or thyroid eye disease (exophthalmos), currently on medication that contributes to an increase in fluid retention within the body (water retention), cataract surgery patients with an intraocular lens (IOL), patients diagnosed with cataracts of a grade higher than one or having amblyopia, diabetes Patient with macula oedema, keratoconus and other corneal diseases that affect the axis of the eye, advanced stage of glaucoma, and total optic-nerve cupping with a diminished field of vision.

2.4 Assessment of refractive error and biometric parameters

Multiple eye examinations were performed on the patient eyes. The HUVITS® auto-refractometer was used to measure all the biometric parameters to determine the presence or absence of refractive errors. The refractive strength was equivalent to the average of the three values used to estimate it. Visual acuity assessment was performed as described in a previous study in [10], using a computerised display screen, and the trial case's lens corrected any vision abnormalities. The results were rated as follows: 6/6, 6/9, 6/12, 6/18, 6/24, 6/36, and 6/60. In cases where the subject had vision issues, the visual acuity was determined by adding lens degrees to the frame. Both assisted and unaided visual acuity readings were reported for each individual.

For further measurements, just one eye with the best vision was chosen. After selecting the clearest eye, the IOL master performed the measurements on the axil length and thickness. For the axial length and lens thickness assessment, the IOL master's achievement was used as the standard, whereby the names and birthdates of the subjects were entered into the device system before the actual check. Data was recorded using assessment sheets, and additional assessment was conducted in radiology employing Canon (aplio i800) instruments to quantify lens elasticity. The data file was stored in the ultrasound machine, and images were downloaded to an external pen drive.

2.5 Data Analysis

All data analyses were performed using IBM SPSS, version 26. The data were initially assessed for normality based on the level of skewness and kurtosis. Since all the continuous data were normally distributed, mean and standard deviation were computed as the measures of central tendency to summarise the dataset. Descriptive analysis determined the minimum, maximum, mean, and standard deviation for all the biometric parameters. Inferential statistics were conducted using the Pearson correlation coefficient, thus presenting the degree, direction and strength of the association between various biometric parameters (elasticity degree, age, refractive error, axial length, lens thickness).

The Spearman correlation coefficient was used to analyse the correlation between different age groups, refraction errors, and other biometric variables.

3.0 RESULTS AND DISCUSSION

3.1 Descriptive results

A total of 84 participants were recruited for this study. The age distribution of the participants varied, with the most significant proportion falling in the 40 to 50 age range, representing 41% of the total subjects. This situation was followed by the 31 to 39 age group, which comprised 32% of the study population. Participants aged 19 to 30 and 51 to 65 comprised 15% and 12% of the sample. These age characteristics are detailed in Table 1, providing a comprehensive overview of the demographic distribution within the study group.

Aligning with the inclusion and exclusion criteria, none of the participants presented any corrective eye surgery for any refractive defect, any history of trauma to the lens, exophthalmos, medication that may promote intraocular pressure and fluid retention, cataract surgery, diabetes, or any corneal diseases. Thus, the participants can be considered appropriate to participate in this study.

Table 1: Floating-point operations necessary to classify a sample

Age group	Frequency	Percentage	Mean (SD)
19-30	13	15.0	
31-39	27	32.0	
40-50	34	41.0	
51-60	10	12.0	
61-65	0	0	39.61(9.60)

3.2 Visual acuity and refractive error data

The investigation into visual acuity among the participants revealed notable findings based on measurements targeting levels 6/6, 6/9, and 6/12. The detailed results are as follows:

(1) VISUAL ACUITY FINDINGS:

- 78 eyes exhibited a visual acuity of 6/6:
  - 34 cases had normal vision without any refractive errors.
  - 44 cases required corrective lenses to achieve 6/6 vision.
- 5 cases had a visual acuity of 6/9:
  - All 5 cases required corrective lenses.
- 1 case had a visual acuity of 6/12:
  - This case also required corrective lenses.

(2) ANALYSIS OF REFRACTIVE ERRORS:

- Myopia:
  - 42 cases were identified with myopia, ranging from simple to moderate.
  - This group included individuals with myopic astigmatism.
- Hypermetropia with Astigmatism:

- 6 cases were identified with simple hypermetropia with astigmatism.

