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CORNEAL TOPOGRAPHICAL AND BIOMECHANICAL INDICES IN MOTHERS OF CHILDREN WITH DOWN'S SYNDROME IN A TERTIARY CARE HOSPITAL OF PAKISTAN

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Abstract

Objective: *To investigate corneal topographical and biomechanical parameters in mothers of children diagnosed with Down's syndrome (DS), and to compare them with mothers of children without Down's syndrome, in a tertiary care hospital in Pakistan.*

Study design: *A comparative cross-sectional study.*

Place and Duration of study: *Armed Forces Institute of Ophthalmology, Rawalpindi, Pakistan, from June 2024 to November 2024*

Methodology: *A comparative analysis was carried out, 188 eyes of 94 patients were studied, forty-seven in Group-A (mothers of Down's syndrome children) and forty-seven in Group-B (mothers of normal children). In this study, the corneal topographical and biomechanical parameters of mothers of children diagnosed with Down's syndrome were studied and compared to their age matched counterparts.*

Results: *The participants average age was 35.8 years in Group-A and 33 years in Group-B. Statistically significant differences were observed between group means for flat simulated keratometry K1 (p value 0.00), steep simulated keratometry K2 (p value 0.00), K maximum (p value 0.024), Belin Ambrosio Enhanced Ectasia Display (p value 0.002) and Topographical biomechanical index (p value 0.02)*

Conclusion: *Our findings reveal a higher prevalence of deranged keratoconus parameters in Group A than in Group B, pointing toward a milder, subclinical presentation of the condition.*

INTRODUCTION

First documented in 1866 by physician John Langdon Down, Down syndrome (Trisomy 21) is a chromosomal disorder caused by an extra copy of chromosome 21. Down's Syndrome is associated with intellectual disability, with an estimated incidence ranging from 1 in 1000 to 1 in 700 births in the general population.

Ocular associations of Down's syndrome include refractive disorders, ectropion, cataract, squint and nasolacrimal duct obstruction. Among these, keratoconus (KC), is a condition marked by corneal thinning and ectasia, leading to a cone-shaped bulge, has been noted in upto 70 percent of individuals with Down Syndrome, varying across different ethnicities[1,2,3]. The prevalence is 10 to 30 times higher in individuals with Down's syndrome compared to the general population, where it is reported to be between 0.05% and 0.1%.[4]. This high prevalence may

be attributed to an increased tendency of eye rubbing as well as a higher reported incidence of collagen disorders seen in these patients.[5,6] This association is well established, however, the link between a mother with keratoconus or subclinical keratoconus giving birth to a child with Down's Syndrome has been poorly studied.

Prevalence of keratoconus in Karachi Pakistan was 8% according to one study, and 2.3% in India.[7,8] A study done in Iran reported a prevalence rate of 6.5% of keratoconus seen in mothers of Down's syndrome children, compared to 1.5% in their normal counterparts.[9]

In a case report by Ambrosio, it was first hypothesized that mothers with keratoconus may be more likely to give birth to children with Down's Syndrome. Maternal genetic factors, such as the presence of mild or subclinical keratoconus, may increase the likelihood of chromosomal abnormalities in offspring, such as trisomy 21.[10]

In this study, the corneal topographical and biomechanical parameters of mothers of children diagnosed with Down syndrome children were evaluated and compared to their counterparts.

Methodology

This comparative cross sectional study was piloted in 2024 at the Armed Forces Institute of Ophthalmology in Rawalpindi, Pakistan. Study duration was six months from June 2024 to November 2024, after permission was granted from the Institutional Review Board and Ethics Committee (reference number 334, dated 24 May 2024).

Inclusion Criteria: Mothers of children with diagnosed Down's syndrome. No age limit was specified.

Exclusion Criteria. Patients with history of other corneal diseases (e.g., Fuchs' dystrophy, herpes simplex keratitis), mothers who are pregnant or breastfeeding during the study period, participants who have undergone any form of ocular surgery or history of eye trauma.

Convenience sampling was carried out. There was no age limit set to the participants enrolled in the study. Only the Pentacam indices and participants age were noted. Informed consent was obtained following a comprehensive explanation of the study's nature and objectives. The required sample size was determined using the WHO sample size calculator. A total of ninety-four patients were studied, forty-seven in each group. Our patients were divided into two groups; mothers of children with diagnosed Down's syndrome (Group-A) and mothers of normal children (Group-B).

