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Original Research

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An insight into corneal button histopathology in dystrophies following keratoplasty: A prospective study

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ABSTRACT

Background: The prognosis and outcome of a tissue transplant is dependent on its pathology and though, penetrating keratoplasty (PKP) is the most successful tissue transplant, most of its studies are genetic/clinical based. This histopathology study on corneal dystrophies is aimed at correlating clinicopathology with graft outcome in an attempt to understand the pathology better. **Materials and Methods:** Corneal buttons from all age groups where PKP was performed for dystrophy/degeneration were prospectively selected over 3½ years by convenient sampling. Corneal buttons of keratoconus and bullous keratopathy (aphakic/psuedophakic) following PKP were also studied, though they are neither specific dystrophy/degeneration and showed non-specific stromal changes. **Results:** One hundred and ten corneal buttons (40.3%) with dystrophy ($n = 44$) and degeneration ($n = 66$) from 273 cases of PKPs were studied histopathologically. 90% of dystrophies and 66% of degenerations showed a very good clinicopathologic correlation. Macular, Lattice and Avellino's dystrophies among dystrophies and Salzmann's nodular degeneration showed specific stromal deposits making them easily diagnosable at histopathology, whereas the rest showed non-specific stromal changes mandating correlation with clinical findings. Seven regraft corneas showed stromal fibrosis making identification of primary dystrophy impossible. However, transmural vascularization and lymphocytic stromal infiltrate were prominently noted in failed grafts though their numbers were few. **Conclusion:** This histopathologic study characterizes classic features of macular, Avellino's, lattice corneal dystrophies and Salzmann's degeneration for their microscopic diagnosis, while the rest showed non-specific changes. Stromal edema was prominently noted in degenerations than in dystrophies. Degree of stromal vascularization and type of cellular infiltrate need attention in regrafts.

KEY WORDS: Cornea, corneal degeneration, dystrophy, histopathology, keratoplasty

INTRODUCTION

One among the corneal diseases causing significant visual impairment and blindness is corneal dystrophies, which is a heterogeneous subset of hereditary corneal disorders that are generally bilateral, non-inflammatory and often result in corneal opacities, requiring corneal transplantation [1]. To add to this group and also which is closely related to dystrophy are the degenerative conditions of the cornea that may be acquired or idiopathic [2].

The prognosis of these corneal lesions depends on the type of pathology affecting the cornea. Hence, histology of biopsy specimens has a role in the assessment of their post-operative management and prognosis. Majority of reported studies are clinical based with an emphasis on genetic workup. Only a few occasional ones are on histopathology. This histopathological study on corneal buttons from clinically diagnosed cases of corneal dystrophies and degenerations presents an attempt to correlate with their graft outcome.

MATERIALS AND METHODS

Full thickness corneal buttons from clinically diagnosed cases of corneal dystrophies and degenerations from patients of all age groups who underwent penetrating keratoplasty (PKP) were selected by convenient sampling. Those who underwent lamellar keratoplasty or those corneal buttons which were improperly fixed/preserved were excluded from the study.

Patient demographics and clinical data were noted from hospital case records. A preliminary gross examination of the corneal buttons was done by documenting the size/dimension, presence of any opacity (extent and type), surface ulceration, pigmentation and perforation if any.

Corneal buttons after routine processing were embedded and cut with a microtome at 5-7 microns, and the serial sections obtained were stained with hematoxylin and eosin stain. The periodic acid-schiff (PAS) stain was also performed routinely to assist in assessing histopathology, visualization of the epithelial

basement membrane, Bowman's and Descemet's membrane. Furthermore, special stains such as Congo red, Crystal violet, von Kossa, Alcian blue (AB), Masson's Trichrome and Grocott's Methenamine Silver were performed wherever necessary.