- Mixed Astigmatism:
  - 2 cases were identified with mixed astigmatism.

(3) OVERALL PREVALENCE:

- 12% of the observed cases had hypermetropia.
- 4% of the observed cases had astigmatism.

These findings provide valuable insights into the prevalence and correction of refractive errors among the study participants, highlighting the need for corrective lenses in a significant portion of the population to achieve optimal visual acuity. Table 2 summarises the visual acuity findings and the distribution of refractive errors among the participants.

Table 2: Distribution of Participants According to Visual Acuity and Refractive Error Evaluation

Visual acuity	Number of the eye	Normal vision	Corrective lenses	Refractive error
6/6	78	34	44	Myopia (42), 84.0% Hypermetropia with astigmatism (6), 12.0% Mixed astigmatism (2), 4.0%
6/9	5	0	5	
6/12	1	0	1	

3.3 Axial length, lens thickness, and lens elasticity data

The mean axial length measured 23.7 mm, ranging from 21.9 mm to 27.0 mm (SD 1.00). Typically, axial length spans from 22.0 to 24.0 mm [40]. In 25 cases, the length exceeded 24 mm, indicating myopia-related complications, with 25% of these cases presenting abnormal values. The mean lens thickness was 3.9 mm, with a range of 3.1 to 4.7 mm (SD 0.30).

During ultrasonic elastography scanning, the elasticity degree, measured in kilopascals (kPa), exhibited distinct patterns among the groups studied. The ultrasound elastography image in Figure 1 presents a color-coded representation. The region of interest (ROI) was identified on the lens tissue, with the sizes of the ROIs fixed at 2 mm in all cases and positioned on four different parts of the eye: the temporal and nasal.

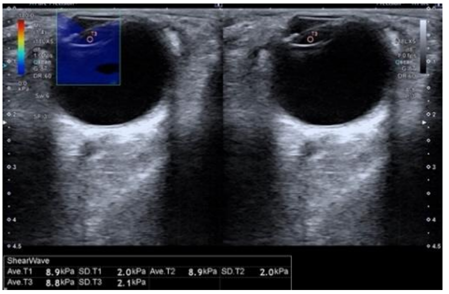

Figure 1: Ultrasound elastography image with a color-coded representation

The overall mean elasticity was found to be 10.24 ± 3.67 kPa. For individuals aged 19 to 39 years (non-presbyopia), the mean elasticity was recorded at 6.98 ± 1.73 kPa, which is lower than the overall mean. In contrast, individuals with presbyopia (40-65 years) exhibited a significantly higher mean elasticity of 13.21 ± 2.09 kPa, surpassing both the overall mean and the elasticity observed in the non-presbyopic group. Lower elasticity values indicate higher elasticity, while higher values indicate less elasticity. There is a significant difference in lens elasticity between the two groups.

3.4 Correlation lens elasticity with age group, refractive error, and biometric parameters

The analysis of the correlation between the degree of lens elasticity and age across the entire sample indicated a strong and significant association ($r = 0.83$, $P < 0.001$). This finding underscores the significant impact of ageing on lens elasticity. Conversely, no significant correlation was observed between refractive error, axial length, and lens thickness with the degree of elasticity, suggesting that these factors do not significantly influence lens elasticity.

A negative correlation was identified between axial length and lens thickness ($r = -0.2334$, $P = 0.033$). This inverse relationship indicates that lens thickness decreases as axial length increases. This finding could have implications for understanding the structural changes in the eye associated with varying axial lengths.

3.5 Discussion

This study is among the few attempts to describe the association between vital biometric parameters and refractive error among various age groups with lens elasticity.

