

**PREVALENCE AND PATTERN OF COMORBIDITIES IN
CHILDREN WITH ALLERGIC CONJUNCTIVITIS AT
KENYATTA NATIONAL HOSPITAL, EYE CLINIC**

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DECLARATION

I, the undersigned declare that this proposal is my original work and has not been submitted to any university or college for an academic award.

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|---|------|
| TABLE OF CONTENTS | |
| DECLARATION | i |
| ACKNOWLEDEMENTS | ii |
| TABLE OF CONTENTS | iii |
| LIST OF FIGURES | v |
| LIST OF TABLES | vi |
| ABBREVIATIONS | vii |
| DEFINITION OF TERMS | viii |
| ABSTRACT | ix |
| 1.0 CHAPTER ONE: INTRODUCTION | 1 |
| 1.1 Background information | 1 |
| 1.2 Subtypes of Allergic conjunctivitis | 1 |
| 1.3 Management of Allergic Conjunctivitis | 3 |
| 1.4 Genetics of Ocular Allergy and Allied Conditions | 4 |
| 1.5 Prevalence of Allergic Conjunctivitis | 4 |
| 1.6 Risk factors for allergic conjunctivitis | 4 |
| 2.0 CHAPTER TWO: | 6 |
| 2.1 Literature Review | 6 |
| 2.2 Study rationale | 9 |
| 2.3 Research Questions | 9 |
| 2.4 Objectives | 10 |
| 2.4.1 Broad Objective | 10 |
| 2.4.2 Specific Objectives | 10 |
| 3.0 CHAPTER THREE: RESEARCH METHODOLOGY | 11 |
| 3.1 Study design | 11 |
| 3.2 Study area | 11 |
| 3.3 Study population | 11 |
| 3.3.1 Inclusion Criteria | 11 |
| 3.3.2 Exclusion Criteria | 11 |
| 3.4 Determination of Sample Size | 12 |
| 3.5 Sampling and recruitment | 13 |
| 3.6 Data collection procedure | 13 |
| 3.7 Study Materials | 14 |

| | |
|--|-----------|
| 3.8 Quality assurance..... | 14 |
| 3.9 Ethics Consideration..... | 14 |
| 3.10 Management of Data and Analysis..... | 15 |
| 3.11 Results Dissemination Plan | 15 |
| 4. RESULTS | 16 |
| 5. DISCUSSION | 25 |
| 6. STUDY LIMITATIONS..... | 29 |
| 7. CONCLUSION..... | 29 |
| 8. RECOMMENDATIONS..... | 29 |
| REFERENCES..... | 30 |
| APPENDIX A: BUDGET..... | 35 |
| APPENDIX B: Questionnaire..... | 36 |
| APPENDIX C: Allergic Conjunctivitis Grading Guide | 38 |
| APPENDIX D: Ocular Allergy Clinical Grading And Management Guidelines | 40 |
| APPENDIX E: UoN Anterior Segment Assessment Tool – For Patients’ file..... | 42 |
| APPENDIX F. Ethical Approval Certificate..... | 2 |

LIST OF FIGURES

| | |
|--|----|
| Figure I : Distribution by Sex | 16 |
| Figure II. Distribution by Age | 16 |
| Figure III: Grade of Allergic Conjunctivitis | 17 |
| Figure IV. Ocular Comorbidities Associated with Allergic Conjunctivitis | 17 |
| Figure V: Ocular Comorbidities Associated with Allergic Conjunctivitis | 18 |
| Figure VI: Refractive errors | 18 |
| Figure VII: Topical Steroid Use | 20 |
| Figure VIII: Systemic Comorbidities Associated with Allergic Conjunctivitis | 21 |
| Figure IX: Systemic Comorbidities Associated with Allergic Conjunctivitis | 21 |
| Figure X: Family History of Ocular Allergy | 23 |
| Figure XI: Family History of Non-Ocular Allergy | 23 |

LIST OF TABLES

| | |
|---|----|
| Table I: Grade of Allergic Conjunctivitis and Ocular Comorbidities | 19 |
| Table II: Grade of Allergic Conjunctivitis and Astigmatism | 19 |
| Table III: Steroid Treatment Complications | 20 |
| Table IV. Number of systemic comorbidities | 22 |
| Table V: Systemic Comorbidities and Sex of the Children | 22 |
| Table VI: Severity of Allergic Conjunctivitis and Systemic Comorbidities | 22 |
| Table VII: Severity of Allergic Conjunctivitis and Family History Atopy | 24 |

ABBREVIATIONS

| | |
|--------------|--|
| AC | Allergic conjunctivitis |
| AKC | Atopic keratoconjunctivitis |
| DES | Dry eye syndrome |
| DS | Diopter sphere |
| DC | Diopter cylinder |
| GPC | Giant papillary conjunctivitis |
| HLA | Human leukocyte antigen |
| IgE | Immunoglobulin E |
| IL | Interleukin |
| ISAAC | International Study of Asthma and Allergies in Childhood |
| KNH | Kenyatta National Hospital |
| OA | Ocular allergy |
| OR | Odds ratio |
| PAC | Perennial allergic conjunctivitis |
| SAC | Seasonal allergic conjunctivitis |
| Th2 | T-helper cells-2 |
| VKC | Vernal keratoconjunctivitis |

DEFINITION OF TERMS

| | |
|-----------------------|---|
| Allergic | Excessively sensitive; susceptible to allergens |
| Child | Any human being under the age of 18 years (Kenya) |
| Comorbidity | A disease or medical condition that is simultaneously present with another or others in a patient due to direct causation or associated risk factors. |
| Conjunctivitis | Is a common condition that causes redness and inflammation of the thin layer of tissue that covers the front of the eye (the conjunctiva). |
| Ocular | Related to the eye |
| Systemic | Relating to or affecting a particular body system. |

ABSTRACT

Allergic Conjunctivitis (AC) is associated with other allergic diseases such as asthma, eczema and rhinitis, which add to the burden of disease and quality of life. Studies on prevalence of AC and its comorbid conditions show high regional differences. This is attributed to differences in latitudinal location, climate, socio-economic factors, diet, hygiene, pollen dispersion and air pollution.

Objective: To determine the prevalence and pattern of ocular and systemic co-morbidities in children with allergic conjunctivitis at Kenyatta national hospital, eye clinic.

Methodology: This was a cross-sectional study reviewing medical records. Simple random sampling was used to select 121 files of children diagnosed with allergic conjunctivitis at Kenyatta National Hospital, eye clinic. Data on all ocular and systemic co-morbid conditions was extracted and recorded in a questionnaire. We defined comorbidity as a disease or medical condition that is simultaneously present with AC due to either direct causation or associated risk factors. The data was analysed using SPSS version 20.0. The frequencies, means and proportions were determined by descriptive analysis. Relationship between different comorbidities, demographic characteristics and AC grade was also analyzed.

Results: Ocular comorbidities were present in 83.5% patients; refractive error 60.3%, dry eye syndrome 52.1%, corneal scars 9.9%, Keratoconus 7.4%, corneal pannus 6.6%, shield ulcer 1.7%, bacterial conjunctivitis 1.7%. AC treatment complications include steroid responders 10.5% and steroid induced cataracts 2.3%. Systemic comorbidities were found in 37.2% of patients; allergic rhinitis in 26.4%, eczema 10.7%, adenoid hypertrophy 8.3%, food allergies 7.4%, asthma 5.0%, and drug allergy 2.5%. Dry eye syndrome (DES) and keratoconus were associated with higher grade of AC.