Imaging was carried with Pentacam and Corneal Visualisation Scheimflug Technology (Corvis ST). Extracted Pentacam indices included maximum keratometry in the central 8.0 mm (Kmax), thinnest pachymetry, Sim K flat and steep and Belin ambrosio total deviation value (BAD-D). Extracted indices from Corvis ST were tomographical biomechanical index (TBI) and corvis biomechanical index (CBI).

Data was analyzed using Statistical Package for the Social Sciences (SPSS) version 27.

For quantitative variables, descriptive measures such as mean and standard deviation were calculated; including age, flat simulated keratometry (K1), steep simulated keratometry (K2), maximum keratometry in the central 8.0 mm (Kmax), Belin ambrosio total deviation value (BAD-D), tomographical biomechanical index (TBI), and corvis biomechanical index (CBI).

Inferential statistics were applied using independent sample t-tests to compare means between Group-A and Group-B. A p-value < 0.05 was considered statistically significant.

RESULTS

Altogether, 94 participants were recruited for the study. The mean age in Group-A (Mothers of Downs Syndrome children) was 35.8 years and Group-B (Mothers of normal children) was 33 years.

Table-I. Demographic Data (n=94)

Variables	Mean age at examination (years)
Group-A	35.8
Group-B	33

The variables studied between the two groups were maximum keratometry (Kmax), thinnest pachymetry, flat simulated keratometry (Simkflat), steep simulated keratometry (Simksteep), Belin Ambrosio enhanced ectasia display index (BAD-D),corvis biomechanical index (CBI), tomographical biomechanical index (TBI). Mean intergroup differences were statistically significant for SimKflat (p value 0.00), simKsteep (p value 0.00), Kmax (p value 0.024), BAD-D (p value 0.002) and TBI (p value 0.003).

The difference between mean value of CBI between the two groups was not statistically significant (p value > 0.05).

Pachymetry also did not show a statistically significant difference between the two groups. (p value > 0.05).

Table-II. Shows comparison of corneal topographical and biomechanical indices in Group A and Group B with normal corneas (Right eyes) (n=94)

Parameters	Group-A	Group-B	p value
Kmax (D)	44.8 ± 1.25	44.1 ± 1.47	0.024
Thinnest pachymetry (µm)	530	530	0.9
SimKflat (D)	43.7± 1.28	42.4± 1.57	0.00
SimKsteep (D)	44.0± 1.68	42.5 ±1.52	0.00
BAD-D	1.5±0.5	1.1±0.9	0.002
CBI	0.14±0.33	0.07±0.23	0.255
TBI	0.29±0.12	0.18±0.29	0.003

Abbreviations: Kmax = maximum keratometry, simKflat = flat simulated keratometry, simKsteep = steep simulated keratometry, BAD-D = Belin Ambrosio enhanced ectasia display index, CBI = corvis biomechanical index, TBI = tomographical biomechanical index, D = Dioptres, µm= micrometer

While evaluating the left eyes of the patients, the intergroup comparison revealed statistically significant mean differences for Kmax (p = 0.002), simKflat (p=0.00), simKsteep (p=0.003) , BAD-D (p=0.01) and TBI (p=0.003). Thus the results observed in the right and left eyes are comparable.

Table III. comparison of corneal topographical indices and biomechanical indices seen in the left eyes of both groups A and B (n=94)

Indices	Group-A	Group-B	p Value
Kmax (D)	45.2 ±1.6	44.2± 1.4	0.002
Pachymetry (µm)	637	529	0.3
SimKflat (D)	44± 1.31	42.5± 1.66	0.00
SimKsteep (D)	44.7± 1.58	43.4± 1.48	0.003
BAD-D	1.53± 0.5	1.04± 0.9	0.01
CBI	0.12±0.30	0.08±0.25	0.48
TBI	0.35±0.31	0.18±0.21	0.003

Abbreviations: Kmax is maximum keratometry, simKflat is flat simulated keratometry, simKsteep is steep simulated keratometry, BAD is Belin Ambrosio enhanced ectasia display index, CBI is corvis biomechanical index, TBI is tomographical biomechanical index, D diopters, µm micrometre

