Review Article

Relevance of IgE, allergy and eye rubbing in the pathogenesis and management of Keratoconus

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Keratoconus (KC) is an ectatic disease of the cornea characterized by localized thinning and protrusion causing irregular astigmatism, which can lead to significant visual impairment. KC has often been associated with allergy and/or atopy, which are immune-mediated inflammatory reactions primarily driven by IgE. A higher proportion of KC patients were reported to have history or suffer from systemic and/or ocular allergy with elevated allergen-specific IgE and/or total serum IgE. Eye rubbing, one of the risk factors for worsening of the disease and developing related complications in KC, is associated with IgE driven conditions. The current review enumerates and contextualizes the evidence related to IgE in mediating KC pathogenesis, including aberrant extra-cellular matrix remodeling. This review also discusses clinical strategies directed at modulating IgE-mediated responses in the management of KC, and the emerging academic and plausible clinical relevance of assessing serum and tear IgE (allergen-specific and total) status in improving the understanding of disease pathobiology, treatment planning, and prognosis.

Key words: Allergy, atopy, eye rubbing, IgE, keratoconus

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Keratoconus (KC) is a corneal ectatic disorder characterized by thinning and forward protrusion of a localized portion of the cornea. In the initial stages the patient may present with varying degrees of irregular astigmatism correctable by glasses but advanced cases can result in a significant drop in vision due to the worsening ectasia and even corneal scarring in some cases.[1-3] KC is usually known to have an onset early in the second decade of life. It can be progressive in a subset of patients or spontaneously stabilize in others.[4] The early stages of KC can be managed by glasses and rigid contact lens for visual rehabilitation, and collagen crosslinking if there is a progression of the disease. Adjunct treatment modalities like intra corneal ring segments or topography-guided treatments have also been described with good effect. The advanced stage of KC may need a corneal transplant to restore vision. Hence, identifying KC in early stages and managing it by treating the known risk factors, may provide ample chance for the disease to stabilize without further deterioration. During the early stages of KC, prior to the use of surgical strategies listed above, it would be beneficial to prophylactically reduce potential risk factors and associated events. Ocular allergy and eye rubbing in particular have been shown as key contributors in the pathogenesis of KC.[5,6] Hence, managing associated ocular allergy and eye rubbing in addition or ahead of other therapeutic strategies would be beneficial in improving the prognosis of KC. The current review collates, contextualizes, and examines an underlying modifiable factor, IgE – which is a key driver of allergic responses, with reference to the pathogenesis and management of KC.

Allergy, Atopy, and Eye Rubbing in KC

Ocular and systemic allergy including atopy have emerged as one of the key modifiable risk factors associated with KC pathogenesis. The pathological role and relationship between ocular allergy and KC has been discussed in detail by Sharma *et al*. earlier.[5] Atopy is a condition associated with the inherent or genetic predisposition to develop allergy due to exaggerated immune response against common allergens. Atopy can have manifestations in skin (dermatitis), respiratory tract (rhinitis, asthma), and the ocular surface (conjunctivitis). Allergy and atopy have long been associated with KC and a summary of findings regarding the relationship between allergy and atopic conditions and KC prevalence from key reports have been enumerated in Table 1. Even though few studies have shown no significant association between KC and ocular allergy, a majority of studies showed a positive association between them.[7-13] The prevalence of allergy across the varying grades of KC ranges from 11.3 to 30% of KC patients.[8,10-12] Studies have shown that KC is more prevalent in children with vernal keratoconjunctivitis (VKC), and VKC has also been found to have effect on progression of the KC. Even though the progression of KC was not affected by the severity of allergic

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Table 1: The status of Atopy/Allergy in Keratoconus