Conclusion: Majority of the AC patients had ocular comorbidities while only about one third had systemic comorbidities. Treatment complications were few.

1.0 CHAPTER ONE: INTRODUCTION

1.1 Background information

Allergic conjunctivitis(AC) also known as Ocular allergy(OA), is a broad group of allergic conditions that involve conjunctival inflammation(1). This is a type 1 hypersensitivity reaction in response to an environmental allergen and has an immediate onset. Some forms have also shown evidence of type IV hypersensitivity reaction, which is a delayed type hypersensitivity response by the cell mediated immunity and usually takes more than 12 hours to develop(2)(3).

AC is often associated with other allergic disease co-morbidities such as asthma and atopic dermatitis (eczema) and rhinitis(1)(2)(4). These conditions contribute to the burden of disease as well as the quality of life and are often underrecognized in the management of OA.

In ocular allergy, hypersensitivity begins with conjunctival exposure to an allergen trapped in the tear film. The allergen is engulfed by antigen presenting cells (APCs) and presented to T helper cells (CD4+) which respond by proliferating and transforming into T helper type 2 cells (Th2). The Th2 cells then release cytokines that cause B lymphocytes to produce the antibody immunoglobulin E(IgE)(3). The then IgE binds to conjunctival mast cells which degranulate and release histamine, prostaglandins, leukotrienes, cytokines, chemokines and proteases. The rapid histamine response causes vasodilation, increased vascular permeability and pruritis., by binding to H1 and H2 receptors on vascular smooth muscle and nerve endings. Increased vascular permeability also causes infiltration by neutrophils and eosinophils from the circulation resulting in chemosis(3)(5).

In chronic ocular allergy, T lymphocytes and eosinophils predominate in addition to mast cells and other inflammatory cells. This is due to persistent allergen- driven inflammation with chemokine release causing attraction of these cells to sites of inflammation(5). In these chronic forms the epithelium is altered with evidence of collagen deposition and tissue remodeling(5).

1.2 Subtypes of Allergic conjunctivitis

Ocular allergy is characterized by two acute disorders and three chronic diseases. The acute ones being perennial allergic conjunctivitis and seasonal allergic conjunctivitis, while chronic ones include atopic keratoconjunctivitis, giant papillary conjunctivitis and vernal keratoconjunctivitis.(6)

These conditions mainly present with tearing, itching, photophobia and redness of the conjunctiva. The symptoms usually depend on severity, with the chronic ocular allergy causing damage to the ocular surface(6)(2). Ocular allergy has also been associated with the development of other ocular conditions such as astigmatism(7) and dry eye syndrome.(8)

1. Seasonal allergic conjunctivitis (SAC)

SAC is intermittent in nature. Usually occurs during the dry season and spring following exposure to allergens, frequently tree and grass pollen. There is frequent association with allergic rhinitis.(1) (2)

2. Perennial allergic conjunctivitis (PAC)

It is a mild persistent form, symptoms occur all year round and is due to constant exposure to allergens such as animal dander, house dust mites and fungal allergen. This condition is also frequently associated with allergic rhinitis. (1)(2)

3. Vernal keratoconjunctivitis (VKC)

VKC represents severe ocular inflammatory disease caused by IgE and cell mediated immune responses. It is a chronic condition with seasonal exacerbations. Affects males more than females with age of onset 5 years to late teens. 95% undergo remission by late teens and 5% develop atopic keratoconjunctivitis. VKC is common in sub-Saharan Africa, Mediterranean and Middle east. In temperate regions VKC is

rare, but is linked with atopic diseases especially eczema and asthma in more than 90% of patients.(2)

Symptoms are intense itching, stringy discharge and matted eyelid on waking up. Corneal involvement causes photophobia, blurred vision and pain. The signs are giant papillae in the tarsal conjunctiva upper eyelid, diffuse conjunctival hyperemia, erosion of the corneal epithelium and limbal inflammation.(1)(2)(5)

VKC is sight-threatening and has been associated with development of corneal shield ulcers, corneal vascularization and scarring resulting in poor vision.(9)

Keratoconus is also frequently associated with VKC due to persistent eye rubbing in response to the sensation of intense itching(10). Herpes Simplex Keratitis also occurs more than average and can be bilateral.(2)

4. Atopic keratoconjunctivitis (AKC)

This is a severe disease that usually develops in adults, peak age between third and fifth decade of life. It can also begin in the late teens. Long history of asthma and

eczema is extremely common and 5% have history of childhood VKC(2). The symptoms ocular itchiness, gritty sensation, blurred vision and soreness. There is usually severe blepharitis, facial eczema involving the eyelids, conjunctival papillae, chronic cicatrizing conjunctivitis and progressive corneal scarring and vascularization(1)(5). AKC causes predisposition to secondary bacterial keratitis, fungal keratitis and herpes simplex keratitis which can be aggressive. Presenile posterior or anterior shield-like subcapsular cataracts are also common and may be worsened by prolonged steroid use.(2)

5. Giant papillary conjunctivitis

This condition is traditionally grouped under ocular allergic diseases, although it is caused by inflammatory response to tissue damage in repetitive microtrauma of the tarsal conjunctiva(9)(11). The variety of stimuli include contact lenses, post-operative sutures and ocular prostheses, scleral buckles, filtering blebs and corneal surface irregularities(2)(9). Symptoms consist of itchiness, redness, contact lens intolerance and mucoid discharge. Hallmark sign of the disease is superior tarsal papillae, although not always giant(>1mm) and erythema. Ptosis may occur due to tissue laxity and irritative spasm secondary to chronic inflammation, but keratopathy is rare. (1) (2)

Allergic conjunctivitis has also been associated with dry eye syndrome evidenced by decreased tear break up time. This has been hypothesized to result from decreased goblet density in the conjunctiva caused by the inflammatory process.(12)

1.3 Management of Allergic Conjunctivitis

There are different systems used globally for the grading and management of allergic conjunctivitis. Bore et al developed a grading guide for use in Kenya based on the ocular allergy clinical grading guide. The grading is based on the most severe sign seen in the worse eye(13). It is based on the signs present but not on the patients' symptoms. This system grades AC into mild, moderate or severe based on four aspects. These include size of papillae on tarsal conjunctiva, degree of corneal hyperemia, limbal involvement and corneal involvement(13). This is because the grade of severity helps to determine the treatment of choice and the follow-up frequency.