The microscopic features were analyzed systematically (layer-wise) starting from epithelium to endothelium and the findings were correlated clinically. With the clinico-pathological correlation, a final diagnosis was made. An attempt to follow-up or obtain information about outcome was tried. The follow-up ranged from 1 month to 1 year. The patients were scheduled for a follow-up visit on the 1st day, at 1 and 3 weeks, at 1, 3 and 6 months, then at 1 year. In addition, they were advised to report back in the event of any problem. At each follow-up visit, the patients underwent a complete ophthalmic examination including recording of visual acuity, graft status, signs of graft rejection, intraocular pressure and fundus examination. The outcome was categorized as clear grafts and failed grafts. A graft was considered as clear, if the cornea was thin with no haze, no Descemet's membrane folds and the endothelium showed no keratic precipitates. A graft was considered failed if the corneal thickness was increased and there were epithelial haze or edema, stromal edema and fresh or old keratic precipitates.

RESULTS

A total of 110 corneal buttons were received after primary PKP for a clinical diagnosis of dystrophy or degeneration over a period of 3 years.

The category of dystrophy and degeneration together constituted 40.3% of the overall indications for PKP, while inflammatory/infective, congenital and miscellaneous causes constituted 47.6%, 1.1% and 10.9% respectively [Table 1].

Dystrophy and Degeneration

Of the 110 corneal buttons, 44 were done for dystrophies (including keratoconus), while 66 were performed for degenerations (including bullous keratopathy) with the histopathology [Figures 1 a-i and 2a-f] confirming changes compatible with the clinical diagnosis.

Of the 44 cases of dystrophy (including keratoconus), 24 corneal buttons were for specific dystrophies, while 20 were from post hydrops keratoconus cases. A male predominance was noted with a male: Female ratio of 1.97:1 [Tables 2 and 3].

Table 1: Indications for PKP in the present study

Indications	Number (*n*=273)	%100
Inflammatory/infective	130	47.6
Dystrophies/degenerations/metabolic	110	40.3
Congenital	3	1.1
Miscellaneous (includes entities suchasxerosis, xeroderma pigmentosa, retinal detachment and unrelated entities)	30	10.9

PKP: Penetrating keratoplasty

Ten were diagnosed with macular dystrophy, eight with congenital hereditary endothelial dystrophy, two each with Stromal and Fuch's dystrophy and one each with Lattice and Avellino's dystrophy. Their age and sex distribution is shown in Table 3. These patients complained of dimness of vision lasting for more than 2 years associated with photophobia. A positive family history could be obtained in three cases. At histology [Figure 1 a-c], the superficial corneal stroma showed granular to mucoid deposits staining positively with AB and were seen to extend subepithelially separating the Bowman's layer from the overlying epithelium. The surrounding stroma showed evidence of edema. The overlying corneal epithelium, the Descemet's membrane and the endothelium were intact and unremarkable.

The case of lattice corneal dystrophy seen in a 9-year-old male who complained of bilateral blurring of vision (right more than left) showed classic corneal lines, on slit lamp examination, forming a lattice configuration primarily around a round, regular, responsive pupil leaving the peripheral cornea clear. At histology [Figure 1d], the intact surface epithelium showed thickened basement membrane. The stroma showed dense sclerosis and fusiform deposits of amorphous, eosinophilic material in mid-stroma, which were PAS and Congo red positive.

The case of Avellino's corneal dystrophy in a 45-year-old male showed collagen disarray with sclerosis and homogenization [Figure 1e]. The stroma showed neovascularization with small spaces containing basophilic material, negative with AB-PAS. They were Congo red negative. This case was diagnosed after clinical correlation.

Two cases of Fuch's dystrophy diagnosed were in a 60-year-old female involving the right eye and the other in a 56-year-old man involving both the eyes. The former was clinically diagnosed as bullous keratopathy secondary to Fuch's dystrophy. The thinned out epithelium at histology [Figure 1f and g] exhibited focal basal cell vacuolation with vesiculation. Both the membranes were markedly thickened and showed evidence of staphyloma. The second case presented with diminished vision of 10 years duration with redness, pain and watering which on histology showed marked stromal sclerosis with a fibrillated to homogenous collagen.