As gleaned from the present study, the participants' ages ranged from 19 to 65 years old, indicating even distribution in various age groups. Overall, 34 (28%) of the individuals' eyes demonstrated normal eye vision (emmetropic) with a corresponding visual acuity 6/6. In contrast, 50 (72%) participants reflected ametropia, which entailed different forms of refractive error issues. Notably, myopia (simple to moderate and myopia astigmatism) was detected in over three-quarters (84%) of the participants with refractive errors were myopic compared to 12% and 4% of hypermetropia and mixed astigmatism, respectively. The high prevalence of myopia in individuals with refractive errors is consistent with previous studies, indicating that it accounts for more than half of all occurrences of refractive error in East Asia, Korea, Japan, Singapore, and China [39]. A previous review also revealed that Southeast Asian countries accounted for the higher prevalence of myopia in the elderly population worldwide [41]. Meanwhile, a wide range of myopia prevalence has been reported in individuals above 40 years old, such as 8% in China [42] and 51% in Myanmar [43].

The low prevalence of hypermetropia is not surprising since the participants were mainly below the age group (55 and above) and, given the inclusion criteria, entailed the absence of eye surgeries or medication that may influence the biometric parameters. Ocular surgeries or ophthalmic interventions are more common in people 60 years and above [41]. However, such older age groups were not recruited in the present study. In addition, the prevalence range of hypermetropia was reported to be wider than myopia in people above 40 years old globally, such as 1.6% in China to > 50% in Iran, the USA and Nigeria [44]. Genetic, lifestyle, racial, and ocular factors may contribute to these discrepancies. The prevalence (10% among those with refractive errors) aligns with the lower bound estimate reported in most Southeast Asian countries [44].

Regarding associations between age and the biometric parameters, participants' age correlated significantly with lens elasticity. These findings demonstrated that age affects the lens's biomechanical qualities and any flaws in the lens tissue that affect the stretching degree (presbyopia) [45, 46]. This result serves as an indicator of the major purpose of the investigation. The correlation between age and lens elasticity corroborates earlier findings [41,43]. Human lens elasticity and the ability to alter shape during accommodation are pertinent for focusing on near objects. Several studies have demonstrated that the human lens's accommodative ability reduces with age and increased stiffness, leading to decreased elasticity [47,48].

This study's refraction error correlated significantly with axial length and lens thickness. In other words, a degree of association was found between myopia and lens thickness, which aligns with several previous research. O'Donnell et al. [49] reported a significant difference in lens thickness between two refractive categories. At the same time, a study conducted in Singapore demonstrated alterations in lens thickness among children of different age categories [50]. The present result supports the theory of a growing and thickening crystalline lens as age increases [51,52]. In contrast, Xie et al. [53] found no association between lens thickness in different refractive age groups. The variation in lens thickness between age groups may result from the alteration in the refractive index of the crystalline lens [49].

Additionally, there was a significant negative correlation between axial length and lens thickness, and both biometric parameters were associated with the degree of refractive errors. This finding is expected since myopia stems from increased axial length [44]. Accumulated evidence from the literature depicts that axial length and lens thickness are among the most critical biometric parameters, influencing the extent to which light bends or refracts when passing via the lens [42, 53].

Likewise, there was no significant correlation between refraction error and elasticity degree. This result implies that the degree of elasticity of the lens is unaffected by any refraction errors. The lens's biometric defaults typically bring on fractional errors; hence, biometric issues with the lens do not compromise its biomechanical qualities.

This study observed no significant association between participants' gender and refraction errors (myopia and hyperopia). A similar result was reported by Donell et al. [49]. Meanwhile, some previous work found a lower prevalence of myopia in women relative to men [55,56] and a wide variation between females and males [44]. This finding might be due to the inclusion criteria in which the effect of vital biometric parameters was controlled. For instance, studies reporting the link between gender and myopia highlighted that the high prevalence of cataracts and longer axial length encouraged such a relationship [41].

In summary, while age strongly influences lens elasticity, other factors, such as refractive error, axial length, and lens thickness, do not significantly correlate with elasticity. The negative correlation between axial length and lens thickness highlights the complex interplay between different biometric parameters of the eye.

4.0 CONCLUSION

The findings indicated that refractive or biometric errors do not influence changes in lens elasticity due to ageing. However, refractive error may be impacted by the effects and irregularities in lens biometric factors. The study highlighted the significance of axial length and lens thickness in determining refractive error, especially in myopic conditions. These insights could be used to develop new diagnostic tools or treatment methods for individuals with refractive errors.

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflicts of interest and fully endorse the contents of this manuscript.

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