The management of ocular allergy depends on the severity of inflammation. Non-pharmacological therapy involves avoidance of allergen, tear substitutes and cold compress. Pharmacological therapy used ranges from mast cell stabilizers, topical antihistamines or combination and steroids. Steroids carry the potential side effects of

cataract and glaucoma, therefore they should only be used in severe cases for short duration.(3) (2)

1.4 Genetics of Ocular Allergy and Allied Conditions

The genesis of allergic diseases is by a composite interaction between environmental and genetic factors(14). Ocular allergy has been associated with allergic diseases such as asthma, rhinitis, and atopic dermatitis (eczema)(2). A number of studies have been done in different regions to show this relation. Association has also been made with food and drug allergies.(15)

Recent genome wide association studies (GWASs) have discovered many loci linked to allergic diseases(16). Candidate genes in the susceptibility loci suggest roles for innate adaptive immunity, epithelial functions, regulatory T cells, IL-1 signaling and vitamin D pathway in the pathogenesis of atopic diseases. HLA, IL13, IL1RL1, and f30 or C11 areas are overlapping susceptibility loci in allergic rhinitis, asthma and atopic dermatitis. Therefore, it is reasonably suggested that this cluster of genes contributes to the genesis of allergic conjunctivitis because the same cytokines have vital role in its pathogenesis.(17)

1.5 Prevalence of Allergic Conjunctivitis

There has been a rise in the prevalence of allergic conjunctivitis worldwide, older studies indicate prevalence of 15-20% and newer studies have shown higher prevalence of 40%(18). In Jos Nigeria Malu found a 32% prevalence of AC which was highest between ages 1 to 16 years(19),while Wade and associates in Gambia established prevalence of 7.9% predominant in children(20). In Rwanda, prevalence of VKC among school children was found to be 4% (21) while in Ethiopia it was 11.10%(22). In Uganda prevalence was 39.5% in a lifetime(23), while in Ghana the prevalence was 9.1%.(24)

In Kenya, the prevalence of AC is 27% as reported in a hospital-based survey. This makes it the leading cause for outpatient visits in eye clinics across the country.(25)

1.6 Risk factors for allergic conjunctivitis

AC has a strong hereditary factor whose inheritance is not consistent with the classic mendelian pattern. Some studies have shown that family history of allergy is as high as 70% for acute AC and 49% for VKC.(26)

The risk is also higher in patient with other allergic conditions such as eczema, allergic rhinitis and asthma. Atopic march concept describes the progression of these allergic disorders in children, which often begins with eczema in infancy.(27)

In Uganda, large case-control study on asthma involving 1,700 school children, 5-17 years, showed extensive overlap and multi-morbidity of the risk factors for AC, eczema and rhinitis(23). The risk factors for rhinitis were: city residence, parents' history atopy, deworming in the previous 12 months, many trucks passing near home and positive skin prick test. These were the same risk factors observed for AC and eczema.(23)

2.0 CHAPTER TWO:

2.1 Literature Review

The international study on asthma and allergies in childhood, (ISAAC) study has shown that there is a close association between allergic rhino-conjunctivitis and asthma with increasing prevalence globally. However, there has been high regional differences in prevalence which have been attributed to different factors. These factors include differences in latitudinal region, climate, mean annual temperature, socio-economic factors, diet, hygiene, pollen dispersion and air pollution.(28)

Gradman et al in 2006(29), carried out a study at an outpatient clinic in Denmark, on AC in children with asthma, rhinitis and eczema. The children were 458 aged between 5-15 years, 316 had been diagnosed with rhinitis, 324 with asthma, 149 with eczema and 137 with AC. They found that AC was co-morbid in 133(42%), 78(24%), 45(30%) of those with rhinitis, asthma and eczema respectively. Of those children with allergic conjunctivitis 133 (97%) had rhinitis with allergic conjunctivitis while 77(56%) had asthma while 45(33%) had eczema. 125(91%) tested positive to at least one allergen, commonest house dust mites, followed by grass. They concluded that allergic conjunctivitis needed to be included in the guidelines on eczema, asthma and allergic rhinitis because it is an important co-morbidity.(29)

In a cross-sectional study in China, the prevalence of OA was found to be 28%. Among these the commonest co-morbid condition was allergic rhinitis in 61%, then asthma and atopic dermatitis in 29% and 25% respectively. Allergen sensitization was highest for mite allergy at 17.6%, then pollen allergy and lastly food allergy at 12.8% and 12.5% respectively.(4)

In another study by Bezerra et al in Brazil on 52 patients with allergic conjunctivitis, ages 3 to 19 years. He found that 25 (48.1%) had bronchial asthma, 20 (35.1%) had allergic rhinitis, and 5 (9.6%) had atopic dermatitis. Eosinophils in conjunctival scrapping was found in 86.5% cases.(30)

In a study by Kim HY et al done in Korea among 615 pre-school children in day-care centers, 3-6 years of age, 64% of those with AC had rhinitis and 23.6% of children with rhinitis had allergic conjunctivitis. 25.3% of those with 'current wheeze' had AC. The study also found the prevalence of food allergy and drug allergy was 18.4% and 2.9%

respectively. Conclusion was that preschool children who had allergic conjunctivitis had a higher prevalence of asthma and allergic rhinitis.(15)

Malu et al in Jos Nigeria conducted a hospital based retrospective study on 972 patients with allergic conjunctivitis both adults and children in 2014. 38.4% were children aged 1-16 years. The commonest ocular co-morbidity was found to be refractive error 151(15.4%). This was followed by pinguecula/pterygium 35(3.6%), bacterial conjunctivitis 22(2.2%), Glaucoma (21) 2.1%, eyelid disorders 17(1.7%), cataract was present in 13(1.3%), and keratopathy in 11(1.1%). Other conditions such as dry eye, were also present in less than 1%. Systemic co-morbidities were very few, eczema in 3 (0.3%)and 1 patient with allergic rhinitis.(19)

In a retrospective study done in a regional eye center in Gambia, by Wade et al (2012) among 7912 patients on the prevalence of allergic conjunctivitis, its associated ocular and systemic comorbidities. 624 (7.9%) had AC, 340 (54.5%) were children. Refractive error was the commonest ocular condition in 92 (7.4%) of eyes, corneal opacities in 14(1.1%), trachoma in 16(1.3%), cataracts in 12(1.0%), keratoconus in 11(0.9%) eyes, pinguecula in 7(0.6%), 6(0.5%) had pterygia, 2(0.2%) eyes had chalazia, while another 2(0.2%) had ptosis. Glaucoma and stye were found in 1 (0.1%) eye each. The commonest systemic condition was asthma, in 9(1.4%) patients. Atopic dermatitis was found in 1(0.2%) patient. No patient had allergic rhinitis which was in contrast to other studies largely from developed countries.(20)

According to a retrospective cross-sectional study done by Abokyi in Ghana, in two referral eye centers, allergic rhinitis was the commonest systemic co-morbidity present in 342(19.9%) of patients with AC, followed by asthma in 57(3.3%) and eczema in 16(0.9%). The ocular complications found were corneal abrasion in 17(1.0%), pannus 7(0.4%), keratoconus 1(0.1%) and steroid induced glaucoma 1(0.1%). Dry eye was present in 89(5.2%) and was the commonest ocular surface disorder. The others included pterygium 31(1.8%), pinguecula 17(1.0%), chalazion 11(0.6%), stye 7(0.4%), and 10(0.6%) had blepharitis.(24)

In a community-based study on allergies in children in Egypt, 114 (14.8%) of the children had seasonal AC while 30 (3.9%) had VKC. Among those with VKC, rhinitis was the commonest comorbidity in 10 (33.3%) of the children, followed by asthma and eczema in 9(30%) and 6(20%) respectively.(31)

According to a study done by Hom et al in Southern California among 689 patients to examine the potential overlap between allergic conjunctivitis and dry eye syndrome as comorbidities. Patients' age ranged between 5 and 90 years. The study found that patients

with symptoms of AC were 2.11 times more likely to have dry eye. Another study found a 12% prevalence of DES in children with AC,(8) while a different study in South-East China showed a much higher prevalence of 97.5%, whereby the severity of DES was associated with duration of AC.(32)

Yangho Kim et al in Korea studied the association of AC with refractive error. The study found that there is indeed association of astigmatism (one cylindrical diopter increase) and AC (OR =1.287).(7)