Key findings	Species	Ref
Case reports describing the presentation of KC and various atopic conditions	Human	[79-83]
Increased frequency of asthma was observed in KC patients compared to controls	Human	[84]
Four cases of cataract with keratoconus were reported in patients suffering from dermatitis including its atopic form.	Human	[85]
Atopy was found in 35% of KC subjects and 12% in the matched control group.	Human	[7]
Increased prevalence of asthma was observed in KC patients compared to controls	Human	[34]
23% of controls and 40% of KC subjects had a history of present or past atopic disease.	Human	[86]
History of systemic atopic disease did not influence the rate of progression of KC to penetrating keratoplasty (PK). However, the progression to PK in one eye resulted in increasing the risk of progression in the contralateral eye.	Human	[87]
KC patients without atopic dermatitis was observed to have better graft prognosis compared to those patients with severe form of atopic dermatitis	Human	[88]
An association was observed between KC and atopy (OR 3.6, 95% CI 0.8-15.8)	Human	[10]
Reducing in anterior keratocyte density was observed to be significantly associated with history of atopy in KC patients	Human	[89]
4 out of 7 KC patients who underwent deep lamellar keratoplasty were atopic	Human	[90]
Corneal topographic and pachymetric features were observed to be significantly worse and distinct in KC subjects with atopy compared to KC subjects without atopy.	Human	[91]
Atopic conditions such as asthma, eczema and hay fever was observed in 23%, 14% and 30% of KC patients, respectively	Human	[11]
KC patients with atopy showed a trend that the rate of graft rejection was twice that of non-atopic KC patients. However, this observation was not statistically significant.	Human	[18]
VKC was significant risk factor for KC. Atopy was observed to be a significant risk factor for developing corneal hydrops in KC patients.	Human	[16]
Graft survival chances in KC patients were not observed to significantly different between KC subjects with and without history of atopy.	Human	[24]
KC associated with atopy (OR 3.0, 95% CI 1.2-7.6)	Human	[92]
History of skin allergy (26.6%), symptomatic ocular allergy (24.45%) and asthma (11.31%) were observed in KC patients	Human	[12]
More severe form of KC was observed in those patients with vernal keratoconjunctivitis (VKC) compared to KC patients without VKC or with allergic conjunctivitis		[13]
KC comprised 6% of the VKC-associated complication	Human	[93]
Of the patients who underwent intrastromal corneal ring segment (ICRS) treatment, complication such as corneal melt or ICRS extrusion was observed in 1.24% of them. All of these 1.24% of patients had history of atopic dermatitis and had episodes of atopic dermatitis exacerbation with itching and burring in the eyes prior to corneal melt/ICRS extrusion	Human	[19]
Atopic keratoconjunctivitis patients exhibited higher rate of corneal thinning and KC	Human	[94]
The odds ratio of asthma, allergic rhinitis, and the combination of allergic conjunctivitis, chronic blepharitis and vernal keratoconjunctivitis with reference to KC was 2.0 (95% CI: 1.6-2.5), 1.6 (95% CI: 1.3-2.0) and 6.0 (95% CI: 4.0-9.2), respectively.	Human	[95]
KC patients exhibited history of allergic disorders (29.7%)	Human	[21]
KC patients with atopy showed corneal densitometry changes compared to KC subjects without atopic disease.	Human	[96]
Case report: History of allergic conjunctivitis and eye rubbing was associated with progression of keratoconus after collagen cross-linking	Human	[97]
The hazard ratio for keratoconus in subjects with severe atopic dermatitis was 10.01 (95% CI, 5.02-19.96)	Human	[98]
In 885 KC subjects, 50.7% had a history of allergic diseases. KC patients with VKC or AC exhibited a more severe form of disease than those without a history of allergic disease	Human	[3]
Significant progression of KC in patients with allergies	Human	[99]
Compared to subjects without allergic conjunctivitis (AC), those with AC exhibited a 37% increase in odds to be diagnosed with KC. However, the opposite relationship was observed between allergic rhinitis and KC.	Human	[100]
The odds ratio of asthma, allergic rhinitis, and atopic dermatitis with reference to KC was 2.21 (95% CI: 1.91-2.55), 3.44 (95% CI: 2.75-4.30) and 7.97 (95% CI: 6.21-10.21), respectively.	Human	[101]
The proportion KC patients with progression of ectasia, 2 years after collage cross-linking was not significantly different between those with (18.5%) and without VKC (16.7%)	Human	[102]
The odds ratio of allergy, asthma, and eczema with reference to KC was 1.42 (95% CI: 1.06-1.79), 1.94 (95% CI: 1.30-2.58) and 2.95 (95% CI: 1.30-4.59), respectively.	Human	[15]

eye disease in one study, there have been other reports where allergic eye disease was found to be associated with higher grade of KC at presentation.[13] Another strongly associated risk factor in KC pathogenesis is eye rubbing and this relationship has been extensively reviewed in many recent articles on the subject.[14,15]

