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One-year epidemiological study of patients with Keratoconus in eastern Iran

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***Abstract*---** Background: Keratoconus is a degenerative and progressive of corneal disease. Unlike other country, studies about epidemiology of keratoconus are limited in the Iran. Aim of the study is survey of keratoconus epidemiology in the eastern Iran. Methods: For doing the cross-sectional study, patients were evaluated at the ophthalmology center of Mashhad County, during 2015-2016 year. Firstly, medical history was obtained from all new patients. Ocular examination was done for detection of keratoconus signs including Scissor reflex, Rizzuti sign, Fischer ring, Vogt striae and any sign of

previous hydrops. For all suspicious patient's topography was done. Also, the required demographic data were recorded. The data were analyzed using SPSS software (version 18). Results: Totally, 90 eyes from 45 patients were studied. The average age of patients was 25.1 ± 6 years and the average age of onset of the disease was 17.72 ± 7.76 years. More than half of patients (55.6%) were female. One-sided Keratoconus was found in 11.1 %. In 10 patients (10 eyes), there was history of penetrating keratoplasty due to advanced keratoconus. Average corneal power of patients was 49.4 ±6. Also, there was Fischer ring, Vogt striae and signs of previous hydrops in the 52%, 21% and 10.7 % of patient, respectively. Conclusion: Overall, the disease must be considered as a cause of unusual and non-correctable gradual visual loss, especially in the young women and age group of less than 20 years in the Iran. Also, many of keratoconus risk factors that were previously reported were not found in the study.

***Keywords*---**Keratoconus, epidemiology, Mashhad, Iran**.**

Introduction

Keratoconus is a non-inflammatory, bilateral, and progressive disease determined by abnormal curvature of the cornea (1). Corneal stroma becomes thin in this disease and may lead to scarring. The most important and first symptom is loss of near and far vision often as the result of astigmatism (2). Over time, astigmatism will be more irregular and cannot be corrected by using glasses (3). In most cases, disease is bilateral and mainly occurs in the second decade of life (4). In most cases, there is no family history of the disease, but inheritance of the disease has been described as inheritance of dominant and recessive autosomal. Several researchers have suggested that keratoconus is not an independent disease and may be a non-specific eye symptom representing broader systemic disease (5). Outbreak of disease has been differently reported in various reports and it has been reported between 50 and 230 cases per 100 thousand populations (6). In Rika et al study, the annual incidence in men is 12.1 and in women have been estimated 5.6 per 100 thousand people (7). The outbreak of this disease in the United States of America has been from 50 to 200 cases per 100 thousand people that this difference may be due to differences in the criteria used in diagnosis of the disease (8). Due to advances in diagnostic techniques, access to medical care, doctors' awareness about the disease in recent years have created a significant increase in diagnosed cases of keratoconus .

Signs and symptoms of the disease vary greatly and some of them depend on the stage of the disease (9). The Mounson Sign and Rizzuti phenomenon are some of findings of the disease that may be seen in external examination (10). Stroma being thinned, severity of Vogt striae, epithelial or sub-epithelial scar and Fisher ring are some of the findings of the disease on Slit-Lamp examination that are visible depending on the severity of the disease (11, 12,13). For diagnosis of the disease, Retinoscopic, Slit-Lamp and topographic surveys are used. Treatment varies at different stages. At the beginning of the disease, by the use of glasses, vision is relatively improved, but in advanced stages of the disease, contact lenses

are required (14). Finally, if dissatisfied with the quality of vision, the patient will be a candidate for surgery that is mainly performed in the form of corneal transplant surgery (15). So far, many studies have been conducted around the world about the epidemiology of this disease, however, in Iran, this type of studies has been very limited. Given the higher prevalence of keratoconus rather than other degenerative corneal diseases, the present study was designed and conducted by the objective of demographic and epidemiological study of keratoconus in patients referred to the greatest ophthalmology center at the eastern Iran country during 2015-2016 year.

Materials and Methods

For doing the cross sectional study, patients that were referred to the greatest ophthalmology center of the Eastern Iran country, at the Khatam Al- Anbia hospital of Mashhad, during January 2015 to March 2016 year. The research project has been approved by ethics committee of Mashhad University of medical sciences. The executive protocol of the study was also carried out based on the Helsinki Declaration and after obtaining informed consent from all participants. Firstly, medical history was obtained from all new patients that were referred to the anterior segment clinic, such as cause of coming to an ophthalmologist, history of any familial or non-familial disease, precedent of ocular or non-ocular surgery, history of using glasses or contact lens and drug history. Then, complete necessary ocular examination including checking uncorrected (UCVA) and best corrected visual acuity (BCVA), intraocular pressure (IOP) by Goldmann Applanation Tonometer (GAT), retinal examination by non-contact slit lamp lenses (90 and 20 diopter), checking of Scissor reflex presence by a Retinoscope, using slit lamp examination for detection of Rizzuti sign, Fischer ring, Vogt striae and any sign of previous Hydrops such as corneal scar or opacity. All examination was done by an anterior segment fellowship of ophthalmology with same setting. Then for all suspicious patients (including unjustified or non-correctable visual loss, history of keratoconus in the family or even presence of an abnormal sign), imaging of the cornea was done, including topography (or Orbscan). Then the required demographic and epidemiological data (gender, age) were recorded on pre-designed questionnaire. Finally, the data were analyzed using SPSS software (version 18).