In Kenya, F. Waweru conducted a study in Kenya in 1991 on 100 patients with VKC at Kenyatta National Hospital, 22% of the patients had rhinitis, 8% had asthma and 3% had eczema. Among these patients 3% had keratoconus, 4% had superficial punctate keratitis and 3% had corneal ulcers.(33) S. Mugho also conducted a study on keratoconus and found a prevalence of 30.9% in patients with AC at Kenyatta National Hospital in 2016. In those with keratoconus, 42.1% had severe allergic conjunctivitis while 34.2% had moderate allergic conjunctivitis.(34)

Long term use of steroids especially in treatment of VKC increases the risk of complications such as steroid induced glaucoma and cataracts. According to a study by Marcus et al in Singapore, 28% of patients with VKC had ocular hypertension due to steroid treatment, and 5.5% developed glaucoma.(35) In another study, steroid induced glaucoma was found in 2% of patients with VKC.(36)

The findings were similar in a study in India whereby 3.3% of children with VKC had steroid induced glaucoma, steroid induced cataracts were 37.8%, 6.3% had keratoconus and 2.1% had shield ulcers on the cornea.(37)

Saleh et al carried out a retrospective hospital-based study in Yemen, on 68 children with VKC. The ocular findings included keratoconus (7),steroid-induced cataract (5), central corneal scars (5) and steroid-induced glaucoma (3).(38)

2.2 Study rationale

Allergic conjunctivitis has been allied with other allergic disease co-morbidities such as asthma, rhinitis and eczema. Most of the data available is from developed countries with different demographics and climate. The few studies done in African populations show that AC is common in African children and probably more severe, as indicated by prevalence of VKC in in countries such as Rwanda and Ethiopia. Currently the few studies that have been carried out in African populations have shown a marked variation with data from the developed countries.

KNH being the largest referral hospital in Kenya is likely to be seeing more severe allergic conjunctivitis which may be associated with severe co-morbidities, but the latter is unclear/unknown.

Treating allergic conjunctivitis and the co-morbidities each in special clinics means they may be missed, not addressed adequately, or complex if patients have to get appointments in other clinics especially in the setting where health access is limited. The typical appointment waiting time in each of these clinics being at least 2 hours, may discourage some and therefore fail to address the burden of disease.

This study aims to look at the patterns of ocular and systemic comorbidities will provide data on the burden of disease, in order to facilitate provision of integrated management through interprofessional collaboration to enhance patient care. Therefore, knowing the co-morbidities associated with allergic conjunctivitis may help to improve co-ordination in triage and multidisciplinary team treatment.

Healthcare professionals may be able to use data from the study to provide patients with individual information about their estimated risk of developing the conditions allied in allergic conjunctivitis. The study will also provide a baseline information for policy makers, and possibly improve health resource allocation.

2.3 Research Questions

- 1) What is the prevalence of ocular and systemic comorbidities in children with allergic conjunctivitis at Kenyatta national hospital, eye clinic?
- 2) What is the pattern of ocular and systemic comorbidities in children with allergic conjunctivitis at Kenyatta national hospital, eye clinic?

2.4 Objectives

2.4.1 Broad Objective

To describe the prevalence and pattern of ocular and systemic comorbidities in children with allergic conjunctivitis at Kenyatta National Hospital, eye clinic.

2.4.2 Specific Objectives

1. To determine the prevalence of ocular and systemic comorbidities in children with allergic conjunctivitis.
2. To describe the pattern of ocular comorbidities in children with allergic conjunctivitis.
3. To evaluate the ocular treatment complications in children with allergic conjunctivitis.
4. To describe the pattern of systemic comorbidities in children with allergic conjunctivitis

3.0 CHAPTER THREE: RESEARCH METHODOLOGY

3.1 Study design

This was a cross-sectional study of medical records.

3.2 Study area

This study was conducted in Nairobi, Kenya at Kenyatta National Hospital (KNH), eye clinic. KNH is Kenya's biggest referral hospital, located at Nairobi Upper Hill area, 3.5 kilometers west of Nairobi central business district. Eye clinic 35 at KNH has specialized pediatric clinic two days a week run by pediatric ophthalmologists, where a large number of the children with allergic conjunctivitis are treated. Some of the children are seen in the outpatient filter clinic which runs every day in clinic 35.

3.3 Study population

Study population included patients diagnosed with allergic conjunctivitis, seen and treated at Kenyatta National Hospital, eye clinic.

3.3.1 Inclusion Criteria

- Children (less than 18 years)(39), diagnosed with allergic conjunctivitis attending KNH, eye clinic.

3.3.2 Exclusion Criteria

Patients diagnosed with allergic conjunctivitis above the age of 18 years.

3.4 Determination of Sample Size

Fischer's formula was used for sample size calculation.

According to records, a total of 1697 patients attended the KNH pediatric eye clinic in the year 2019. The hospital-based prevalence of allergic conjunctivitis in Kenya is 27% (25) and the most recent proportion of comorbidity is keratoconus at 30%. (34)

$$n = \frac{z^2 P(1-P)}{d^2}$$

$$n = \frac{1.96^2 \cdot 0.3(1-0.3)}{0.07^2}$$

n = sample size

N = population size 458 (27% of 1697)

d = degree of precision 7%

z = z score 1.96 (95% confidence interval)

P = proportion = 0.3

The calculation gave a sample size of **164**

Corrected for population less than 10,000

$$n = \frac{n}{1+(n-1)/N}$$

$$n = \frac{164}{1+(164-1)/458} = \mathbf{121}$$

Therefore, a sample size of **121** files was used.

3.5 Sampling and recruitment

Simple random sampling was used in selection of files. The sampling frame included all file numbers of patients with allergic conjunctivitis for the period between January and December 2019. These were obtained from the clinic 35 attendance records and each assigned a serial number. These were then entered into Microsoft excel computer program to generate a random sample of 121. The files of the corresponding serial number were then used in the study. The filter clinic cards were not included sampling frame, because there is no strict adherence to format of documentation used in specialized pediatric eye clinic therefore some data may be missing. The files were checked for AC diagnosis and exclusion done appropriately.

3.6 Data collection procedure

Coding of eye diseases at KNH uses ICD10 only for inpatients. Eye diseases for patients seen in outpatient eye clinic 35 are not coded. They are recorded in the clinic attendance records from where file numbers were taken and files retrieved from the records department. These were used to retrieve medical records of all pediatric patients who attended the any of the two clinics with diagnosis of allergic conjunctivitis. Data collection was done using a formulated questionnaire, which included: demographic data on age, and sex. The grading given for allergic conjunctivitis and history of steroid use were recorded. Any ocular comorbid condition diagnosed and systemic comorbid condition either diagnosed or indicated in the past medical history was recorded.

All this information was in the file because there is a standard format for documentation used in the pediatric eye clinic. There is also a standard tool used for evaluation and treatment for allergic conjunctivitis; the ‘Ocular Allergy Clinical Grading and Management guide’(13). These two tools are attached at the appendix.

The following were recorded as subtypes of allergic conjunctivitis and the ‘Ocular Allergy Clinical Grading and Management Guide’ was used to assign a grade of severity to those without, based on the clinical findings recorded.

- Perennial allergic conjunctivitis
- Seasonal allergic conjunctivitis
- Atopic keratoconjunctivitis
- Giant papillary conjunctivitis
- Vernal keratoconjunctivitis

All known ocular comorbid conditions associated with AC were recorded as indicated in the file. Clinically significant refractive errors were recorded; myopia -0.5DS and above, astigmatism 0.5DC were recorded(40). Consideration was made to eliminate normal refractive status for age in hyperopia(41)(42). Presence of dry eye syndrome, if not indicated, was considered as tear break-up time less than 10 seconds. Keratoconus was accepted if there is recorded presence of Munson sign, oil droplet reflex, scissoring on retinoscopy and presence of a positive corneal topography report. The presence of shield ulcers, pannus and non- traumatic corneal scars was recorded as indicated in the file. Microbial keratitis was recorded and specified by causative organism if indicated in the records.