KC patients with ocular allergy are also at a higher risk of developing other ocular complications like acute hydrops and corneal scarring, which could be related to the associated eye rubbing in these patients. These patients may require surgical intervention including intrastromal corneal ring segments or

keratoplasty for visual rehabilitation.[16,17] Ocular allergy and eye rubbing can also have a detrimental effect on the outcomes of surgical procedures on the eye due to the associated inflammation and mechanical trauma. Allergy and atopy have also been linked to complications related to KC management such as graft and intrastromal corneal ring segment outcomes.[18,19] Collagen crosslinking is a procedure done to halt the progression of KC. Studies have shown an increased risk of progression of KC even after collagen crosslinking in patients with ocular and systemic allergy.[20-22] This could be related to the mechanical trauma due to eye rubbing and the inflammation and cytokines released. These patients could require repeat collagen crosslinking.[20,22] In addition, the outcomes of keratoplasty for advanced KCwas evaluated in various studies.[23,24] It was found that the there was no difference in the outcomes of keratoplasty including visual outcomes and graft survival or the risk of graft rejection among the KC patients with and without (VKC).[23,24] However, certain complications like early loosening of sutures, epithelial breakdown, and steroid related complications showed an increased incidence in the KC patients with associated ocular allergy who underwent keratoplasty.[23]

Serum IgE and KC

A key factor that is a common mediator to the major risk factors (allergy, atopy, and eye rubbing) associated with KC is Immunoglobulin E (IgE). It is well known that the signs and symptoms associated with allergy and atopy including ocular manifestations are primarily driven by IgE-mediated cellular responses.[25-27] Hence, a detailed review of literature was conducted to evaluate the status of IgE in KC patients with and without allergy or atopy across different studies [Table 2]. It is evident that a significant number of KC patients do have higher levels of serum IgE. It has also been shown that KCs patients who have allergy have significantly high serum IgE levels than those without clinical signs and symptoms of allergy.[7,13] Elevated serum IgE is also associated with a subset of KC patients even without significant signs of ocular allergy.[7,8] The association of serum total IgE and s pecific IgE levels in KC patients has been evaluated by Rahi A *et al*.[7,13] along with association to other immunoglobulins. No significant association or trend was found in the serum levels of other immunoglobulins. Kemp *et al*. evaluated the association of total serum IgE and allergen specific IgE in patients with keratoconus and found a 52% incidence of elevated levels of total serum IgE in patients with keratoconus and 59% of raised serum specific IgE levels.[8] Increased serum IgE was also reported to be associated with the progression of the disease and graft rejection in KC patients.[28,29] Based on reports listed in Table 2, it is important to note that there could very well be a subset of KC patients with raised IgE, but without any history or ongoing allergy/atopy. However, the reason underlying this observation is yet to be ascertained and could be attributed to sub-clinical allergy or measurement variation. Irrespective of the etiology underlying the raised IgE in KC patients, it would be beneficial to reduce IgE levels and mitigate IgE mediated effects to improve KC prognosis.

