

Frequency of corneal dystrophies on the basis of histopathology in surgically removed corneas

Iram Sohail,¹ Fozia Noreen,² Samia Nawaz,³ Safina Ahmed,⁴ Humaira Zafar,⁵ Mahwish Niaz⁶

Abstract

Objective: To assess the frequency of corneal dystrophies on the basis of histopathology in surgically-removed corneas.

Methods: The descriptive study was conducted at Foundation University Medical College, Islamabad, and Al Shifa Eye Hospital, Rawalpindi, Pakistan, from May to October 2011, and comprised post-keratoplasty corneal specimen irrespective of age and gender. The surgically-removed corneas were processed according to the standard guidelines of histopathological processing. The histopathological sections were examined for various corneal dystrophies. Data was recorded on a proforma and was analysed using SPSS 17.

Results: Of the 63 patients in the study, 12(19%) were diagnosed as having corneal dystrophies. In these 12 patients, 6(50%) were diagnosed as stromal corneal dystrophies and 5(42%) had posterior corneal dystrophies, and 1(8%) had anterior corneal dystrophy.

Conclusion: Histopathological examination of corneas is a reliable method to diagnose and classify corneal dystrophies.

Keywords: Cornea, Corneal dystrophy, Keratoplasty, Histology. (JPMA 65: 1056; 2015)

Introduction

According to a recent study, 80% of world's blind people live in developing countries. In these countries corneal diseases constitute 8% to 25% cases of blindness which are responsible for 20% of childhood blindness.¹

The cornea is a transparent, avascular, crystal clear structure that forms the anterior 1/6th of the outer surface of the eye ball. A transparent cornea on the front surface of the eye is very essential for a clear retinal image.² As far as the histology of cornea is concerned, it is composed of five different layers from anterior to posterior (epithelium, Bowman's layer, stroma, Descemet membrane and endothelium).³⁻⁵ Any change in the anatomy/physiology of cornea results in loss of transparency to some extent. The importance of cornea is often neglected because of its transparent nature, because it lacks the neurobiological sophistication of retina and the dynamic nature of lens, but still without its clarity a proper and clean vision is not possible.⁶

The corneal dystrophies are a group of bilateral, non-inflammatory, inherited diseases confined to cornea. Clinically they present as variably shaped corneal opacities due to accumulation of different types of deposits in the cornea which may culminate in blindness. Corneal

dystrophies may not affect vision in the early stages of disease but it can affect vision in advanced stages and that is why proper evaluation, correct diagnosis and treatment are necessary for the restoration of optimal vision.

According to a study conducted in the USA, corneal dystrophies are divided into 3 main groups; anterior, stromal and posterior corneal dystrophies on the basis of histopathology. In anterior corneal dystrophy, corneal epithelium, basement membrane and superficial corneal stroma are involved. These include Messmann dystrophy and gelatinous drop-like dystrophy. In stromal corneal dystrophies, corneal stroma is involved. It includes macular corneal dystrophy and granular corneal dystrophy. In posterior corneal dystrophies, Descemet membrane and corneal endothelium are involved. They include Fuchs corneal dystrophy and congenital hereditary endothelial corneal dystrophy.^{7,8}

Corneal dystrophies are one of the major indications of corneal transplant in eastern as well as in the western world.⁹ Penetrating keratoplasty is a very safe and reliable surgical procedure for patients with corneal dystrophies. Keratoplasty is a surgical procedure in which the patient's diseased cornea is replaced by donor's healthy cornea. It also provides us corneal tissue for histopathological study. Accuracy of provisional diagnosis of corneal dystrophies can be increased by histopathological examination of surgically-removed corneas.¹⁰

The prevalence of corneal dystrophies is diverse and

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^{1,5}Al-Nafees Medical College & Hospital, Islamabad, ²Margala Hospital, Taxila Cantt, ³Shifa International Hospital, Islamabad, ^{4,6}Fauji Foundation Hospital, Rawalpindi.