DISCUSSION

The connection between keratoconus and Down's Syndrome has been explored extensively in DS patients but remains underexplored in the maternal population. To date, there has been limited research addressing this issue within our local context. This is the first study of its kind being conducted in our region, highlighting a significant gap in the existing

literature. The closest comparable study was carried out in Iran.[9]

A comparative study done in Tehran in 2021 provided preliminary evidence to support this hypothesis.[9]. The study observed a 6.5% prevalence of keratoconus in mothers of children with Down's syndrome, which was significantly higher than the 1.6% prevalence observed in mothers of typically developing children. (p=0.04) Their study reported mean intergroup differences to be significant for Index of height Aymmetry IHA (P=0.01), irregularity index (P = 0.026), anterior Q-value (P = 0.043), Pentacam Random Forest Index PRFI (0.049), Stiffness Parameter A1 SP-A1 (P = 0.048), Deformation Amplitude ratio DA ratio-1 mm (P = 0.001), Deformation Amplitude ratio DA ratio-2 mm (P = 0.003), integrated radius 1-mm (P = 0.015), Highest Concavity Deflection HC deflec. amp. (P = 0.026), pattern deviation PD (P = 0.008), and radius (P < 0.001). On the other hand, the indices that were found to be statistically different between the two groups in our study were not significant in their study population. BAD-D in their study was 0.9 in both study groups, while our study reported a higher BAD-D value of 1.5 in Group-A and 1.1 in Group-B. Similarly, TBI in their study was noted to be 0.14 in both study groups, while it was higher in our study, at 0.29 and 0.18 in Group-A and Group-B respectively. There was no significant difference in corneal pachymetry at the thinnest point between the groups in both studies, reported at 542 µm in Iran and approximately 530 µm in our study. Likewise, Kmax values in both studies were similar, at 44 D. Additionally, although keratoconus could not be diagnosed in any of our study subjects, steeper corneas were observed. These findings suggest that the relationship between maternal keratoconus and Down's Syndrome may be more than coincidental, warranting further investigation into the genetic and environmental factors that may contribute to this association.

Genetic associations of keratoconus are being studied, and a variety of single nucleotide polymorphisms and loci on chromosomes are under investigation. The antioxidant superoxide dismustase gene (SOD1), located on chromosome 21, is one such gene associated with keratoconus.[11] An enzyme expressed from this gene is localized to the cytoplasm, responsible for mitigating oxidative stress in cells by neutralizing superoxide radicals, a form of reactive oxygen species. It has been suggested that a mutation in SOD1 promotes oxidative stress which in turn predisposes corneas to ectatic disorders over time. However, the role of SOD1 in keratoconus is not universally accepted, and there are conflicting pieces of evidence regarding it.[12]

While blepharitis-related eye rubbing is a common contributor to keratoconus in Down syndrome patients [13], genetic abnormalities in the structure and content of their corneas can also be a risk factor for ectatic disorders. The candidate gene for keratoconus, the Superoxide dismustase SOD1 gene, is located on chromosome 21, thus an association with Down's syndrome can be proposed.[14]

It is important to note that the severity of keratoconus varies from case to case. Early stage keratoconus may be difficult to diagnose clinically and it is possible that this early stage keratoconus is more prevalent in this population than clinically overt keratoconus. The results reinforce the importance of integrating corneal topography and biomechanical analysis into screening protocols for high-risk populations to support early detection and intervention.

A study conducted by Mathan et al. compared Pentacam based parameters of normal corneas in Down's syndrome patients (n=64) with a non-Down's syndrome cohort (n=431).[15] It was revealed that the Down's syndrome cohort had higher values in front steep simulated keratometry (K1), anterior corneal astigmatism, maximum keratometry (Kmax) and posterior elevations at the thinnest point when correlated to their normal counterparts. Therefore, widespread corneal assessment and follow up is needed in these groups, as additional other studies have also reported steeper corneas in Down's syndrome group even in the absence of keratoconus.[16]

A study conducted by Hamayun et al. in Armed Forces Institute of Ophthalmology and published in 2020, documented mean anterior segment values in a normal population reporting to the refractive department.[17] Normal mean anterior segment values were as follows: Flat simulated keratometry (K1) 42.1±1.84 diopters (D), steep simulated keratometry (K2) 43.8 ± 1.93 D, K maximum 44.4 ± 1.93 D. The mean values documented in the Mothers of Down's syndrome population in our study are

comparatively greater than those reported in this study, K1 was 44D in our study, K2 was 44.7D, Kmax was 45.2D.