Tear IgE and KC

Ocular surface IgE levels in KC patients would provide the much-needed relevant information pertaining to the actual role of allergy in causing KC. Measuring IgE level from the tear fluid would be an ideal strategy to determine the status of IgE on the ocular surface of patients. Altered tear fluid IgE levels have been reported in a variety of ocular surface conditions including ocular allergy, dry eye, and corneal dystrophies.[30-33] However, the information regarding the status of tear IgE in KC patients is almost nil, expect for a couple of reports. A study by Rahi A *et al*. showed that there was higher levels of IgE in serum, but not in tear fluid of KC patients compared to controls.[7] However, a more recent finding stated in a conference proceedings reports a significant increase in both serum and tear IgE levels were observed in KC patients without allergy compared to controls.[34] More studies assessing tear IgE levels in KC are required to improve this knowledge base. There is mounting evidence regarding the usefulness of tear IgE assessment in ocular surface conditions, and tear IgE levels are reported to associate with the severity of ocular surface conditions and allergenic factors.[32,35-38] Further, correlation between tear and serum IgE levels[39,40] and a significant positive relationship between allergen-specific tear IgE and skin prick test[41,42] were

Table 2: The status of IgE in Keratoconus

Key findings	Species/Sample	Ref
IgE was raised in 17% of the KC studied.	Human/Serum	[103]
IgE levels >200 IU/ml was observed in 47% of the KC subjects and 6% in controls. 60% of the KC subjects with higher IgE were atopic and 40% of the KC subjects with higher IgE were non-atopic. IgE in KC patients ranged between 10-4000 IU/ml and in controls ranged between 10-272 IU/ml.	Human/Serum	[7]
Levels of IgE on the ocular surface of KC and controls were not significantly different	Human/Tear fluid	[7]
30% of the KC subjects and 20% of controls showed higher IgE (>120 UI/ml) levels.	Human/Serum	[86]
High IgE levels (>120 IU/ml) was observed in 52% of the KC subjects and 7% in controls. IgE in KC patients ranged between 6.5->1000 IU/ml and in controls ranged between 5-185 IU/ml. Significantly higher levels of specific IgE was observed in 59% of the KC subjects and 13% of the controls.	Human/Serum	[8]
Prospective survey of a family with KC members: 2/12 members presented with KC and they also exhibited elevated total and allergen specific IgE. 2 of 3 other members (with no KC at initiation of the study) with higher levels of IgE developed KC over the course of the study period	Human/Serum	[28]
Clinical atopy was observed in 44% of the KC patients in the study. Relatively higher frequency of atopic KC patients underwent keratoplasty. 4/5 atopic patients with graft rejection had IgE levels >1000 U/ml	Human/Serum	[29]
Case report: KC with hyperimmunolgoublin E syndrome. IgE=28900 IU/ml	Human/Serum	[104]
Case report: IgE=38000 IU/ml	Monkey/Serum	[105]
Case report: IgE levels in KC subjects (*n*=2) with vernal keratoconjunctivitis was 706 IU/ml & 825 IU/ml	Human/Serum	[6]
Significantly higher levels of serum and tear IgE was observed in KC subjects compared to controls. Higher levels of tear IgE were observed with increasing grades of KC.	Human/Serum/ Tear fluid	[70]

also reported. Tear IgE measurements for diagnostic purpose needs further standardization that would requires large scale population studies to determine normative data and the type of tear collection method (Schirmer's strip or capillary tube). Until then tear IgE measurement will remain a supplemental tool in diagnosis and treatment planning. However, total and allergen-specific IgE levels in the tear fluid of KC patients would be of immense value in studying the mechanistic role of allergy or IgE in KC pathogenesis and prognosis.

IgE Associated KC Pathogenesis

KC was previously considered as a non inflammatory condition. However, in the last decade, various studies have confirmed the inflammatory basis of KC pathogenesis.[43-47] The local (ocular surface) manifestation of a IgE-based systemic immunological imbalance common in allergy or atopy could possibly be related to the underlying inflammatory nature of KC leading to changes in the collagen and keratocytes in the ectatic region. IgE exerts its function including protection against parasites by the binding of the Fc portion of the antigen bound IgE to Fc-epsilon receptor (FcεR) present on the surface of variety of cells such as mast cells, basophils, eosinophils, epithelial cells, and neurons.[27,48,49] Mast cells, basophils, and eosinophils primarily in the tissues degranulate when stimulated by binding of IgE-bound to an allergen (IgE-IC; IgE immune complex) to FcεR on their surface.[26] Fig. 1 outlines the proposed IgE-mediated events that may underlie KC pathogenesis. Briefly, (i) IgE-FcεR degranulates granulocytes resulting in the release of itch factors and inflammatory mediators; (ii) the released inflammatory mediators such as the allergy associated cytokines and chemokines can orchestrate the trafficking of immune cells further propagating the inflammatory milieu on the ocular surface; (iii) itch factors along with additional inflammatory mediators results in eye rubbing, which delivers mechanical trauma to the corneal tissues and also stimulates inflammatory factors, and (iv) inflammatory milieu along with proteases compromises extra-cellular matrix remodeling processes resulting in ectasia.

