Original Article

The Relationship between Keratoconus and Joint Hypermobility

Seyed - Hashem Daryabari *[1], MD; Sajad Mansourian [2], MD; Atefeh Shiravandi [3], BS

1. Chemical Injuries Research Center, Systems biology and Poisonings Institute, Baqiyatallah University of Medical Sciences, Tehran, Iran.
2. Eye research Center, Farabi Eye Hospital, Tehran University of Medical Sciences, Tehran, Iran.
3. Department of Ophthalmology, Baqiyatallah University of Medical Sciences, Tehran, Iran.

***Corresponding Author:** Seyed - Hashem Daryabari
E-mail: shdarya50@yahoo.com

Abstract

Purpose: To evaluate the relation between joint hypermobility and keratoconus.
Patients and Methods: This case-control study was conducted at the ophthalmology department of Baqiyatallah hospital, Tehran, Iran, from September 2020 to April 2021. The case group consisted of patients with keratoconus, while the control group included healthy individuals. The hypermobility score (Beighton test) was calculated for patients in both groups.
Results: A total of 127 keratoconus patients were enrolled as the case group. Additionally, 34 healthy individuals were evaluated as the control group. When comparing joint hypermobility individually, the case group showed significantly higher spinal column forward flexion hypermobility ($P < 0.01$) and elbow joint hypermobility ($P = 0.03$). In the case group, 43 patients (33 %) had a Beighton mobility score of more than 4, implying general joint hypermobility, compared to 8 patients (23.5 %) in the control group, indicating no statistically significant difference between the two groups ($P = 0.22$). Despite the lack of correlation between general joint hypermobility and the presence or absence of keratoconus, a significant correlation was observed between the severity of keratoconus and joint hypermobility in patients with keratoconus, such that higher stages of keratoconus were associated with greater joint hypermobility ($P < 0.001$).
Conclusion: Based on our findings, it can be concluded that although joint hypermobility and keratoconus may not necessarily be related diseases, there might be a correlation between the severities of these two conditions.

Keywords: Keratoconus; Joint Hypermobility Syndrome; Correlation.

Article Notes: Received: Nov. 08, 2022; Received in revised form: Dec. 05, 2022; Accepted: Jan. 14, 2023; Available Online: Apr. 02, 2023.

How to cite this article: Daryabari SH, Mansourian S, Shiravandi A. The Relationship between Keratoconus and Joint Hypermobility. Journal of Ophthalmic and Optometric Sciences . 2023;7(2): 9-13.

Introduction

The ability of a joint to move beyond its normal range of motion along physiological axes is called joint hypermobility [1, 2]. General joint hypermobility (GJH) is a common condition, found in 2-57 % of the population, but individual joint hypermobility may be observed in various degrees in a higher percentage of the population [3]. It has been suggested that individuals with joint hypermobility exhibit an abnormal ratio of type III to type I collagen [4]. Type I collagen, which has high tensile strength, is the most common collagen in the body and is abundantly present in tendon receptors, joint capsules, skin, bone, and nerves [5]. Type III collagen is highly stretchable and fragmented, found in organs such as the intestines, skin, and blood vessels [6]. Mutations in genes encoding type I collagen play a significant role in the pathogenesis of joint hypermobility [7]. Joint hypermobility occurs 1.5 to three times more often in women than in men and is also more prevalent in Asian and African ethnicities [2].

Keratoconus, the most common cause of primary corneal ectasia, is a bilateral, and asymmetric progressive disease characterized by corneal ectasia, thinning, and protrusion [8,9]. It has a varied prevalence around the world, with an estimated prevalence of about 1 in 2000. However, it can be as high as 5 % of the population in the Middle East [10,11]. Keratoconus typically manifests in the second and third decades of life, progressing rapidly before slowing down [12]. In this disease, the collagen fibers weaken and lose their ability to maintain the shape of the cornea, resulting in the cornea becoming thinner and its shape changing [13].

It has been suggested that there might be a relation between keratoconus and joint hypermobility, since both conditions arise from irregularities in collagen tissue [14, 15]. We performed the present study to further evaluate the possible relation between these two diseases.

Patients and Methods

Study Population

The present study included patients with keratoconus who visited the ophthalmology clinic of Baqiyatallah Hospital, Tehran, Iran, from September 2020 to April 2021. These patients comprised the case group, while the control group consisted of healthy individuals without any apparent eye diseases.