Six buttons diagnosed as congenital hereditary endothelial dystrophy were from patients between 6 months and 9-year-old male children who presented with congenital corneal opacity involving both eyes. They had blue sclera and nystagmus. History of consanguineous marriage was obtained in both. Histologically, they had thickened corneal wall with epithelial

Table 2: Age and sex distribution in cases treated with PKP

Groups	Number (*n*=110)	Male (*n*=73)	Female (*n*=37)
Dystrophy(+keratoconus)	24+20=44	19+10=29	5+10=15
Degeneration (specific+PBK/ABK)	19+47=66	13+31=43	6+16=22

PBK: Pseudophakic bullous keratopathy , ABK: Aphakic bullous keratopathy, PKP: Penetrating keratoplasty

Table 3: Details of cases with corneal dystrophies and keratoconus, and their relation to age and sex

Dystrophy (*n*=44)	Number	Male	Female	Age<30 years	Age>30 years
Specific dystrophy (*n*=24)	(*n*=24)	(*n*=19)	(*n*=5)	(*n*=18)	(*n*=6)
Macular dystrophy	10	7	3	7	3
Lattice dystrophy	1	1	0	1	0
Avellino's dystrophy	1	1	0	0	1
Fuch's dystrophy	2	1	1	0	2
Congenital hereditary endothelial dystrophy	8	8	0	8	0
Stromal dystrophy	2	1	1	2	0
Keratoconus (*n*=20)	20	10	10	16	4
Total (*n*=44)	44	29	15	34	10

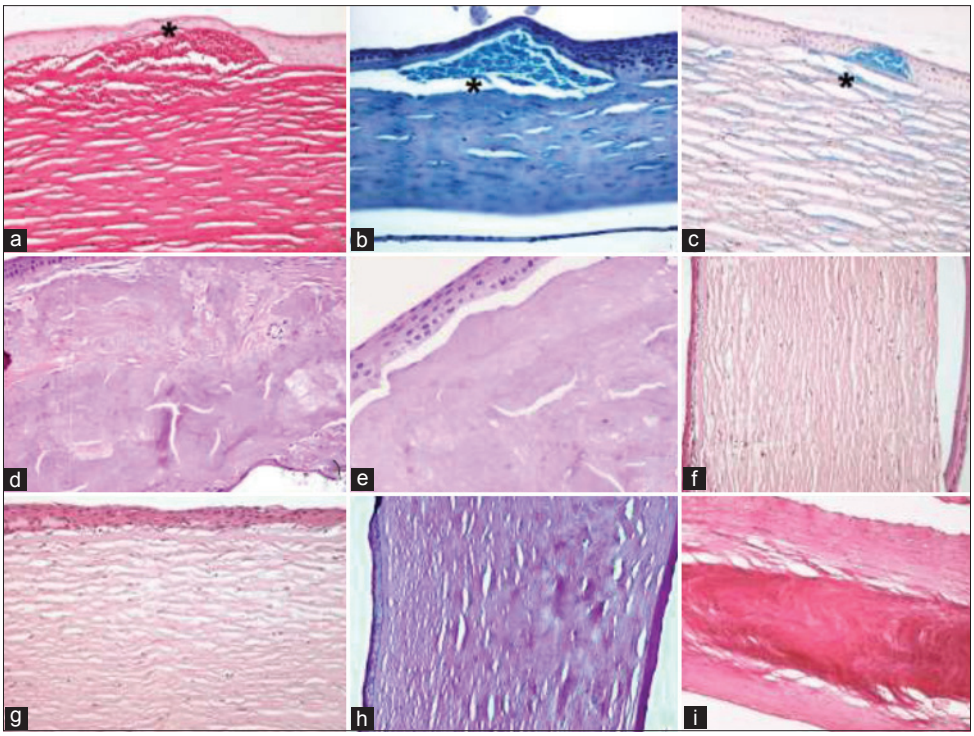

Figure 1: Photomicrographs showing various types of corneal dystrophies. (a-c) Macular dystrophy: Asterix shows granular deposits which are Alcian blue (AB) positive (a: H and E stain ×200; b and c: AB stain, ×200 and × 100, respectively), (d) Lattice corneal dystrophy (H and E stain, ×200), (e) Avellino corneal dystrophy (H and E stain, ×200), (f and g) Fuch's corneal dystrophy (H and E, ×100 and ×200, respectively), (h) Congenital hereditary endothelial dystrophy (H and E, ×200), (i) Congenital stromal dystrophy

atrophy. The Bowman's membrane was thickened. The stroma showed marked hyalinization associated with thickening of Descemet's membrane. No obvious deposits were identified [Figure 1h].