Conjunctival biopsies from ocular allergy exhibits several degranulating mast cells and infiltration of inflammatory cells.[50] Since, mast activation results in the production of cytokines that facilitates immune cell trafficking and further the release of potent inflammatory mediators.[30,51,52] The eye rubbing in response to itchy eyes has been suggested as an important link between KC and allergy.[53] Such itch sensations are often mediated by inflammatory or immune factors that stimulate the release of itch factors. Therefore, it is possible that an allergy and immune mediated release of itch factors is causal in KC. Although, it is not understood whether the eye rubbing alone can initiate or worsen KC directly due to mechanical trauma, or if the inflammation due to subclinical ocular allergy causes the eye rubbing and consequently KC.[3] Elevated serum IgE levels in patients with allergy triggers the release of mediators such as histamine and IL-13, which activate transient receptor potential channels on sensory nerve endings to trigger an itch response.[54] Thus, in patients with clinical or subclinical ocular allergy, elevated serum IgE levels can be associated with KC, particularly those who have ocular surface inflammation or eye rubbing. Studies demonstrate that tear levels of matrix metalloproteinases (MMP)-13, IL-6, and TNF- alpha have been increased by eye rubbing even in normal eyes,[12,53] suggesting an inflammation mediated mechanism linking eye rubbing with KC. More recently, the activation of FcεR on the peripheral nociceptive neurons by IgE-IC was reported to result in an itch response.[49]

Cytokines related to ocular allergy has been reviewed extensively elsewhere,[55] and IL-4, IL-5, and IL-13 are the common cytokines that was reported to be elevated in the different forms of ocular allergy. A variety of cytokines, including IL-1β, IL-4, IL-5, IL-6, IL-8, IL-13, IL-17, TNFα, IFNγ, chemokines, and MMPs was observed to elevated in the tears and ocular surface of KC patients.[47,56-61] In addition, increased proteolytic, gelatinolytic, and collagenolytic activity was also observed in the tears of KC patients.[62] Inflammatory mediators are also known to be associated with KCand could be driving the underlying inflammatory pathology.[46,53,63] These inflammatory signals also lead to an increase in the tissue protease activity and progression in KC, which is evidenced by the severity dependent increase in MMP9.[46,54] In addition, KC corneas show altered collagen arrangement and extracellular matrix properties, which is suggested to be due to increased expression of lysosomal and proteolytic enzymes and decreased concentration of protease inhibitors.[53] While, IL-17 is known to induce MMP9,[64,65] TNFα reduces collagen synthesis and lysyl oxidase (LOX) expression.[66,67] Reduced LOX expression in the corneal epithelium was reported to be associated with sub-optimal outcome following cross-linking in KC patients.[68] Hence, inflammation associated increase in MMPs and decrease in LOX have resulted in compromised extra cellular matrix (ECM) remodeling (increased degradation and reduced synthesis of collagen), plausibly resulting in corneal ectasia.