Any intraocular pressure 22mmHg and above was considered steroid response in patients treated with steroids. Steroid induced glaucoma was indicated by recorded history of steroid response with optic nerve damage or glaucomatous visual field defects. Steroid induced cataracts were also recorded.

Systemic comorbidities case definition was recorded as follows:

1. Asthma; wheezing, persistent dry night coughs
2. Rhinitis; persistent blocked nose, persistent sneezing or running nose
3. Eczema (atopic dermatitis); itchy rash, recurrent itchy rash

Family history of ocular allergy or any other atopic condition was also recorded.

3.7 Study Materials

- A predesigned questionnaire will be used to collect the data.
- Patient files
- Ocular Allergy Clinical Grading and Management Guide.

3.8 Quality assurance

Data was collected using a predesigned questionnaire by the principal investigator. This is in order to avoid wrong classification of data, misinterpretation or exemption of vital data from the patient files.

3.9 Ethics Consideration

Ethical approval to undertake this study was sought from Kenyatta National Hospital/ University of Nairobi Ethics and Research Committee. Authorization to use the patient's files was sought from the deputy Director clinical services and deputy Director, health information, KNH.

Patient's file identity and details were kept anonymous at all times by the use of coded questionnaires. Files were not photographed and no material was be taken out of the

records department. Data was stored in one computer and protected with a password only accessible by the principal investigator in order to facilitate confidentiality.

3.10 Management of Data and Analysis

The collected data was coded and then entered into the computer. Analysis was done using the statistical package for social sciences programme (SPSS). This data was then be analysed using quantitative techniques, whereby the findings were exhibited in frequency distribution tables, pie charts and bar graphs.

The proportion of patients with asthma, eczema and rhinitis was calculated collectively as well as for each condition. Proportion of those with food and drug allergy was also calculated. Proportion of patients with each ocular comorbidity was also determined. Patterns for comorbidities were described, in terms of age distribution and sex predilection if any and the most prevalent grade of allergic conjunctivitis. Analysis was done to identify association of any of the comorbidities with the severity of AC. The prevalence steroid treatment complications among those treated with topical steroids was also computed.

3.11 Results Dissemination Plan

The findings of this study were presented in the ophthalmology department. Submission would be made to ophthalmology scientific journals for publishing. A copy of the dissertation would be deposited in the University of Nairobi research repository, the College of Ophthalmology of Eastern Central and Southern Africa (COECSA)research repository and the research office at KNH.

4. RESULTS

Records of 121 patients with allergic conjunctivitis seen in the pediatric eye clinic, in the year 2019 were reviewed and below are the findings.

Figure I : Distribution by Sex

There were 51 females and 70 males. M:F ratio was 1.4:1 and the difference was not statistically significant.

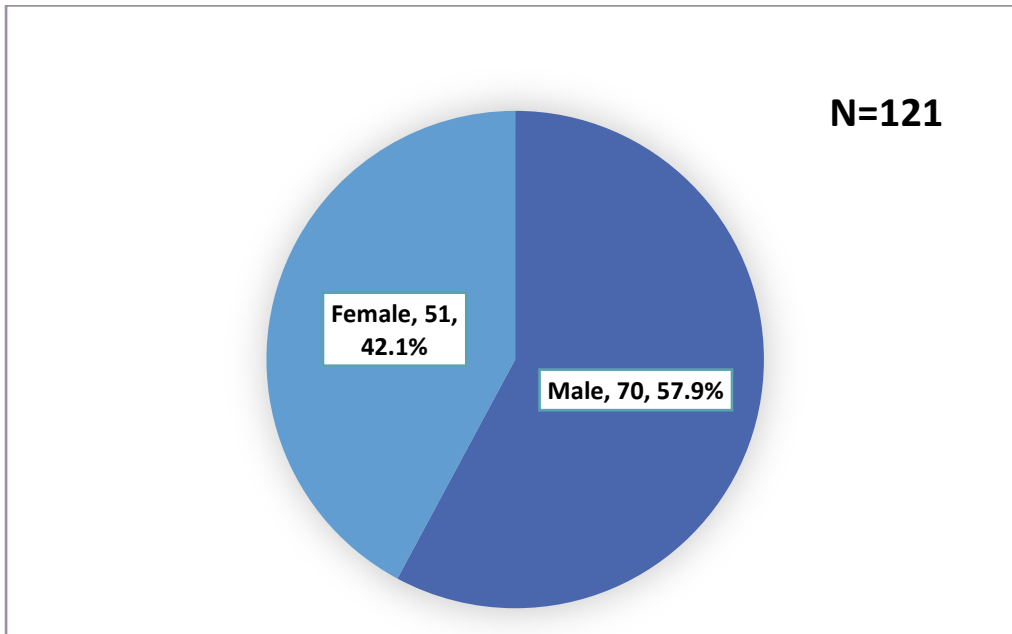


Figure II. Distribution by Age

The mean age was 9.7 (SD 3.5) years. The youngest was 2.0 years, and the oldest was 17.0 years. The largest age groups were between 6 and 13 years.

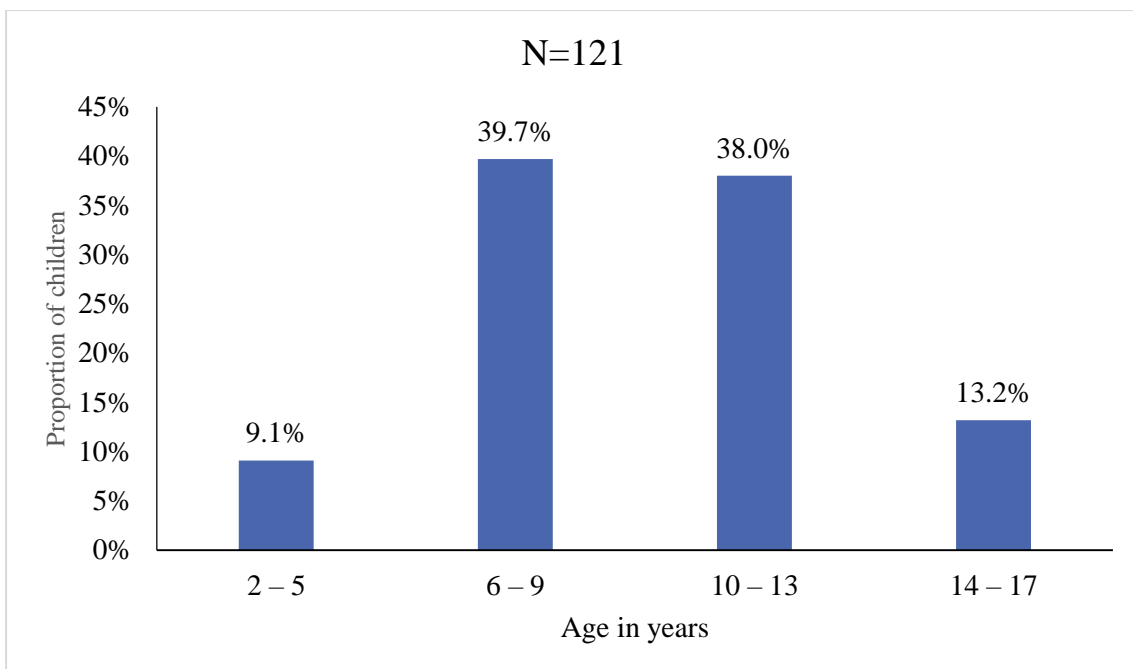


Figure III: Grade of Allergic Conjunctivitis

The most common grade of allergy was moderate allergic conjunctivitis.