Two cases of congenital hereditary stromal dystrophy were encountered in 11-year-old female and 15-year-old male with a history of dimness of vision since childhood and a positive history of consanguineous marriage in one of them. The excised corneal button showed thickened Descemet's membrane and marked stromal sclerosis [Figure 1i].

Twenty cases of clinically diagnosed post hydrops keratoconus were seen in ten males and eight females. Majority (more than 80%) were aged <30 years and gave a history of gradual progressive dimness of vision in one eye more than the other resulting in frequent change of glasses and were associated clinically with distorted corneal curvature and scarring. A positive family history was present in four out of 20 cases of keratoconus (20%). Histologically [Figure 2e], the corneal epithelium was thinned out. The Bowman's membrane showed breaks in continuity with underlying stroma showing sclerosis. Edema in the stroma was noted in eight cases in addition.

Degenerations

Sixty-six buttons (both specific types and bullous keratopathy) excised after PKP showed degenerative changes in corneal stroma constituting 24% of the overall indications. 19 buttons showed specific changes; bullous spheroidal keratopathy [Figure 2a and b] in 11, Salzmann's nodular degeneration in six, and two with pellucid marginal degenerative changes and the details are depicted in Table 4. One case of Salzmann's nodular degeneration in particular was diagnosed in a 19-year-old male who had corneal opacity in both eyes and had a positive sibling history as well. At histology [Figure 2c], the corneal stroma

showed globular homogenous basophilic deposits which were both AB and PAS negative. The corneal edema was significant. The case diagnosed to have pellucid marginal degeneration showed full thickness asymmetric sclerosis of the corneal stroma.

Though bullous keratopathy (aphakic bullous keratopathy [ABK]/pseudophakic [PBK]) are not specific degenerations, yet they are studied under degenerations in this study as they are thought to be a consequence of endothelial dysfunction and mimic corneal degenerations in all aspects. 35 cases of clinically diagnosed PBK [Figure 2d] showed marked stromal degeneration with associated edema. 12 cases of ABK showed a similar histology, but four of them showed intense stromal edema.

Table 4: Details of cases with corneal degenerations and bullous keratopathy and its relation to age and sex

Degenerations (*n*=66)	Male	Female	Age<30 years	Age>30 years
Specific (*n*=19)	(*n*=13)	(*n*=06)	(*n*=07)	(*n*=12)
Salzmann's nodular degeneration (06)	04	02	4	2
Bullous spheroidal degeneration (11)	08	03	2	9
Pellucid degeneration (02)	01	01	1	1
Bullous keratopathy (*n*=47)	*n*=31	*n*=16	*n*=5	*n*=42
PBK* (35)	23	12	4	31
ABK* (12)	08	04	01	11
Total (66)	44	22	12	54

*PBK and ABK are not specific degeneration but grouped together for histopathology, PBK: Pseudophakic bullous keratopathy, ABK: Aphakic bullous keratopathy

