Anterior chamber dimensions, angles and pupil diameter in patients with Down syndrome: A comparative population-based study

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Purpose: To study the anterior chamber (AC) dimensions, angles and pupil diameter (PD) in patients with Down syndrome compared to normal controls. Methods: Prospective study is comparing the AC parameters in patients with Down syndrome aged 10-30 years and age-matched controls. Extracted indices included average anterior chamber depth (ACD), volume (ACV), angle (ACA), and PD measured by Pentacam. Results: Data from 202 patients with Down syndrome (age 17.2 ± 4.8 years) were compared with 190 normal controls (age 17.2 ± 4.5 years). In Down and normal groups, mean ± SD were 2.51 ± 0.31 and 2.83 ± 0.34 mm for ACD-2 mm, 1.65 ± 0.30 and 1.93 ± 0.31 mm for ACD-4 mm, and 3.03 ± 0.29 and 3.24 ± 0.26 mm for endo-ACD, 3.54 ± 0.29 and 3.80 ± 0.26 mm for epi-ACD, mean 169.31 ± 30.38 and 200.17 ± 33.20 mm² for ACV, 40.69 ± 4.50 and 39.97 ± 4.12° for ACA, and 2.79 ± 0.62 and 3.59 ± 0.80 mm for PD, respectively (all P < 0.001). None of the studied indices significantly correlated with age, except for ACA (P = 0.011). All parameters, except for PD, were significantly higher in males compared to females (all P < 0.001). Temporal ACA was significantly wider in male subjects (44.61 ± 6.52 vs. 42.24 ± 6.52°; P < 0.001). Conclusion: The AC in patients with Down syndrome is smaller than normal individuals. AC in females with Down syndrome is smaller than males, and the narrower ACA is attributable to the difference in the temporal angle and not the ACA in other meridians.

Key words: Anterior chamber angle, anterior chamber dimension, anterior chamber volume, down syndrome, pupil diameter

The anterior chamber (AC) is the space between the cornea and the anterior lens surface, and it is defined by the indices of anterior chamber depth (ACD), volume (ACV), angle (ACA), and can be influenced by pupil diameter (PD). The dimensions and angles of this chamber are measured using a variety of devices, including ultrasound A-scan devices, the Spectralis optical coherence tomography (OCT) system, IOLMaster, Biograph, Orbscan, and Pentacam. Studies have shown high accuracy for Pentacam measurements of ACV and ACA compared with OCT and even ultrasound. Some advantages of this device include the good repeatability in measuring these indices and its independence from the experience and skill of the examiner. Accurate measurements of the AC have various applications in ophthalmology. In refractive surgery candidates or patients undergoing cataract surgery requiring intraocular lens (IOL) implantation, in addition to being one of the main components of the formula for lens power calculation and increasing the accuracy of the estimation, it is used to determine the exact position of the lens to prevent damage to the endothelial cells. Another application of AC measurements is screening for angle-closure glaucoma (ACG). These cases usually have shallower chambers. Nolan et al. have shown that using ACD in the screening and prophylactic treatment of ACG can reduce the incidence of glaucoma.

Based on World Health Organization’s report, the incidence of Down syndrome is 1 in 1000 to 1 in 1100 live births worldwide, which was reported 1 in 700 by centers for disease control and prevention. Previous studies showed the prevalence of cataract and lens opacity is 4.0% for aged 0-16 years, 20.0% for <25 years, and 42.0% for >30 years. The prevalence of glaucoma was also reported 0.8% for <17 years and 7.7% for <15 years, respectively. It was demonstrated the prevalence of refractive error is 25.3% for <17 years and 76.2% for >30 years. Current study also showed the congenital lens opacity in 37.8% of the patients with Down syndrome. To our knowledge, there has been no population-based study to evaluate AC parameters in 10- to 30-year-old patients with Down syndrome. In a study by

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Aslan et al.,[17] ACV, ACD and PD were reported in 38 patients with Down syndrome aged 5-13 years. Also, Haugen et al.[18] evaluated mean ACD in 39 patients with Down syndrome aged 14-26 years. High prevalence of cataract, glaucoma, and refractive error in addition to ocular structural differences in these patients show the necessity of knowing the reference range for AC dimensions and angles.