Correspondence: Iram Sohail. Email: iramriazaq@yahoo.com

different in different parts of the world because of many factors, like family history; eye care etc.¹¹ In Canada, the prevalence is 12.8% among corneal diseases. Germany has got 19.8% while in Japan and Australia the prevalence is 12.6% and 7% respectively.

In developing countries, the data for corneal dystrophies are deficient probably because of less number of corneal transplantation centres, late diagnosis and poverty.¹

The current study was planned to find the frequency of corneal dystrophies in surgically-removed corneas. Previously the diagnosis of corneal dystrophies was made clinically only because corneal biopsy material after keratoplasty was thrown away and wasted. The study was also used as an adjunct to clinical findings to make the final diagnosis of a corneal dystrophy to enhance the rate of diagnostic accuracy.

Patients and Methods

The descriptive study was conducted in the Department of Pathology, Foundation University Medical College, Islamabad, and Al-Shifa Eye Trust Hospital, Rawalpindi, Pakistan, from May to October 2011, and comprised post-keratoplasty corneal specimen irrespective of age and gender. Inadequate corneal biopsy material and inadequately fixed biopsies were excluded.

By applying non-probability consecutive sampling technique, the sample size was calculated as 63. Data about patient's name, age, gender and clinical presentation was collected on a proforma after informed consent was obtained from the patients.

All corneal samples were processed as per standard guidelines of histopathological processing, including fixation in 10% formalin, dehydration in ethyl alcohol by increasing concentration (70%, 80% and 90%), clearing by xylene, paraffin embedding by wax, section cutting by microtome and then stained with routine Haematoxylin and Eosin (H&E). Special stains such as Periodic Acid Schiff (PAS) and Congo Red were also used as per requirement. The stained slides were examined by experienced histopathologists. The corneal biopsies were systematically reported, beginning with a macroscopic description (colour, diameter and consistency) along with microscopic details and noted in a systematic manner from epithelium, basement membrane, stroma, Descemet membrane and endothelium. These cases were categorised as anterior, stromal and posterior corneal dystrophies.

Data was analysed using SPSS17. Descriptive statistics (frequencies along with percentages) were used to describe categorical variables (gender, clinical features

and types of corneal dystrophies) and summarised as mean±standard deviation. $P < 0.05$ along with 95% confidence interval (CI) was considered significant.

Results

Of the 63 patients in the study, 12(19%) were diagnosed as having corneal dystrophies. The mean age was 31 ± 24.2 years and the gender distribution was almost equal 7 (58%) were males and 5 (42%) were females. In the 12 patients, 6(50%) were diagnosed as stromal corneal dystrophies, 5(42%) had posterior corneal dystrophies, and 1(8%) had anterior corneal dystrophy.

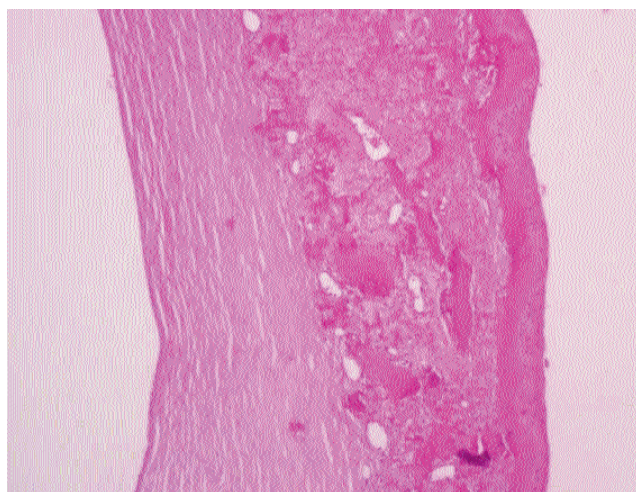


Figure-1: Photomicrograph of corneal tissue revealing gelatinous drop-like dystrophy (anterior corneal dystrophy) with thickened Bowman's membrane and amorphous material in anterior stroma. (Haematoxylin and Eosin stain X 10).