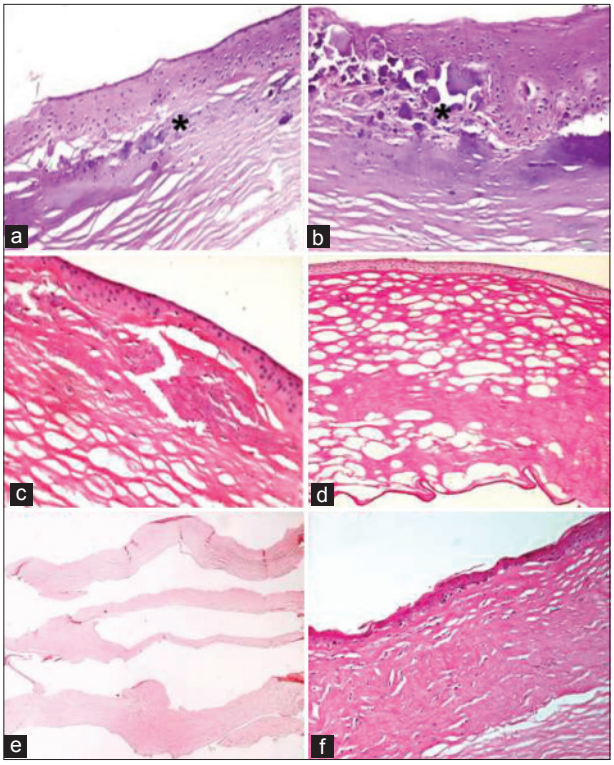

Figure 2: Photomicrographs showing degenerative lesions of cornea and keratoconus. (a and b) Spheroidal degeneration: Asterix showing globular basophilic deposits (H and E, ×100 and ×200 respectively), (c) Salzman's nodular degeneration (H and E, ×100), (d) Bullous keratopathy (H and E, ×100), (e) Keratoconus (H and E, ×100), (f) Stromal degeneration (H and E, ×100)

Ninety percent of all dystrophies and two-third of all degenerations showed findings well correlated with clinical features. The rest were not considered as discordant but reflected the non-characteristic histopathology spectrum, which included total collagen disarray and dense chiefly stromal fibrosis/degeneration [Figure 2f] confirming the clinical evidence of scarring. A total of 43 cases of the total 273 corneal buttons (inclusive of all indications) following previous PKP had failed and were subjected for regraft [Figure 3]. Of these, seven corneal buttons (16.2%) were received after regraft PKP for a clinical diagnosis of dystrophy/degeneration. Five of these were degenerative lesions; two were clinically confirmed as spheroidal degeneration and three as PBK. Only two cases of dystrophy namely congenital hereditary endothelial dystrophy and stromal dystrophy needed a regraft. These cases histologically showed chiefly stromal scarring with mild focal lymphocytic infiltrate and minimal neovascularization.

DISCUSSION

Corneal transplant (keratoplasty) is the most successful tissue transplant known to mankind [1]. The prognosis/outcome of the graft is dependent on its pathology. Hence, a histopathologic evidence/confirmation of the disease process is necessary. However, histopathological studies on cornea are only a few, and most of the studies are clinical based [2]. The present study has been attempted to document the corneal dystrophies and degenerations seen at our institute over 3-year period.

Corneal dystrophies involve the formation of corneal opacities that are most often characterized by bilateral, inherited, non-inflammatory progressive diseases restricted to the cornea. The opacities are caused by progressive accumulation of nonnative protein or other material, both intracellular and extracellular

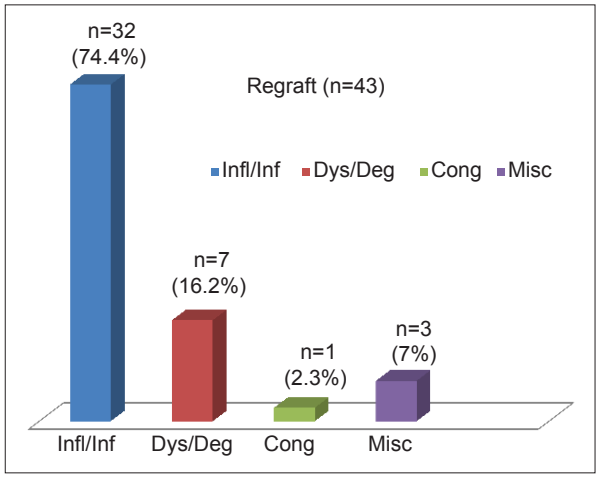

Figure 3: Bar chart showing the graft failure occurring among keratoplasty performed for various corneal lesions
(Infl/Inf: Inflammatory/infectious, Dys/deg: Dystrophy/degeneration Cong: Congenital, Misc: Miscellaneous)

deposits in the cornea resulting in loss of transparency and visual impairment. Dystrophies are classified based on the anatomical location of the lesions as: Anterior corneal dystrophies (affecting the epithelium and extending into the superficial stroma), stromal dystrophies (that involve the stroma only) and posterior corneal dystrophies (which include the Descemet's membrane and endothelium). In general, the stromal and endothelial dystrophies are commonly encountered by the histopathologist.