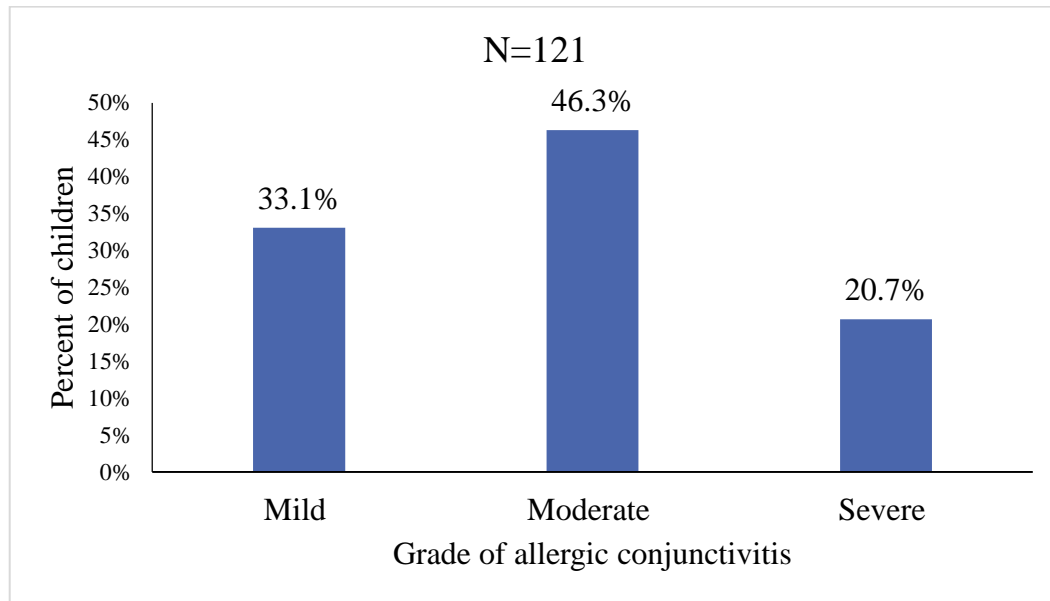


Figure IV. Ocular Comorbidities Associated with Allergic Conjunctivitis

Majority of the patients had associated ocular comorbidities as shown below.

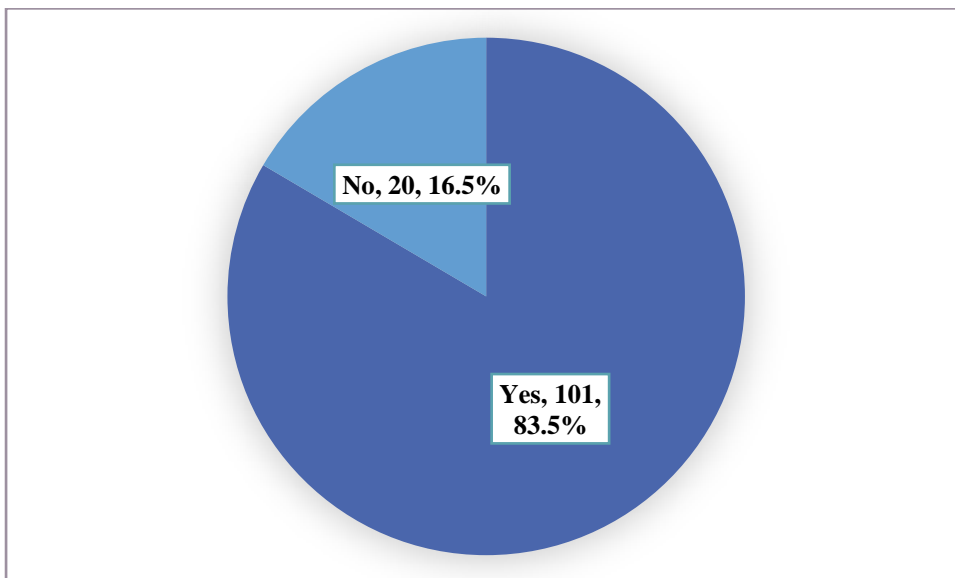


Figure V: Ocular Comorbidities Associated with Allergic Conjunctivitis

Refractive errors and dry eye syndrome were the most common ocular comorbidities as shown below.

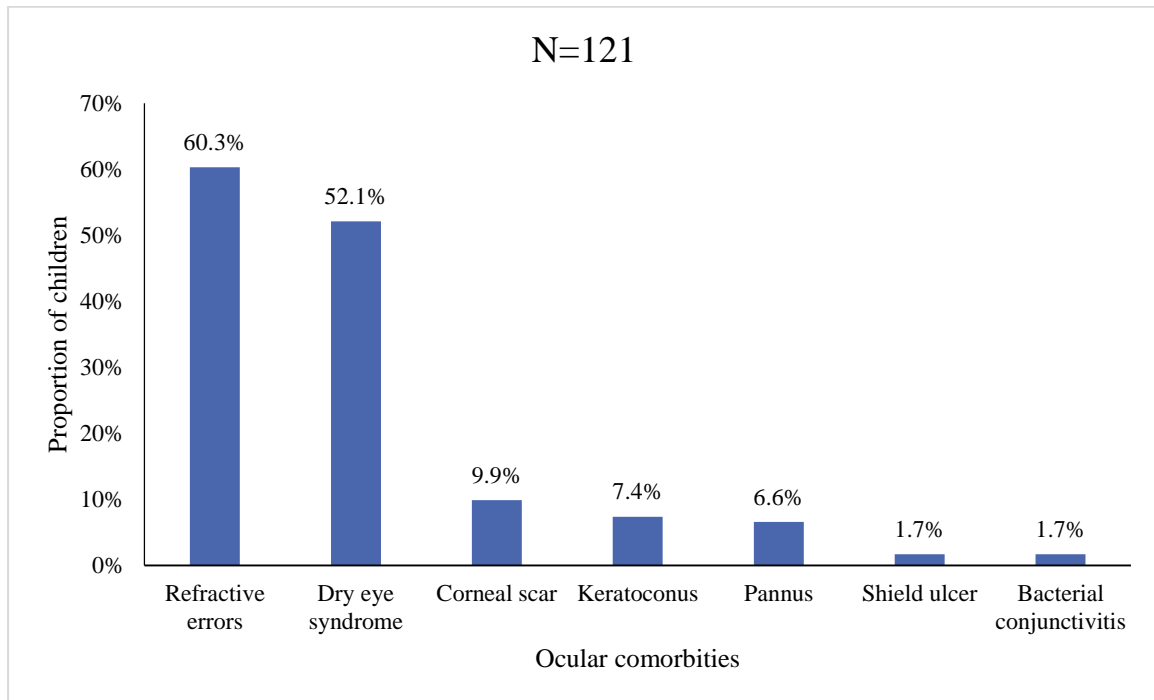


Figure VI: Refractive errors

The graph below shows the distribution of the different refractive errors, astigmatism being the most common.