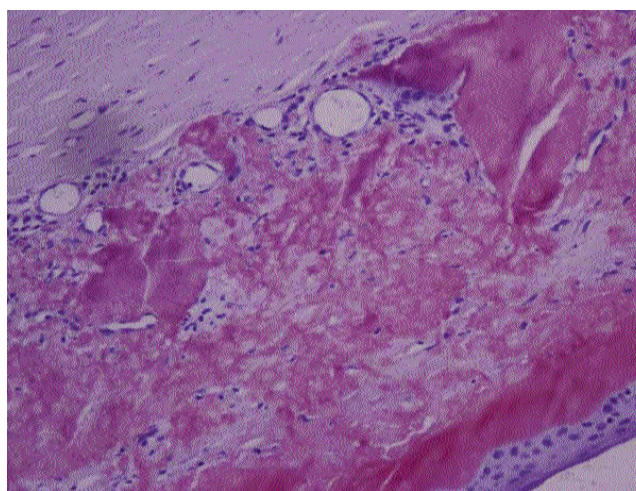


Figure-2: Photomicrograph of corneal tissue with gelatinous drop-like dystrophy (anterior corneal dystrophy) showing amorphous material (amyloid) stained with Congo red, giving brown colour in anterior stroma. (Congo red stain X 40).

Of the 12 patients, blurring was the most common symptom 12(100%), followed by deterioration of vision 10(83.3%), irritation and watering 8(66.6% each), photophobia 4(33.3%) and pain 3(25%). Only 1(8.3%) case had recurrent erosions.

The lone (8%) patient diagnosed and labelled as gelatinous drop-like dystrophy presented with complaints of blurring, decrease vision and photophobia along with some raised areas on cornea. On microscopic examination the epithelium was atrophic and the area just below the Bowman's membrane and anterior stroma contained amorphous material (Figure-1). This material was positive for Congo Red stain and under polarised light it revealed apple green birefringence (Figure-2). Descemet membrane was intact and endothelial cells were normal in number and morphology.

Among the 6(50%) patients diagnosed with macular corneal dystrophy, the most common symptoms were discomfort, blurring and reduced vision with opaque corneas. On histopathological examination, stroma of all the corneas revealed focal and patchy deposition of amorphous material. This basophilic material was PAS-positive. Epithelium and Descemet membrane were unremarkable.

Of the 5(42%) patients with posterior corneal dystrophy, 2(40%) were labelled as Fuchs corneal dystrophy, while the other 3(60%) were diagnosed as congenital hereditary endothelial dystrophy. In both cases of Fuchs corneal dystrophy, the patients represented with blurring of vision and opaque corneas. On microscopy, the epithelium, Bowman's membrane and stroma were unremarkable. The Descemet membrane was markedly thickened along with loss of endothelial cells and local guttae formation. The patients of congenital hereditary endothelial dystrophy had complaints of blurring and deterioration of vision with opaque corneas. On histopathology, the epithelium and Bowman's membrane were unremarkable with mild stromal oedema. Focal absences of endothelial cells were obvious in all cases.

Discussion

Cornea is a crystal clear, avascular structure present at the anterior 1/6th of outer eye ball.² The transparency of cornea is very necessary for a clear image.¹² Histologically, cornea is composed of 5 layers: epithelium, Bowman's layer, stroma, Descemet membrane and endothelium.¹³ Any deposition in these layers will result in loss of transparency.