Corvis ST determines the corneal biomechanical properties by calculating the distortion of the cornea in response to air puff.[18] A study was carried comparing Pentacam indices and Corvis ST of 73 subclinical keratoconus eyes to 69 normal eyes. Results showed that Corneal Biomechanical Index (CBI), tomographic biomechanical index (TBI) and Ambrosio relational thickness to the horizontal profile (ARTh) were good indicators when it came to differentiating early stage keratoconus cases from standard counterparts. Their study reported TBI value of 0.23 in normal eyes and 0.55 in subclinical keratoconus eyes. In our study although TBI values were comparatively lower at 0.29 in Group-A and 0.18 in Group-B, the subclinical keratoconus eyes had a higher TBI value. Similarly CBI in the international study was 0.43 and 0.61 in the normal eyes and subclinical keratoconus eyes respectively, and 0.14 and 0.07 in Group-A and B respectively. [19]

A study done by Padmanabhan et al. reported that Topographical biomechanical index (TBI) was the most accurate parameter to differentiate subclinical keratoconus from normal eyes.[20] These findings, when aligned with our study can indicate that the Group-A cohort may have a sub clinical form of keratoconus.

This is the first clinical study of its kind in our region, to compare corneal topographical indices between Group-A (mothers of children diagnosed with Down syndrome) and Group-B (mothers of normally developing children), the results of our study show that atypical Keratoconus parameters are more prevalent in Group-A than in Group-B.

Limitations:

Sample size in our study was limited.

Conclusion:

The results of our study show that irregular corneal topographical parameters are more commonly seen in Mothers of children diagnosed with Down syndrome children (group A) than in Mothers of typically developing children (Group B), and they point towards a milder more sub clinical form of keratoconus.

Author's contribution:

NN - Substantial contributions to study design, acquisition of data, manuscript drafting or reviewing it critical for important intellectual content, has given final approval of the version to be published

AF- Substantial contributions to acquisition of data, Manuscript drafting or reviewing it critical for important intellectual Content, Has given final approval of the version to be published

FH - Substantial contributions to analysis and interpretation of data, critical review, has given final approval of the version to be published

IS- Substantial contributions to concept, study design, Critical review, has given final approval of the version to be published

AH - Substantial contributions to concept, study design, critical review, has given final approval of the version to be published

AH- Substantial contributions to concept, study design, Critical review, has given final approval of the version to be published

REFERENCES:

Kristianslund O, Drolsum L. Prevalence of keratoconus in persons with Down syndrome: a review. BMJ Open Ophthalmol 2021;6(1):e000754 https://doi.org/10.1136/bmjophth-2021-000754

Roizen NJ, Mets MB, Blondis TA. Ophthalmic disorders in children with Down syndrome. Dev Med Child Neurol 1994;36(7):594-600 https://doi.org/10.1111/j.1469-8749.1994.tb11896.x

van Splunder J, Stilma JS, Bernsen RM, Evenhuis HM. Prevalence of ocular diagnoses found on screening 1539 adults with intellectual disabilities. Ophthalmology 2004;111(8):1457-1463 https://doi.org/10.1016/j.ophtha.2003.12.051

Little JA, Woodhouse JM, Saunders KJ. Corneal power and astigmatism in Down syndrome. Optom Vis Sci 2009;86(6):748-754 https://doi.org/10.1097/OPX.0b013e3181a59d5d

Yu SN, Gad R, Kutler R, Trief D. Scheimpflug-Based Tomographic Risk Factors for the Development of Acute Corneal Hydrops in Keratoconus. Cornea 2024;43(9):1150-1153 https://doi.org/10.1097/ICO.0000000000003508

Akoto T, Li JJ, Estes AJ, Karamichos D, Liu Y. The Underlying Relationship between Keratoconus and Down Syndrome. Int J Mol Sci 2022;23(18):10796 https://doi.org/10.3390/ijms231810796