Results

A total of 55 patients with keratoconus were recorded during the study period that 10 cases were excluded due to lack of sufficient information about them or lack of compliance. Out of the remaining 45 patients, 90 eyes were examined, that among these 90 cases, evidence of keratoconus was not observed in 5 cases. In 10 eyes, we were also looking for advanced keratoconus, penetrating keratoplasty surgery (PK) that has already been done for them, which these 10 eyes were for 10 patients (22.2% of total patients). Out of 45 of studied patients, 11.1 % of them had one-sided Keratoconus. Totally, 25 cases (55.6%) were female. The average age of patients was 25.1 ± 6 and the average age of onset of the disease was 17.72 ± 7.76. According to age of onset of the disease, Patients were divided into five groups of 0-9, 10-19, 20-29, and 30-39 and more than 40 years. The relative

frequency distribution of patients by age and duration of disease outbreaks has been shown in the table 1.

Of the 45 patients, three patients (6.7%) had a family history of keratoconus among first degree family members, and 15 patients (33.3%) reported wearing glasses among their first degree family members. Table 2 show the frequency distribution of patients based on medical history and eye diseases. In the evaluation of visual acuity, out of 90 examined eyes, 15 eyes were excluded because of corneal normality and history of cornea transplants. In 75 examined keratoconic eyes, the lowest visual acuity was 0.5 mcf (meter counted finger) and the highest was 8/10. Of these, 23 eyes (31.1%) had visual acuity 2/10 to 4/10 and 41 eyes (55.4%) had visual acuity of less than 2/10. In terms of astigmatism, in 14 eyes (18.9%), astigmatism value was less than 4 diopters, and in 18.9 %, it was between 5 and 8 diopters. 46 eyes of patients (62.2%) had astigmatism of over 11 diopters.

Regarding keratometry, average corneal power of patients (based on topographic findings) was 49.4 ±6. Also, the maximum and minimum keratometry was 61 and 45, respectively. In the examination of patients' eyes by Slit-Lamp in the 52%, 21% and 10.7 % of patient, Fischer ring, Vogt striae and signs of previous hydrops were observed, respectively. In the study, there was no significant correlation between age and gender in the keratoconus. (P= 0.78). Also in this study, there was no significant relationship between the disease incidence age and corneal transplant history (P= 0.3), Also, association between duration of the disease and corneal transplant history was not significant. (P= 0.4). The relationship between variables of the study with history of corneal transplant has been shown in table 3. On the other hand, in the study, no relationship was observed between unilateral or bilateral disease with a family history of wearing glasses or keratoconus (P = 0.441). Table 4 show Correlation between the studied variables with first related-family history of wearing glasses and keratoconus.

Discussion

In this study, more than half (55.6 %) of keratoconus cases were females that is in contrast with most of similar study (18-20). Based on report of Salouti et al from Southern Iran (18), 57 % of patients with keratoconus were male. Also, in the study of Zadnik et al (19) in the New Zealand, 23.5 % of patients were female and one of the lowest women involvements has been reported in the study of Dao et al (20) that was 22 %. Although the involvement of more women have been reported in older studies. Thus, regarding ratio and gender percentage of patients, the present study results is similar to studies in the past (21). In this study, mean age of patients at diagnosis time and highest percentage of age group was lower than 20 years that is similar to a study that was done in the southern Iran (18.5 ± 5.7) (18) that is lower than most of studies in the other country (12, 14, 21). In the few studies (22), the age of disease incidence is close to the results of present study (19).

In this study, 11% patients with keratoconus didn't have any findings (even in the imaging) in favor of keratoconus in another eye. This value in the study of Salouti et al (18) has been 6% and in the other studies, this range varies between 10%

and 20% (16, 19, 23). In the study of Holland et al (24), the imaging (topography) has been used to detect disease and unilateral involvement has been reported as 1.83 %. In this study, 22.2 % of patients had a history of corneal transplant, of course neither of them had the transplant in both sides of cornea. In the similar studies in Iran (18), this value was reported 21.2 %. The percentage of keratoconus patients with corneal transplant varies based on the nature of the center where the study has been conducted. for example, in this study, because the Eye Center of Mashhad University of Medical Sciences is considered as the corneal transplant center in Mashhad, so percentage of patients is significantly high.

There was no relationship between age of disease incidence and history of corneal (P= 0.303).Also, the disease duration was not correlated with corneal transplant history (P= 0.415). Given that the higher women involvement in this study and considering that the most of women were housewives (6.35%), thus, possible reduction in their social activities resulting in a high percentage of housewives falling into far-fetched, However, to study the relationship of the disease among housewives needs to more studies such as comparison with normal population. Also with respect to the involvement of students (26.7%), assessment of academic failure and school dropout of keratoconus patients seem necessary. In this study, a family history of keratoconus was 6.7 %, which is higher than similar studies in the Iran (18) and less that Lee et al study (15%). If used from imaging, this may be increased in the first-degree relatives of patients with keratoconus. Dominant inheritance pattern of the disease has been mentioned in the form of autosomal in some studies with influence of 20%.