In the present study, dystrophy and degeneration together formed the second commonest indication (40.3%) for corneal transplant with infective/inflammatory conditions being the most common (47.6%) indication. This is in contrast to the Western literature, where PBK/ABK is the leading indication. Approximately, 64% of patients with dystrophy/degeneration in the present study were <30 years (excluding bullous keratopathy) with a male: female = 1.97:1. Dandona *et al.*, in their study on 1964 corneal buttons, observed that 69% were males, and 62% of the subjects were <50 years [2]. A similar observation by Pandrowala was made wherein the mean age was 34 years [3]. This is in contrast to the Western studies where mean age group of patients undergoing PKP was 50-60 years with a female predominance.

In the present study, dystrophy alone as a group (including keratoconus) constituted 16 % of the indication that is very similar to observations made by Cursiefen *et al.* and Lois *et al.* [4,5]. Table 5 shows the comparison of two important indications of keratoplasty in addition to graft failure rates, with observations from other studies to highlight the contrasting findings between the Western and Asian studies [2,6-14].

Topographically, among the corneal dystrophies, the epithelial types are the rarest, and none was seen in the present study whereas the stromal endothelial dystrophies are the commonest. They include the classic types namely macular, lattice, and granular type as well as the rarer Schneider's crystalline dystrophy and congenital hereditary stromal dystrophy. In the present study, nine cases of macular dystrophy were noted

Table 5: The comparison of rates of infective/inflammatory lesions with dystrophy and graft failure across various studies in the literature

Authors	Infective/inflammatory scarring (%)	Dystrophy (%)	Regraft (%)
Robin *et al.*[6]	25	6	15.1
Mamalis *et al.*[7]	8.9	5.8	13
Leger *et al.*[8]	25	7.8	11.1
Flowers *et al.*[9]	17	7.1	21.3
Dandona *et al.*[2]	40	14.4	17.1
Lindquist *et al.*[10]	19	12.5	8.1
Cursiefen *et al.*[4]	21	16.6	15.5
Godeiro *et al.*[11] (2007)	51	13.8	-
Chen *et al.*[12]	46	4.5	21
Al-Yousuf *et al.*[13]	23.5	27.9	40.9
Sony *et al.*[14]	66	3.85	11.5
Present study (2014)	47.6	8.8	15.7

forming the commonest type of specific dystrophy. This finding supports the report by Kanavi *et al.* from Iran and Zare *et al.* from Middle East [15,16]. This is in contrast to the western literature where Fuch's dystrophy appears to be the most common [4,10,17,18].

Macular dystrophy is an autosomal recessively inherited disorder mapped to chromosome 16 which is characterized by the accumulation of keratin sulfate related glycosaminoglycan in corneal structures. The deposits may be present within keratocytes or endothelial cells but are usually most prominent as extracellular subepithelial deposits that stain well with AB and Hale's colloidal iron stain. Macular corneal dystrophy is clinically subclassified based on the reactivity of serum and cornea with an antibody against keratin sulfate. The disease may recur in the graft [19].

One each case of lattice corneal dystrophy and granular corneal dystrophy, which are a rare group of dystrophies, were noted in the present study. The lattice corneal dystrophy is a group of autosomally dominant inherited disorders characterized by the accumulation of amyloid, which shows positive staining with Congo red and the typical apple-green birefringence, in a lace-like fashion within the corneal stroma. In most Types (I, III, IIIA), the deposition of amyloid is limited to the cornea, but in Type II the corneal amyloid deposition is part of a systemic disease.

The granular dystrophies are autosomally inherited and are characterized by extracellular deposits of the mutated gene's product, keratoepithelin, mostly within the anterior stroma. These deposits are eosinophilic and stain red with Masson trichrome stain. The granular corneal dystrophy Type II may additionally show amyloid deposition. These dystrophies have a tendency to recur in the graft [19].

The endothelial corneal dystrophies include Fuchs' endothelial dystrophy, which is the most common corneal dystrophy noted in some of the studies. It occurs in two forms, autosomal dominant and autosomal recessive. It starts manifesting at birth and is present in infancy/childhood. The disease is more common in females, and familial clustering has been observed. Histologically, it is characterized by Hassall-Henle bodies in the central thickened cornea and abnormally thickened and laminated descemet's membrane, which may be thick enough to bury the excrescences and edematous stroma. Associated are the secondary features of endothelial cell loss, namely, bullous changes of the surface epithelium. The prevalence of Fuch's endothelial corneal dystrophy differs markedly in different parts of the world. It is the most common corneal dystrophy in western countries, accounting for about 10% of all corneal transplants in North America, but appears to have a lower prevalence (1.2-4.5%) in the Middle East and Asia [3,11,20,21].