Emerging Perspectives in the Management of KC

Various strategies for the treatment of KC have been comprehensively reviewed in existing literature.[69] Most often, the management options are based on the grade of KC, which includes topography and pachymetry. An important adjunct to the the success of these treatment strategies relies on careful identification and the management of the associated risk factors. Allergy, atopy, and eye rubbing are key modifiable risk factors that would impact KC prognosis and treatment outcomes. Hence, we propose an addendum [Fig. 2] to the currently available and preferred practice algorithms for KC. Since, IgE mediated factors like allergy and eye rubbing are evolving to be key drivers of KC pathogenesis, one approach to the management of KC could be to objectively identify and manage allergy and altered IgE status in KC patients to slow the progression of disease and improve the clinical outcome of surgical interventions. KC patients with associated allergy are more likely to have progressive KC and complications like acute hydrops due to the associated inflammation and eye rubbing.[17] Since, IgE levels correlate with the increasing grades of KC,[70] it is important to control the ocular and systemic allergy adequately. Controlling allergy may lead to reduced eye rubbing and the associated inflammation of the ocular surface. Therefore, controlling the ocular allergy along with systemic allergy could help attain better treatment outcomes. The management of ocular and systemic allergy would depend upon the severity, duration, and the frequency of episodes. The symptoms, depending on systemic involvement, like that of nose (allergic rhinitis) or that of lung (asthma) needs a multi-centric approach. It involves local therapy like intranasal steroids/decongestants/antihistamines or inhalers accordingly, or systemic antihistamines, leukotriene receptor antagonists, respectively.[71] Environmental avoidance measures, once a triggering allergen, is identified, is known to reduce the exacerbations.[71] High serum IgE, though the indicative of higher sensitization for atopy, warrants detailed systemic evaluation and the possible identification of locally relevant common allergens.[71]