Methods

In this prospective population-based study, the patients with Down syndrome between the ages of 10 and 30 years were recruited from special needs schools and non-governmental organizations dedicated to the patients with Down syndrome. The diagnosis of Down syndrome was stated in their medical records. Exclusion criteria from the study included the presence of other intellectual disabilities (16 cases), including Klinefelter syndrome, autism, and physical and mental disability. Also, 200 age- and gender-matched normal subjects as the control group were selected from candidates of refractive surgery presenting for their first work-up session (87 cases) as well as normal cases presenting for a vision check-up (113 cases) in the referral Eye Hospital. This group had no history of Down and other intellectual disabilities neither themselves nor their families. Both groups underwent a complete ophthalmic and optometric examination.

This project was approved by the Ethics Committee of Tehran University of Medical Sciences (ID: 1397-091). The methods and objectives of the study were explained to the healthy participants and parents of the patients with Down syndrome; informed consent forms were signed by parents and verbal assent was obtained from patients with Down syndrome before examinations.

In this report, cases with pterygium, keratoconus, and glaucoma, as well as those with any history of corneal surgery were excluded from the analysis. Enrolled cases underwent imaging with Pentacam HR (Oculus Optikgeräte GmbH, Wetzlar, Germany) between 8:00 A.M. and 12:00 noon. The Oculus software version 6.08r27 and 1.21r24 was used to extract the data. Imaging acquisitions were repeated until OK quality status seen in the image report. When there was a need for more than three repetitions, imaging was postponed for 2-3 days to avoid errors. All imaging was done in a study room with an ambient light source and patients stayed there 10-15 minutes to adapt the light condition (physiologic mydriasis).

In this report, we present the results in terms of the following indices:
1. The average ACD measured from the endothelium at 12 meridians (0-30° intervals) on a ring 2 mm from the center (ACD-2 mm).
2. The average ACD measured from the endothelium at 12 meridians (0-342° at 18° intervals) on a ring 4 mm from the center (ACD-4 mm).
3. The ACD measured from the endothelium at the corneal apex (endo-ACD).
4. The ACD measured from the epithelium at the corneal apex (epi-ACD).
5. The volume of the AC defined as the space between the posterior corneal surface and the anterior lens in the central 12 mm zone (ACV).
6. The average AC angle measured at four meridians (superior, inferior, nasal and temporal) (ACA).
7. The PD as measured during imaging.

In the analysis, given the high correlation between fellow eyes (lowest = 0.831 with ACA and highest = 0.916 with ACD-2 mm) only the right eye data were used. For the descriptive analyses, we determined the mean ± standard deviation (SD), 95% confidence intervals (CI) of the mean, range, and median of the studied indices. The multiple linear regression model was used to examine correlations of quantitative indices with age (continuous variable), gender (binomial variable), spherical equivalent/SE (continuous variable), and groups (Down and normal).

Results

After applying the study inclusion criteria, 234 of the 250 patients with Down syndrome and 200 normal controls were enrolled in this study. After applying exclusion criteria of this report (pterygium, keratoconus, glaucoma, and history of corneal surgery), data from 202 patients with Down syndrome and 190 normal controls were used in this report. In the Down syndrome group, congenital lens opacity was observed in 37.8% (76 patients). The mean age of Down and normal controls were 17.1 ± 4.8 and 17.2 ± 4.5 years (P = 0.806); 75.2% and 78.4% were under 20 years old (P = 0.457) and 53.0% and 48.4% were male (P = 0.368), respectively. The mean SE in patients with Down syndrome (-0.37 ± 3.99, range: -17.25 to 7.88 D) was lower than normal group (-3.25 ± 3.19, range: -18.00 to 6.75 D) (P < 0.001).

In Down and normal groups, mean ± SD were 2.51 ± 0.31 and 2.83 ± 0.34 mm for ACD-2 mm, 1.65 ± 0.30 and 1.93 ± 0.31 mm for ACD-4 mm, and 3.03 ± 0.29 and 3.24 ± 0.26 mm for endo-ACD, 3.54 ± 0.29 and 3.80 ± 0.26 mm for epi-ACD, mean 169.31 ± 30.38 and 200.17 ± 33.20 mm² for ACV, 40.69 ± 4.50 and 39.97 ± 4.12° for ACA, and 2.79 ± 0.62 and 3.59 ± 0.80 mm for PD, respectively (all P < 0.001) [Table 1].