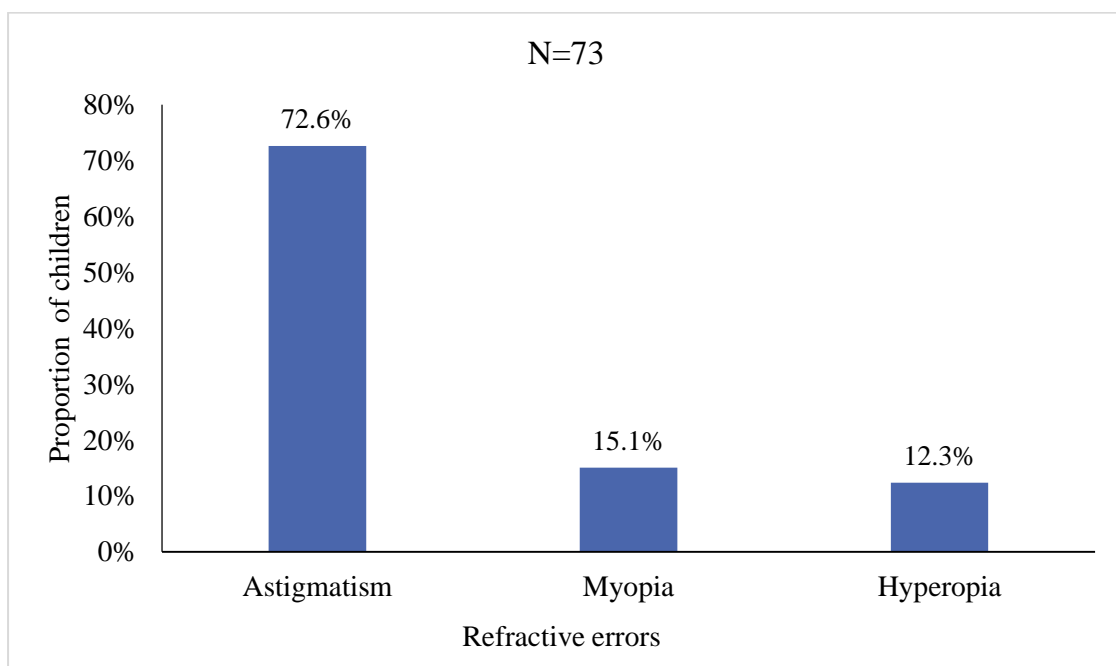


Table I: Grade of Allergic Conjunctivitis and Ocular Comorbidities

Each comorbidity was independently tested with the severity of AC and a p-value result is shown for each association. The p values for dry eye syndrome, pannus, corneal scar and keratoconus showed that they are associated with increase in severity of allergic conjunctivitis.

| Ocular comorbidity | Mild AC | Moderate AC | Severe AC | p-value |
|---------------------------|-----------|-------------|-----------|------------------|
| | n (%) | n (%) | n (%) | |
| Dry eye syndrome | 7 (11.1) | 40 (63.5) | 16 (25.4) | 0.001 |
| Refractive errors | 18 (24.5) | 37 (51) | 18 (24.5) | 0.724 |
| Shield ulcer | 0 | 0 | 2 (100) | 0.107 |
| Pannus | 0 | 1 (12.5) | 7 (87.5) | <0.001 |
| Corneal scar | 1 (8.3) | 3 (25) | 8 (66.7) | 0.003 |
| Keratoconus | 0 | 2 (22.2) | 7 (77.8) | <0.001 |
| Bacterial conjunctivitis* | 1 (50) | 1 (50) | 0 | 0.465 |

Table II: Grade of Allergic Conjunctivitis and Astigmatism

Grade of AC was tested to determine whether there was an association with astigmatism. The results show no association as shown by the p-value below.

| Allergy grade | Astigmatism | | p-value |
|----------------------------------|------------------|-----------------|---------|
| | Present n (%) | Absent n (%) | |
| Mild allergic conjunctivitis | 13 (24.5) | 27 (39.7) | 0.093 |
| Moderate allergic conjunctivitis | 25 (47.2) | 31 (45.6) | |
| Severe allergic conjunctivitis | 15 (28.3) | 10 (14.7) | |

Figure VII: Topical Steroid Use

Majority of the patients had history of treatment with topical steroids as shown;

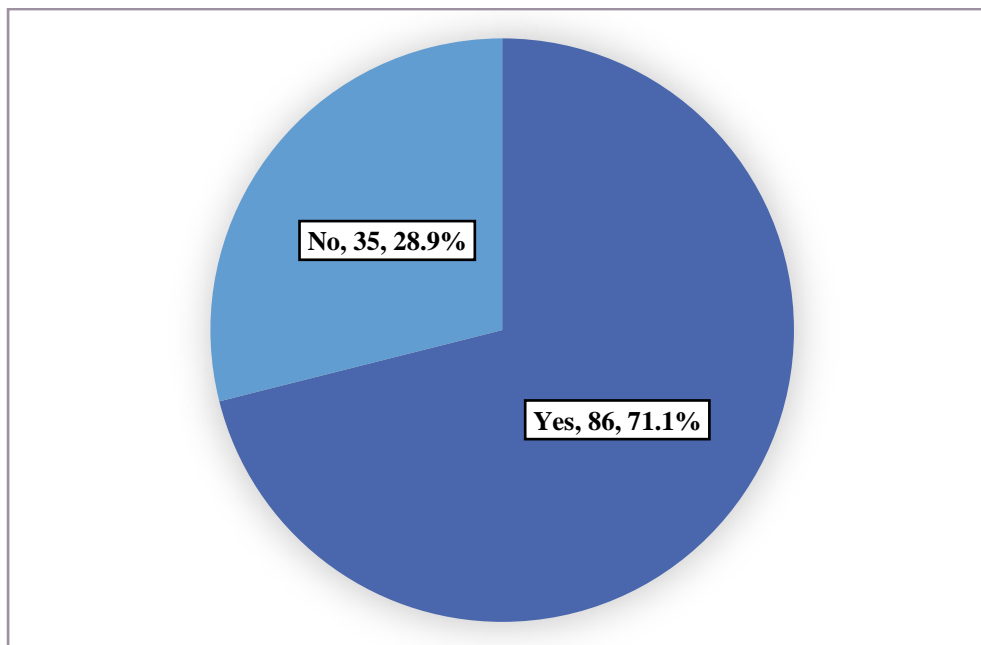


Table III: Steroid Treatment Complications

Among all the patients treated with topical steroids, only few developed complications.

| Steroid induced complication | N=121 |
|-------------------------------------|--------------|
| | n (%) |
| Non-responders | 76 (88.4) |
| Steroid responders* | 9 (10.5) |
| Steroid Induced cataracts | 2 (2.3) |

*1 child was both steroid responder with steroid induced cataract

Figure VIII: Systemic Comorbidities Associated with Allergic Conjunctivitis

Presence of systemic comorbidities was as shown in the pie chart.