Inclusion criteria for the case group were patients diagnosed with keratoconus by a corneal specialist, aged 15 to 60 years. Exclusion criteria included individuals with soft tissue joint and connective tissue disorders (myopathies, rheumatic diseases, etc.), and those taking corticosteroids. This study was conducted in accordance with the Declaration of Helsinki. The study protocol was approved by the institutional ethics committee, and all participants provided written consent before entering the study.

Data Collection Tools

We employed a SIRIUS device for corneal imaging, a slit lamp for eye examinations, and a goniometer for joint examinations.

Research Methodology

Patients diagnosed with keratoconus based on tomography imaging with a SIRIUS device were included in the study group. All study participants, both in the case and control groups, were surveyed through questionnaires for demographic characteristics, history of rheumatological diseases, allergies, athletic

activities, and corticosteroid use. Subsequently, patients were referred to the physical medicine clinic and examined by a physical medicine specialist for joint hypermobility in the elbows, knees, first and fifth metacarpals, and forward bending ability of the spine. Also the mean body mass index (BMI) was calculated for all participants.

If the range of motion of a joint exceeded the normal range for that joint, it was recorded as hypermobile. Overall Beighton mobility scores for all joints were summed up and expressed as a fraction out of 9, with scores higher than 4 out of 9 considered general joint hypermobility.

Statistical Analysis

All analyses were performed using SPSS version 19 (IBM, Armonk, NY, USA). Statistical indicators such as mean, standard deviation, percentage, frequency, and related metrics were utilized. P values less than 0.05 were considered statistically significant.

Results

A total of 127 keratoconus patients were enrolled in the study. Additionally, 34 healthy individuals served as the control group. The average age in the patient group was 32.14 ± 8.2 years (age range 18 to 57 years), and in the control group, it was 32.8 ± 9.6 years (age range 23 to 52 years), showing no statistically significant difference. In the case group, 64.8 percent were male and 35.2 percent were female. In the control group, 59.1 percent were male and 40.9 percent were female. There was no statistically significant difference between the case and control groups regarding sex distribution. The mean BMI in the case and control groups was 26.44 and 25.29, respectively, showing no statistically significant difference between the two groups. In the patient group, the highest hypermobility was noted in the spinal column's forward flexion, affecting 93 individuals (73 %), followed by elbow joint hypermobility in 71 individuals (55 %), little finger metacarpophalangeal joint hypermobility in 46 individuals (36 %), knee joint hypermobility in 19 individuals (14 %), and thumb metacarpophalangeal joint hypermobility in 5 individuals (4 %) (Table1). In the control group, the highest hypermobility was noted in spinal column forward flexion hypermobility in 18 individuals (52 %), followed by elbow joint hypermobility in 12 individuals (35 %), little finger metacarpophalangeal joint hypermobility in 12 individuals (35 %), knee joint hypermobility in 4 individuals (11 %), and thumb metacarpophalangeal joint hypermobility in 4 individuals (11 %) (Table1). When comparing joint hypermobility individually, the case group showed significantly higher spinal column forward flexion hypermobility ($P < 0.01$) and elbow joint hypermobility ($P = 0.03$) (Table1). In the case group, 43 patients (33 %) had a Beighton mobility score of more than 4, implying general joint hypermobility, compared to 8 patients (23.5 %) in the control group, indicating no statistically significant difference between the two groups ($P = 0.22$). Despite the lack of a correlation between general joint hypermobility and the presence or absence of keratoconus, there was a significant correlation between the severity of keratoconus and joint hypermobility in keratoconus patients, such that higher stages of keratoconus were associated with greater joint hypermobility ($P < 0.001$).

Table 1: Comparison of joint hypermobility between patients with keratoconus and healthy individuals

Joint	Case group	Control group	P- Value
Spinal Column Forward Flexion	93 (73 %)	18 (52 %)	< 0.01
Elbow joint	71 (55 %)	12 (35 %)	0.03
Little finger metacarpophalangeal joint	46 (36 %)	12 (35 %)	> 0.05
Knee joint	19 (14 %)	4 (11 %)	> 0.05
Thumb finger metacarpophalangeal joint	5 (4 %)	4 (11 %)	> 0.05

Discussion

It is often suggested that keratoconus might be associated with joint hypermobility, but there is surprisingly little literature confirming or refuting this connection. In this study, a total of 127 patients with keratoconus were compared to 34 individuals without keratoconus regarding joint hypermobility. The mean age was 32.14 ± 8.2 years in the patient group and 32.8 ± 9.6 years in the control group, showing no significant difference. There was also no significant difference in sex distribution or BMI between the case and control groups. When comparing joint hypermobility individually, the case group showed significantly higher spinal column forward flexion hypermobility and elbow joint hypermobility, but no difference was observed regarding little finger metacarpophalangeal joint, knee joint, or thumb metacarpophalangeal joint hypermobility.