Keratoconus is not a true dystrophy, but a bilateral disorder characterized by progressive central stromal scarring and thinning of the corneal stroma resulting in a cone-shaped cornea. This is thought to represent the common final path

to different pathologic processes involving abnormalities of matrix proteins. A genetic predisposition as well as associations with systemic disease, such as trisomy 21 has been shown. An intraepithelial iron ring (Fleischer's ring) may be present. Bowman's layer shows variation in thickness, deficits, breaks, and pannus formation associated with stromal thinning, while the endothelium is typically unremarkable. Recurrence of keratoconus in the graft rarely occurs. In some cases, no histologic abnormality can be seen in corneas excised for keratoconus [22]. It is wise to remember that the keratoconus is a clinical diagnosis and that one may not exclude keratoconus histologically. In the present study, keratoconus alone as a group formed seven percent of the overall clinical indication for PKP, similar to the observation by Dandona *et al.* [2]. Table 6 shows the overall comparison of the important indications for PKP from among the dystrophies and degenerations in different parts of the world with special reference to bullous keratopathy, keratoconus, Fuch's and non-Fuch's dystrophy. Bullous keratopathy was highest in France (28.7%) [27] and lowest in UK (7.6%) [13]. Keratoconus and Fuch's dystrophy were more common in the West [4,23] (Germany [4] and USA [23], 21% and 15%, respectively) as compared to South India [27] (1.9% and 1.2%, respectively). In comparison, our results were in par with Dandonna *et al.* [2] from South India with respect to all dystrophies and degenerations namely bullous keratopathy, keratoconus, Fuch's and non-Fuch's keratopathy but did not match with results noted in other Indian studies namely, Sony *et al.* [14] and Dasar *et al.* [27].

Salzmann's nodular degeneration is unilateral, but it may be bilateral with single or multiple lesions that usually measure between 1 and 3 mm in size. It is usually asymptomatic, but patients may develop recurrent corneal erosions or decreased vision from scarring. The nodules are sometimes arranged in a spoke-like pattern. Sections of the cornea show thinning of the epithelium or denudation, destruction of Bowman's layer, duplication of the epithelial basement membrane and disorganization of collagen lamellae in the superficial anterior stroma. These histologic findings are entirely non-specific and can be seen in scarring from any cause [28].

Table 6: The comparison of specific indications to penetrating keratoplasty with reference to dystrophies and degenerations namely bullous keratopathy, keratoconus, Fuch's dystrophy and non-Fuch's corneal dystrophy in different regions of the world

Country	Indications (%)			
	ABK+PBK	Keratoconus	Fuch's dystrophy	Other dystrophies
South India 1997[2]	22	6	1.2	7.2
Germany 1998[4]	17	20.9	14.9	1.7
Canada 2000[24]	15.3	16.1	9.6	3.1
France 2001[25]	28.7	12.1	7.8	15.4
Taiwan 2001[21]	17.6	2.5	4.5	1.6
USA 2002[23]	27.2	15.4	15.2	1.3
UK 2004[13]	7.6	15	9.3	3.6
North India 2005[14]	13.5	2.4	-	3.9
Pakistan 2011[26]	12.3	8	1.31	2.09
South India 2013[27]	8.8	1.9	-	2.8
Present study 2014	17.2	7.3	0.73	8.1