Bhatti N, Fawad MU, Hussain M, Qidwai U, Hasan MU, Rehman AU. Three Years Clinical Audit of Patients Presenting in Cornea Clinic at a Tertiary Care Pak J Ophthalmol 2011;27(4):191–194 https://www.pjo.com.pk/27/4/nasir%20Bhatti%204.pdf

Jonas JB, Nangia V, Matin A, Kulkarni M, Bhojwani K. Prevalence and associations of keratoconus in rural maharashtra in central India: the central India eye and medical study. Am J Ophthalmol 2009;148(5):760-765 doi:10.1016/j.ajo.2009.06.024

Hashemi H, Asgari S, Panahi P, Mehravaran S, Fotouhi A, Ambrósio R. Corneal ectasia in mothers of Down syndrome children. Sci Rep 2021;11(1):22436 https://doi.org/10.1038/s41598-021-02035-2

Salomão MQ, Ambrósio R, Lopes BT, Faria-Correia F, Höfling-Lima AL, Dawson DG. Mild Keratoconus in the Mother of a Patient with Down Syndrome: Case Report and Clinical Hypothesis Int J Kerat Ect Cor Dis 2018;7(2):115-120 https://doi.org/10.5005/jp-journals-10025-1167

Lucas SEM, Burdon KP. Genetic and Environmental Risk Factors for Keratoconus. Annu Rev Vis Sci 2020;6:25-46 https://doi.org/10.1146/annurev-vision-121219-081723

Moschos MM, Kokolakis N, Gazouli M, Chatziralli IP, Droutsas D, Anagnou NP, et al. Polymorphism Analysis of VSX1 and SOD1 Genes in Greek Patients with Keratoconus. Ophthalmic Genet 2015;36(3):213-217 https://doi.org/10.3109/13816810.2013.843712

Rabinowitz YS, Galvis V, Tello A, Rueda D, García JD. Genetics vs chronic corneal mechanical trauma in the etiology of keratoconus. Exp Eye Res 2021;202:108328 https://doi.org/10.1016/j.exer.2020.108328

Mouli K, Liopo AV, Suva LJ, Olson KR, McHugh EA, Tour JM, et al. SOD1 Is an Integral Yet Insufficient Oxidizer of Hydrogen Sulfide in Trisomy 21 B Lymphocytes and Can Be Augmented by a Pleiotropic Carbon Nanozyme. Antioxidants (Basel) 2024;13(11):1361 https://doi.org/10.3390/antiox13111361

Mathan JJ, Gokul A, Simkin SK, Meyer JJ, McGhee CNJ. Keratoconus in Down syndrome: Prevalence, risk factors, severity and corneal tomographic characteristics. Clin Exp Ophthalmol 2024;52(1):22-30 https://doi.org/10.1111/ceo.14316

Vega-Estrada A, Fariselli C, Alio JL. Posterior corneal features in patients with Down syndrome and their relation with keratoconus. Br J Ophthalmol 2020;104(12):1683-1689 https://doi.org/10.1136/bjophthalmol-2019-314939

Humayun S, Fawad A, Ishaq M, Humayun Q, Arzoo S, Mashhadi SF. Screening Thresholds for the Corneal Tomography in Hyperopic Pakistani Population. J Coll Physicians Surg Pak 2020;30(9):951-955 https://doi.org/10.29271/jcpsp.2020.09.951

Ren S, Xu L, Fan Q, Gu Y, Yang K. Accuracy of new Corvis ST parameters for detecting subclinical and clinical keratoconus eyes in a Chinese population. Sci Rep 2021;11(1):4962 https://doi.org/10.1038/s41598-021-84370-y

Peyman A, Sepahvand F, Pourazizi M, Noorshargh P, Forouhari A. Corneal biomechanics in normal and subclinical keratoconus eyes. BMC Ophthalmol 2023;23(1):459 https://doi.org/10.1186/s12886-023-03215-6

Kataria P, Padmanabhan P, Gopalakrishnan A, Padmanaban V, Mahadik S, Ambrósio R. Accuracy of Scheimpflug-derived corneal biomechanical and tomographic indices for detecting subclinical and mild keratectasia in a South Asian population. Journal of Cataract and Refractive Surgery 2019 ;45(3):328-336 https://doi.org/10.1016/j.jcrs.2018.10.030