Based on linear regression model, all indices were significantly smaller in patients with Down syndrome compared to the age-matched control (all P < 0.001), except for ACA (P = 0.147). All parameters were significantly smaller in female (all P < 0.05), except for PD (2.78 ± 0.63 mm in male vs. 2.75 ± 0.60 mm in female, P = 0.253) [Figs. 1 and 2]. None of the indices showed a significant correlation with age (all P > 0.05), except for ACA (β = -0.12, P = 0.009). Also, none of the indices were correlated to SE (all P > 0.05).

This model showed that ACA was marginally correlated with gender (P = 0.053). ACA was 40.83 ± 4.60° and 39.88 ± 3.98° in males and females, respectively. ACA in the temporal meridian was significantly higher in males (44.61 ± 6.52° vs. 42.24 ± 6.52°, P = 0.041), but in superior, inferior, and nasal meridians were comparable between genders (all P > 0.05).

Discussion

The present study describes the ACD—as measured from the epithelium and endothelium—ACV, ACA, and PD in a population of the 10- to 30-year-old patients with Down syndrome in comparison with age- and gender-matched normal controls. Studies in this area are limited and the findings of this study can provide a useful guide for clinicians
in different fields of ophthalmology such as cataract surgery, refractive error correction (intraocular lens implantation), and glaucoma treatment in patients with Down syndrome.

The normal range of AC dimensions has been reported from normal population-based studies of different age groups. A comparison of indices of AC and PD in normal population-based studies shows that AC is shallower in Iranian populations\[19-21\] compared to Turkey’s.\[22\] The ACD, ACV, and ACA were reported 2.62, 139.0 and 34.3, respectively, for the normal adult population in Iran and 3.03, 185.50 and 37.12 in Turkey with the same age and gender. There is a report showing Iranians have smaller eye globes.\[21\] To our knowledge, there has been no study on this topic in patients with Down syndrome except for the study by Aslan et al.\[17\] in Turkey and Haugen et al.\[18\] in Norway.

In a study of 38 Turkish children aged 5-13 years (mean of approximately 9 years),\[17\] mean ACD, ACV, ACA, and PD were 3.08 mm, 181.65 mm\(^3\), 39.7\(^{\circ}\), and 2.95 mm. The former three indices did not differ between the patients with Down syndrome and normal controls, but PD was significantly smaller in patients with Down syndrome (3.29 ± 0.45 mm) than normal controls. In the present study, which was conducted in the 10- to 30-year age group (mean 17 years), these indices were 3.07 mm, 169.31 mm\(^3\), 40.69\(^{\circ}\), and 2.78 mm, respectively. All indices were smaller in patients with Down syndrome than normal group. ACA was not affected by Down syndrome. One-sample t-test indicated that the smaller chamber volume, wider angle, and smaller PD in our patients with Down syndrome were statistically and significantly different compared to the study by Aslan and colleagues.\[17\]

Table 1: AC indices in 10- to 30-year-old the patients with Down syndrome and normal controls with no corneal pathology

|                  | Mean (CI 95% of mean) | Range     | Median | P*  |
|------------------|-----------------------|-----------|--------|-----|
| ACD-2 mm (mm)    | Down                  | 2.53 (2.48-2.57) | 1.68-3.58 | 2.52 | <0.001 |
|                  | Normal                | 2.83 (2.78-2.88) | 1.77-3.75 | 2.82 |       |
| ACD-4 mm (mm)    | Down                  | 1.65 (0.61-1.69) | 0.88-2.44 | 1.64 | <0.001 |
|                  | Normal                | 1.93 (1.89-1.98) | 1.07-2.72 | 1.92 |       |
| Endo-ACD (mm)    | Down                  | 3.03 (2.99-3.07) | 2.21-3.81 | 3.03 | <0.001 |
|                  | Normal                | 3.24 (3.20-3.28) | 2.49-3.96 | 3.25 |       |
| Epi-ACD (mm)     | Down                  | 3.54 (3.50-3.58) | 2.75-4.37 | 3.54 | <0.001 |
|                  | Normal                | 3.80 (3.76-3.83) | 3.02-4.51 | 3.82 |       |
| ACV (mm\(^3\))   | Down                  | 169.31 (165.13-173.50) | 97.0-251.0 | 167.0 | <0.001 |
|                  | Normal                | 200.17 (195.43-204.91) | 121.2-297.0 | 204.0 |       |
| ACA (\(^{\circ}\))| Down                  | 40.69 (40.07-41.31) | 28.8-53.7 | 40.9 | <0.001 |
|                  | Normal                | 39.97 (39.38-40.56) | 28.2-51.6 | 39.7 |       |
| PD (mm)          | Down                  | 2.78 (2.70-2.87) | 1.58-4.90 | 2.70 | <0.001 |
|                  | Normal                | 3.59 (3.47-3.70) | 2.12-6.31 | 3.40 |       |