PBK: Pseudophakic bullous keratopathy, ABK: Aphakic bullous keratopathy

Recent literature in the field of genetics and molecular basis of the dystrophies has led to the evolution of a new classification which incorporates genotypic-phenotypic features. As histopathology continues to be evidence-based and the gold standard for the diagnosis, other techniques do help provide additional information in this area. Corneal dystrophies can be considered unique as the association of gene-protein-disease has been approached both in the forward direction as well as the reverse order [29]. The degenerations accounted for 24% of cases in this study. Histopathology was able to confirm the clinical diagnosis in two third of the cases with maximum concordance (100%) in cases of Salzmann's nodular degeneration. Bullous keratopathy occurs most commonly after cataract removal and is called pseudophakic (i.e. if an intraocular lens implant is present) or ABK (i.e., if no intraocular lens implant is present). It is characterized by the formation of fluid-filled blisters on the surface of the cornea. The blisters rupture, causing pain, often with a foreign body sensation and impairment of vision. The clinical diagnosis is made from the typical appearance of a swollen, cloudy cornea with blisters on the surface. While at histopathology, the changes include desquamating epithelial cells from the anterior surface and separation of the epithelium from Bowman's layer creating the bullous detachment. The Bowman's layer is irregularly thinned probably related to the bullae. The stroma shows areas devoid of keratocyte nuclei, irregular lamellae and features indicative of scarring. The endothelium is markedly attenuated; there are fewer endothelial cells than normal. Additional findings that may be seen include a thickened and redundant epithelial basement membrane. In general, the key finding is paucity of endothelial cells, and those cells remaining are flattened and attenuated. The Descemet's membrane is usually intact. ABK is a less frequent indication than PBK probably due to extracapsular lens extraction with intraocular lens implantation having become the standard practice in cataract lens surgery. As expected, PBK outnumbered ABK and showed high concordance with histopathology and bullous keratopathy accounted for 18% of the overall clinical indications in similarity with a few of the western studies [4]. The incidence of pseudophakic bullous keratopathy is on the increase as there is strong effort to eliminate avoidable blindness due to cataract. With the increasing cataract surgical rate in India, more intraocular lenses are implanted in a large number of eyes, and they are at risk of going blind due to corneal decompensation [30].

Morphological alterations in keratocytes are minimal or none in both corneal degeneration and dystrophy. However, the keratocytes in ABK and PBK may show intracellular edema and vacuolar change in Fuch's dystrophy. Hence, one may not observe significant changes in keratocyte morphology to differentiate between dystrophy and degeneration but prominent stromal edema is more often seen in degenerations than in dystrophy.

In the study of our regraft cases, the stromal scarring was predominant. The present study also indicated that graft failure secondary to dystrophy is less as compared to infective/inflammatory causes. Inflammation and the associated vascularization process were minimal in those cases of graft failure due to dystrophy. When present, one needs to assess the degree of the stromal neovascularization. As cornea is an avascular organ, transmural vascularization probably due to reparative process may indicate poorer prognosis in comparison to the focal areas. In addition, neutrophilic exudation may indicate an early and better host response rather than an infiltrate of lymphocytes. In most of the cases, graft failure is due to poor maintenance of graft after PKP by the patients rather than actual recurrence of the primary pathology [27].

While histopathologic study is the gold standard for the diagnosis, various other techniques such as bright field, fluorescence, and confocal microscopy on sections of corneal buttons have been of great help especially in the evaluation of early onset Fuchs corneal dystrophy with antibodies against *COL8A1*, *COL8A2*, *COL4*, laminin, and fibronectin [31]. Corneal dystrophies have been considered unique as the association of gene-protein-disease has been approached both in the forward direction as well as the reverse order [20]. Recent additions in the field of genetics and molecular basis of the dystrophies have led to the evolution of a new IC3D classification for corneal dystrophies, integrating up-to-date information on phenotypic description, pathologic examination, and genetic analysis [32].

CONCLUSION

The present study has attempted to aid in understanding the histopathology of corneal dystrophy, characterize the various subtypes and add to the limited data available from India. Macular dystrophy, lattice dystrophy, Avellino's dystrophy and Salzmann's nodular degeneration show specific stromal deposits; mucoid and granular AB positive deposits in macular, AB-PAS and Congo red negative deposits in Avellino's, PAS and Congo red positive eosinophilic deposits in lattice dystrophies and basophilic AB-PAS negative deposits in Salzmann's nodular degeneration and are easily diagnosable at histopathology, while the rest need to be supported by clinical correlation. Dystrophy and degeneration together form the second commonest indication for corneal transplant with infective/inflammatory conditions being the most common indication in contrast to the Western literature where PBK/ABK is the leading indication followed by keratoconus and regrafts.

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