Contrary to our findings, Woodward et al., [14] reported no statistically significant differences between the groups for the trunk or knee joints, although differences were found for the metacarpophalangeal and wrist joints. On the other hand Street et al., [16] detected no statistically significant differences in the prevalence of hypermobile joints in keratoconus patients and controls for any of these five joints.

We observed 43 patients (33 %) in the case group with a Beighton mobility score of more than 4, implying general joint hypermobility, compared to 8 patients (23.5 %) in the control group, indicating no statistically significant difference between the two groups (P = 0.22). Despite the lack of a correlation between general joint hypermobility and the presence or absence of keratoconus, we observed a significant correlation between the severity of keratoconus and joint hypermobility in patients with keratoconus, with higher stages of keratoconus associated with greater joint hypermobility.

The main limitation of this study was the relatively small number of participants. Considering the limited number of previous studies on the subject and the contradictory results, performing future studies with a larger sample size is warranted.

Conclusion

Based on our findings, it can be concluded that although joint hypermobility and keratoconus may not necessarily be related diseases, there

might be a correlation between the severities of these two conditions.

Authors ORCIDs

Seyed - Hashem Daryabari:
https://orcid.org/0000-0002-7264-8637

References

1. Castori M. Joint hypermobility in children: a neglected sign needing more attention. Minerva Pediatr. 2020;72(2):123-33.
2. Ituen OA, Anieto EM, Ferguson G, Duysens J, Smits-Engelsman B. Prevalence and Demographic Distribution of Hypermobility in a Random Group of School-Aged Children in Nigeria. Healthcare (Basel). 2023;11(8):1092.
3. Blajwajs L, Williams J, Timmons W, Sproule J. Hypermobility prevalence, measurements, and outcomes in childhood, adolescence, and emerging adulthood: a systematic review. Rheumatol Int. 2023;43(8):1423-44.
4. Simmonds JV, Keer RJ. Hypermobility and the hypermobility syndrome. Man Ther. 2007;12(4):298-309.
5. Buckley MR, Evans EB, Matuszewski PE, Chen YL, Satchel LN, Elliott DM, et al. Distributions of types I, II and III collagen by region in the human supraspinatus tendon. Connect Tissue Res. 2013;54(6):374-9.
6. Kuivaniemi H, Tromp G. Type III collagen (COL3A1): Gene and protein structure, tissue distribution, and associated diseases. Gene. 2019;707:151-71.
7. Malfait F, Hakim AJ, De Paepe A, Grahame R. The genetic basis of the joint hypermobility syndromes. Rheumatology (Oxford). 2006;45(5):502-7.
8. Vazirani J, Basu S. Keratoconus: current perspectives. Clin Ophthalmol. 2013;7:2019-30.
9. Romero-Jiménez M, Santodomingo-Rubido J, Wolffsohn JS. Keratoconus: a review. Cont Lens Anterior Eye. 2010;33(4):157-66.
10. Marx-Gross S, Fieß A, Münzel T, Wild PS, Beutel ME, Schmidtmann I, et al. Much higher prevalence of keratoconus than announced results of the Gutenberg Health Study (GHS). Graefes Arch Clin Exp Ophthalmol. 2023;261(11):3241-7.
11. Gomes JAP, Rodrigues PF, Lamazales LL. Keratoconus epidemiology: A review. Saudi J Ophthalmol. 2022;36(1):3-6.
12. Duncan JK, Belin MW, Borgstrom M. Assessing progression of keratoconus: novel tomographic determinants. Eye Vis (Lond). 2016;3:6.
13. Sinha Roy A, Shetty R, Kummelil MK. Keratoconus: a biomechanical perspective on loss of corneal stiffness. Indian J Ophthalmol. 2013;61(8):392-3.
14. Woodward EG, Morris MT. Joint hypermobility in keratoconus. Ophthalmic Physiol Opt. 1990;10(4):360-2.
15. Robertson I. Keratoconus and the Ehlers-Danlos syndrome: a new aspect of keratoconus. Med J Aust. 1975;1(18):571-3.
16. Street DA, Vinokur ET, Waring GO 3rd, Pollak SJ, Clements SD, Perkins JV. Lack of association between keratoconus, mitral valve prolapse, and joint hypermobility. Ophthalmology. 1991;98(2):170-6.

Footnotes and Financial Disclosures

Conflict of interest:

The authors have no conflict of interest with the subject matter of the present manuscript.