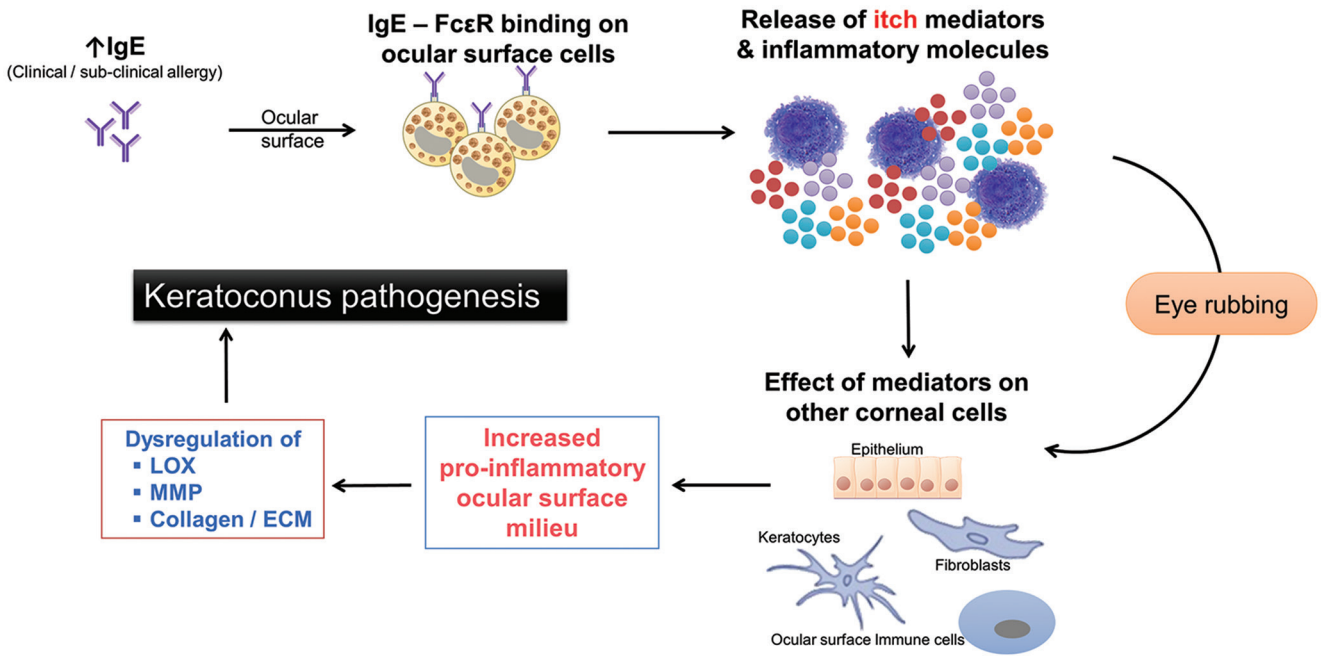

Figure 1: Proposed role of IgE in keratoconus pathogenesis. Schematic hypothesizes that raised IgE will bind to its receptor (FcεR) on the ocular surface immune cells including mast cells. Binding of IgE to FcεR results in the degranulation of FcεR expressing cells, releasing itch factors. These factors -enzymes and cytokines can trigger eye rubbing and degranulated factors along with mechanical force of eye rubbing can have an effect on epithelium, keratocytes and fibroblasts of cornea resulting in an inflammatory molecular milieu contributing to dysregulated focal ECM remodeling resulting in keratoconus pathogenesis

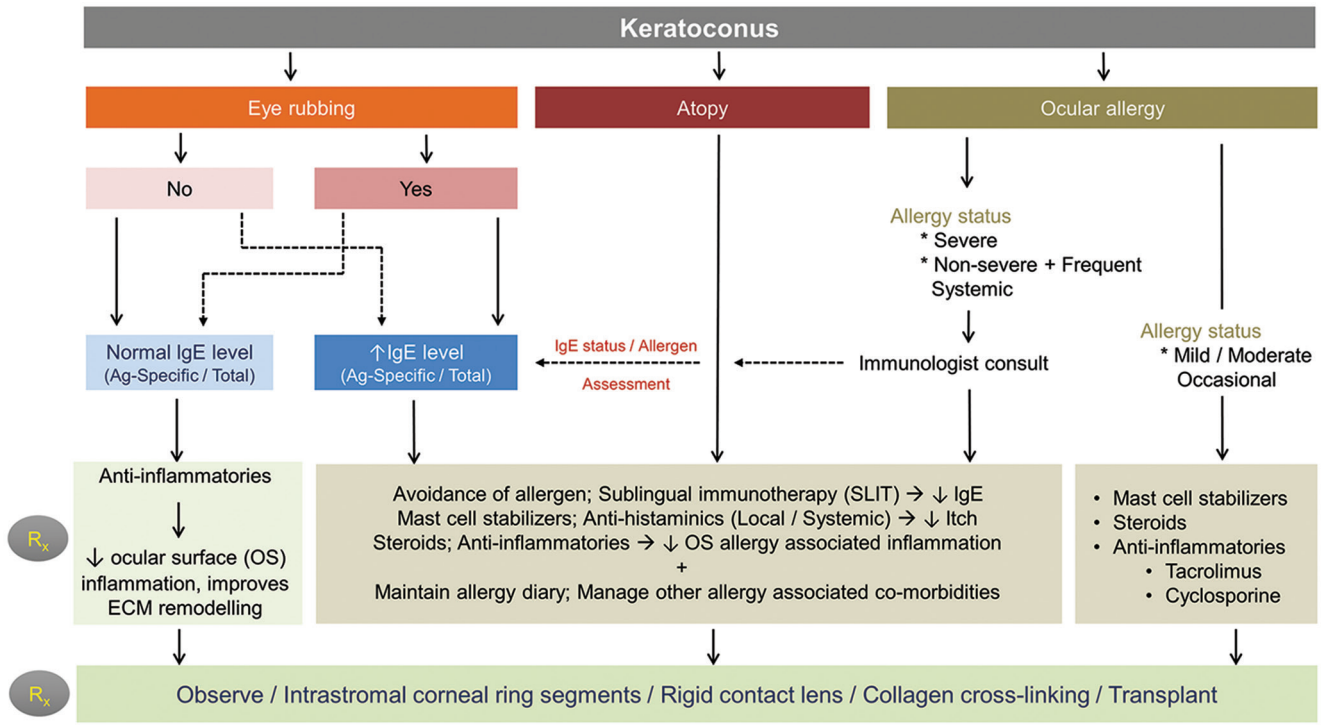

Figure 2: Algorithm for clinical management of Keratoconus, raised IgE and Allergy. The relationship between allergy and KC is important in KC management. Treatment planning involves triaging KC patients based on allergy signs, history and eye rubbing. A multidisciplinary team with an immunologist is useful in patients with recurrent, severe allergy or history of atopy. Identification of allergen (skin prick or patch test; allergen specific IgE) and control (sublingual immunotherapy; avoidance of exposure) is possible. Total IgE status aids as well. Reducing ocular surface inflammation, IgE and induced effectors prior to treatment would improve outcome. Ag – Antigen/Allergen