Corneal dystrophies are bilateral, non-inflammatory, progressive corneal diseases, characterised by deposition of non-native proteins in the different layers of cornea. They can be a cause of blindness in all age groups. The prevalence of corneal dystrophies is different from

country to country.¹¹ They are the leading cause of blindness not only in adults, but also in children. It is estimated that approximately 1.5 million children in the world are blind and corneal dystrophies are a major cause of blindness in these children.^{14,15} In USA, the burden of corneal dystrophies is 897 per million.¹⁶ In Europe, the prevalence is 13.9%.¹⁷ Studies conducted in Japan and Australia revealed frequencies of corneal dystrophies 12.6% and 7% respectively.^{18,19}

On the basis of histopathological and biomicroscopic features, corneal dystrophies are classified into anterior, stromal and posterior corneal dystrophies. In anterior corneal dystrophy the deposition mainly occurs in epithelium or anterior stroma. Stromal corneal dystrophy mostly occupies the mid-stromal portion of corneas. The site of deposition in posterior corneal dystrophy is Descemet membrane or endothelium.

In the West a number of studies have been conducted on corneal dystrophies. In the current study we not only confirmed the diagnoses of corneal dystrophies but also classified these corneal dystrophies on the basis of histopathology. After keratoplasty, corneas of 63 patients were included. Out of 63 patients, 12 were diagnosed as corneal dystrophies. The most common symptoms in descending order of frequency were difficulty in vision, reduced vision, watering, photophobia, pain and recurrent erosions.

Among the 12 patients, 50% were diagnosed with stromal corneal dystrophy (macular corneal dystrophy). In this type, the main deposition of amorphous material was present in stroma. This deposit was positive for PAS stain. The overlying epithelium was focally thin in 3 cases and remaining 3 cases had unremarkable epithelium. The Bowman's membrane was intact in 5 cases while showing focal breaks in 1 case. Descemet membrane was unremarkable and intact. The endothelial cells were also normal in number and morphology.

Five patients were diagnosed as posterior corneal dystrophy and further classified into Fuchs corneal dystrophy and congenital hereditary endothelial dystrophy. The epithelium and Bowman's membrane were unremarkable, the stroma showed mild interstitial oedema, the Descemet membrane was markedly thickened with loss of endothelial cells and guttae formations were seen in both cases of Fuchs corneal dystrophy. While in 3 cases of congenital hereditary endothelial dystrophy the epithelium and Bowman's membrane were unremarkable in all cases, mild stromal oedema with thickened Descemet membrane in 2 cases and focal absence of endothelial cells in all cases.

Many studies have been conducted worldwide to determine the frequency of corneal dystrophies. A study²⁰ in USA determined the prevalence of corneal dystrophies as 897 per million. They noted that corneal dystrophies are common in white females with average age of 35 years. Anterior and endothelial dystrophies were more common compared to stromal type. In the current study anterior and stromal dystrophies are more common so it shows dissimilarity in the presentation of anterior and stromal dystrophies and this dissimilarity may be due to difference in the races of both studies; the current study having Asians only. So from the results of these studies, conclusion can be drawn that the endothelial dystrophy is common in both Asians and Americans, while stromal dystrophies are more commonly present in Asians, with the same age of presentation but difference in gender terms.²⁰

A study²¹ conducted in India found 9.6% prevalence of corneal dystrophies. Males were more commonly involved and stromal dystrophies were more prevalent in India. One more important parameter socioeconomic status was also observed in that study. Corneal dystrophies were more common in high socioeconomic group (67%) and less common in low socioeconomic group (33%). Like the current study, the Indian study also showed that stromal and posterior corneal dystrophies were more common, and anterior dystrophies were less common in India.

Our study had a limitation as it ignored Western literature^{22,23} in which most of the corneal dystrophies are caused by molecular genetic defects. Future studies should explore this aspect for further confirmation and classification of corneal dystrophies.

Conclusion

Histopathological examination of corneas after keratoplasty was a good and reliable method not only to confirm the diagnosis of corneal dystrophies but also to properly classify them into anterior, stromal and posterior types. This histopathological examination can be used as an adjunct to clinical findings to reach a more accurate diagnosis.

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