In this study, high rate of wearing glasses in the first-degree relatives of patients (33.3%), may show association of significant refraction error and high incidence of keratoconus in the family, but the issue must be proved with prospective study by doing imaging from the family of patients with the keratoconus. There was no significant correlation between other systemic diseases and keratoconus incidence. Also, In the other studies, similar results were obtained (16, 18, 23). History of allergy in the patients of the study was 6.7 %, while in the study of Owens et al (25) this amount was 35%. Congenital heart disease was not observed in this study due to lack of suitable methods of diagnosis, such as related echocardiography. In the study of Kenedy et al, 5% of patients were with MVP (16). Vernal keratoconjunctivitis outbreaks in this study was (21.2 %) that is lower than similar studies in Iran (18) (29.5%) and abroad (35%) (16). Cataract associated with keratoconus has already been proven (26). In this study, cataracts were observed in 3.5 % of the eyes examined that in this study, it was not known whether it was congenital or not.

In terms of visual acuity, the survey results showed that only 13.5% of the examined eyes had vision better than 5.10, which was 58%, in the study of Zadnik et al (19) and 79% in study of Lass et al (23) and in Salouti et al study (18), it was 34%. The difference in the amount of astigmatism in this study is consistent with other studies. In terms of keratometry, average corneal power of patients (based on topography) was 49.4 ±6 in this study, which is consistent with most of studies in this field (16, 19). The findings of Slit-Lamp (73.3 %) are slightly higher than the results of the study of Zadnik et al (19) (68%). The total

amount of scar observed in this study was 24% that was higher than study of Salouti et al (17.2%) (18) and less than of Zadnik et al study (43%) (19). Also, no significant relationship was observed between gender and age of the patients in this study, while in the study of Owens et al (25), the disease occurred in younger age groups in men.

Conclusion

Overall, based on the study results and comparing with similar study, a certain geographical distribution was not observed for keratoconus in the Iran; the disease must be considered as a cause of unusual gradual visual loss, especially in the young women and age group of less than 20 years. Also, many of accompaniments with keratoconus that were reported in the previous studies were not found in the present study; such as gender, correlation between age of onset and chronic duration of disease with increasing risk of keratoplasty, association of systemic disease with keratoconus. However, based on specific characters of any region, more comprehensive and large studies are needed to discovering the chief risk factors of keratoconus.

Conflict of Interest

None of the authors has conflict of interest with the submission.

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Table 1
The relative frequency distribution of patients by age and duration of disease outbreaks (up to referring time) based on year.

	Age groups	number	percent
Disease onset age	0-9	6	13.3
	10-19	26	57.8
	20-29	9	20
	>30	4	9.8
	Total	25	100
Disease duration	0-4	20	44.4
	5-9	14	31.1
	10-14	6	13.3
	15-19	1	2.2
	>20	4	8.9

Table 2
Frequency distribution of patients based on medical history and eye diseases. (*Mental retardation,ϕHypertension,€Ischemic heart disease,**Vernal keratoconjunctivitis)

Medical history	Number	percent
Allergies	3	6.7
Asthma	1	2.2
MR*, Down syndrome	1	2.2
HTNϕ, IHD€	1	2.2
DM	1	2.2
Normal	38	84.4
Total	45	100
Eye disease	**Number**	**percent**
VKC**	18	21.2
Chorioretinal atrophy	4	4.7
Cataract	3	3.5
Trauma	3	3.5
Seborrhic blepharitis	2	2.4
Epithelial erosions	1	1.2
Strabismus- Amblyopia	1	1.2

Table 3
The relationship between variables of the study with history of corneal transplant (*Number)

Keratoconus		Keratoplasty(+) N*	%	Keratoplasty (-) N*	%	P value
Onset age	0-9	2	4.4	4	8.9	0.138
	10-19	4	8.9	22	48.9	
	20-29	4	8.9	5	11.1	
	>30	0	0	4	6.9	
	Total	10	22.2	35	77.8	
Duration	0-4	3	6.7	17	37.8	0.268
	5-9	5	11.1	9	20	
	10-14	2	4.4	4	8.9	
	>15	0	0	5	11.1	
	Total	10	22.2	35	77.8	

Table 4
Correlation between the studied variables with a first relative-family history of wearing glasses and keratoconus (*Number)

Keratoconus	value	Family history (+)		Family history (-)		P
		N*	%	N*	%	
onset age	0-9	1	2.2	5	11.1	
	10-19	13	28.9	13	28.9	
	20-29	2	4.4	7	15.6	0.101
	>30	0	0	4	8.9	
	Total	16	35.6	29	64.4	
Type	Unilateral	1	22	4	8.9	
	Bilateral	15	33.3	25	55.6	0.440
	Total	16	35.6	29	64.4	