The approach to allergic eye disease is targeted at the pathomechanism of the disease. Seasonal allergic conjunctivitis (SAC) and perennial allergic conjunctivitis (PAC) are IgE mediated reactions to allergens.[72] Targeting IgE, IL-4, and IL-13 by using monoclonal antibodies (mAb, e.g. anti-IgE antibody, Omalizumab) against these factors, mast cell stabilizing agents, antihistaminics and steroids have been successful in the management of systemic allergy and atopic conditions. In the event of KC associated with severe/frequent ocular allergy or the history of systemic allergy, measurement of allergen specific IgE would be useful in identification of the trigger. Allergen specific immunotherapy (SIT) is a treatment recommended by the World Health Organization as an important addition to existing management protocols for severe allergy. Sublingual immunotherapy (SLIT) is a relatively new technique of immunotherapy to reduce the specific IgE load, which has been found to have high safety and efficacy. It works by making the patient more tolerant to the allergen, giving symptomatic relief, and reducing the need for medications especially steroids. An immunologist consultation for these patients would improve effectiveness in diagnosis and managing these subjects. SLIT has been found to be useful in treating patients with recalcitrant or chronic allergy not responding to regular treatment. It changes the phenotype of T cells from Th2 to Th1 as happens in when anergy or tolerance develops as a natural course of the disease.[72,73] More severe cases or acute exacerbations can be treated when topical steroids are used in pulsed and tapering fashion. The type of topical steroid would again depend upon the severity of disease and can range from loteprednolol 0.5% to prednisolone 1% eye drops for varying frequencies and durations. The biggest drawback of using topical steroids are the potential side effects of long-term usage like rise in intraocular pressure and cataract formation. To avoid such complications, there are steroid sparing agents like cyclosporine 0.05% and 0.1% eye drops and tacrolimus 0.03% and 0.1% eye ointment, which act by calcineurin inhibition.[74,75]

Topical mast cell stabilizers like sodium cromoglycate and anti-histamines, either alone or in combination can be effective in the managing milder/moderate form of allergies and eye rubbing. Mast cell stabilizers act primarily by stabilizing mast cell membranes and inhibiting degranulation, thereby preventing histamine release. They prevent the signs and symptoms of type 1 allergic reactions including acute and chronic allergic conjunctivitis.[76] Newer molecules like olopatadine have a dual mode of action by both mast cell stabilization and antihistaminic action. It inhibits the release of histamine, tryptase, and PGD2 with decreased H1 receptor binding activity *in vitro*. Another possible method of action is by inhibiting anti-IgE antibody-mediated release of tumor necrosis factor alpha (TNFα) from human conjunctival mast cells, which plays an important role in allergic ocular inflammation via increasing intercellular adhesion molecule (ICAM)-1 on epithelial cells and triggering other proinflammatory events. These medications are effective as a stand-alone medication in milder ocular allergy and as an adjunct in more acute allergy with topical steroids.[77,78]

Conclusion

Since KC is often associated with allergy and eye rubbing, it is important to control allergy while treating the KC. Measuring serum IgE could be an important parameter in the management of KC especially if the patient has chronic ocular allergy and is a frequent eye rubber. However, in certain patients, the serum IgE may be elevated even without any symptoms or signs, thereby making IgE testing relevant even in such cases. The inflammation induced extracellular remodeling associated with KC may therefore be reduced if the allergy or IgE induced inflammatory stimulus is controlled medically. However, the cost of doing the serum specific IgE test is a limitation as it may not be affordable for many patients. With advancing technologies and the use of tear fluid, a more affordable and non invasive means to assess IgE status would be possible to aid informed decision making in the management of KC.

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Conflicts of interest

There are no conflicts of interest.

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