ACD: Anterior chamber depth; epi-ACD: Chamber depth from the epithelium; ACV: Anterior chamber volume; ACA: Mean anterior chamber angle; PD: Pupil diameter. *Comparison of mean of indices between the patients with Down syndrome and normal controls

Figure 1: Inter-gender comparison of anterior chamber depth in 10- to 30-year-old the patients with Down syndrome and normal controls. Endo-ACD: AC depth from the endothelium; epi-ACD: Chamber depth from the epithelium

Figure 2: Inter-gender comparison of chamber volume in 10- to 30-year-old the patients with Down syndrome and normal controls
In comparing these two studies, one should note a few points. In addition to racial and sample size differences, the age difference between the two samples, which is almost a decade, can be an influential factor. However, reports concerning age-related AC changes have been inconclusive. Some believe the dimensions and angles of the AC reduce with age.\textsuperscript{[20,23]} Wang et al. have reported correlations for ACD and ACAV with age and lack of any ACA correlation with age in normal Chinese children.\textsuperscript{[25]} In our study, no significant correlations were found between indices and age, except for ACA. Multiple regression analysis could show the age-related change of indices more accurately. It seems that the pattern of AC variation by age is not similar in the age range of the present study (10- to 30-years) and other samples were aged 20-73,\textsuperscript{[23]} 30-89,\textsuperscript{[24]} and 6-18 years.\textsuperscript{[25]} A study by Aslan et al.\textsuperscript{[17]} showed ACA less than ours. It may be due to reporting ACA in 0° in their study and mean ACA in ours. Also, multiple analyses showed that ACA was only affected by age and that it decreased with age.

In a study of 39 Down syndrome patients with average age 20 (14-26 years),\textsuperscript{[19]} mean ACD was 3.45 mm for 35 patients with no keratoconus and similar to the normal group. It may be related to small sample size and low power of statistical analysis. Although other dimensions of AC were not mentioned in study by Haugen,\textsuperscript{[18]} it can be said that AC is smaller in our population. Similar to us, they have refused the age-elapsed changes of ACD.

The results of this study showed that inter-gender differences in AC indices in patients with Down syndrome have a pattern similar to normal individuals, and females have shallower AC compared to males; this difference is independent of age.\textsuperscript{[16,22,25,26]} In addition, the ACA gender difference was only observed in the temporal quadrant, and there were no inter-gender differences in the other three meridians. In a study by Aslan,\textsuperscript{[17]} the correlation of AC indices to gender was not evaluated but Haugen et al.\textsuperscript{[18]} reported the correlation between ACD and gender was not significant. Owing to low sample size (35 cases) and not adjusting the correlation between two eyes,\textsuperscript{[18]} non-significant correlation with gender is expected.

A limitation of this study was non-randomized sampling and low generalizability of results to the Down syndrome population. The strengths of the current study compared to previous studies\textsuperscript{[15,17]} were the size and structure of the study population. Given the large sample of the patients with Down syndrome with normal and non-pathologic corneas, who were recruited from different sources to the present study, and no use of sedatives for imaging, our results can be considered as a reference range of AC dimensions and angles in patients with Down syndrome.

**Conclusion**

In conclusion, in patients with Down syndrome, AC is smaller than the normal population. AC dimension and angle is stable between the ages of 10 and 30 years and does not change significantly. In patients with Down syndrome, similar to the normal population, females have a smaller AC compared to males. The narrower ACA is due to the difference in the temporal meridian. There are no differences between the two genders in other meridians.

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**Conflicts of interest**

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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