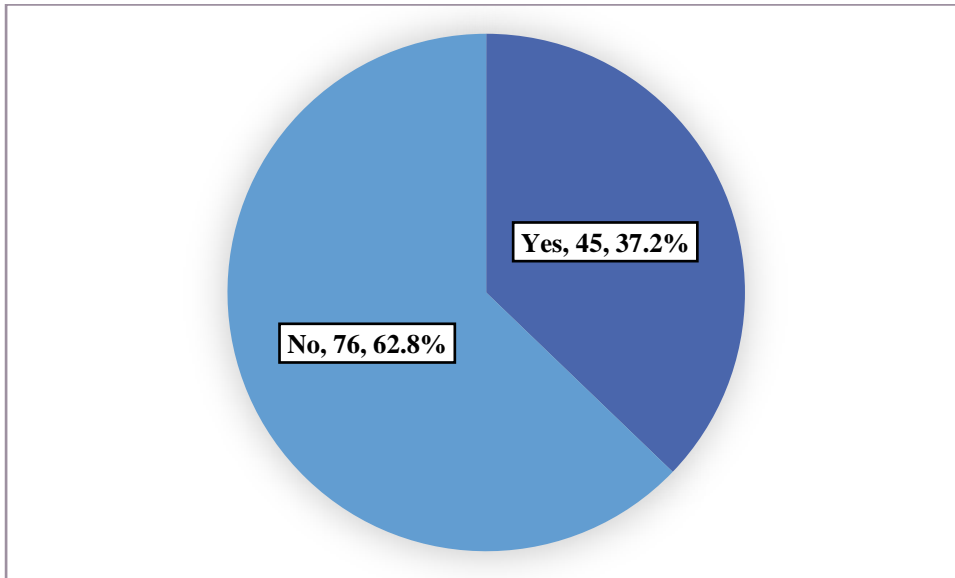


Figure IX: Systemic Comorbidities Associated with Allergic Conjunctivitis

Allergic rhinitis was the most common systemic comorbidity as shown in the graph below.

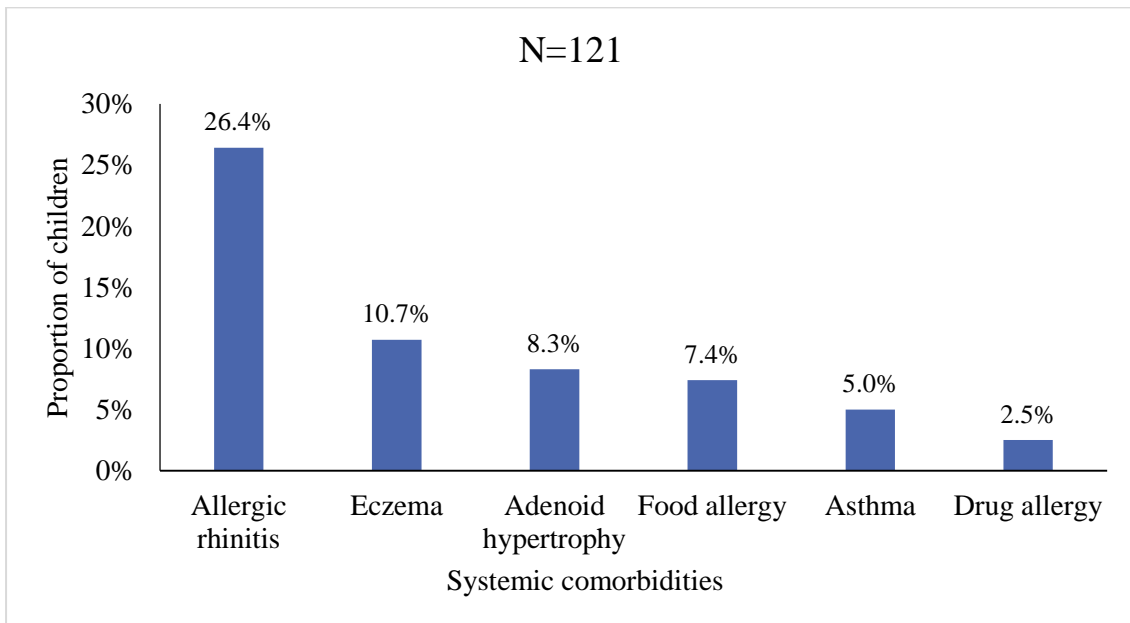


Table IV. Number of systemic comorbidities

Some of the patients had more than 1 comorbidity as shown below.

| Systemic comorbidities | N=121 n (%) |
|-------------------------------|------------------------|
| No comorbidity | 76 (62.8) |
| 1 comorbidity | 21 (17.4) |
| 2 comorbidities | 20 (16.5) |
| 3 comorbidities | 4 (3.3) |

Table V: Systemic Comorbidities and Sex of the Children

There was no sexual predilection regarding the presence of systemic comorbidities as shown by the p value below.

| Systemic Comorbidities | | | |
|-------------------------------|--------------------------|-------------------------|----------------|
| Sex | Present n (%) | Absent n (%) | p-value |
| Male | 26 (57.8) | 44 (57.9) | 0.990 |
| Female | 19 (42.2) | 32 (42.1) | |

Table VI: Severity of Allergic Conjunctivitis and Systemic Comorbidities

Higher grade of allergic conjunctivitis was associated with the presence of systemic comorbidities as shown by the p value below.

| Systemic comorbidity | | | |
|----------------------------------|--------------------------|-------------------------|----------------|
| Allergy Grade | Present n (%) | Absent n (%) | p-value |
| Mild allergic conjunctivitis | 7 (15.6) | 33 (43.4) | 0.007 |
| Moderate allergic conjunctivitis | 27 (60.0) | 29 (38.2) | |
| Severe allergic conjunctivitis | 11 (24.4) | 14 (18.4) | |

Figure X: Family History of Ocular Allergy

Figures below shows positive and negative family history of ocular allergy. The Unknown category is of 24 patients whereby the family history was not indicated in the records. Majority of the children did not have family history of ocular allergy.

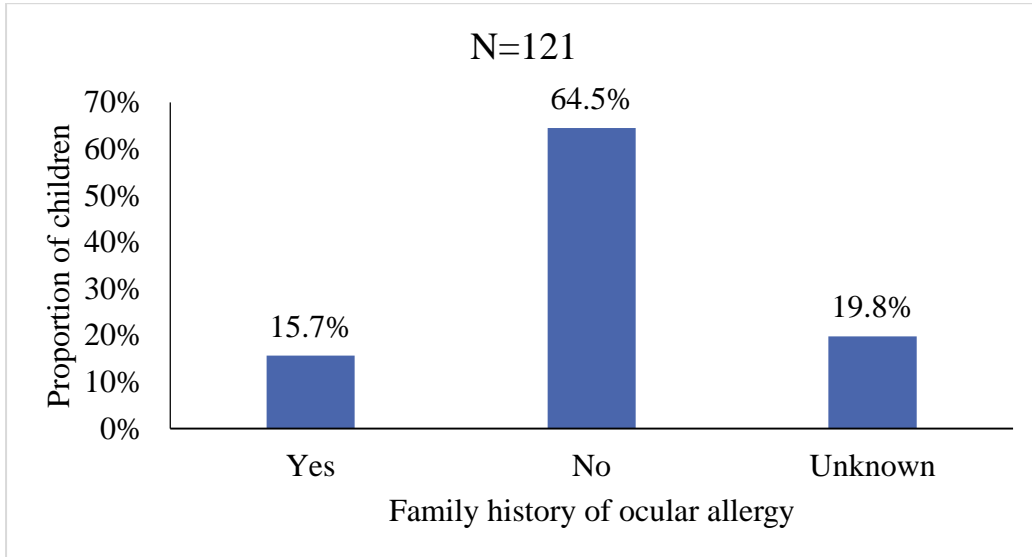


Figure XI: Family History of Non-Ocular Allergy

Majority of the children did not have family history of non-ocular allergy as shown in the graph below.

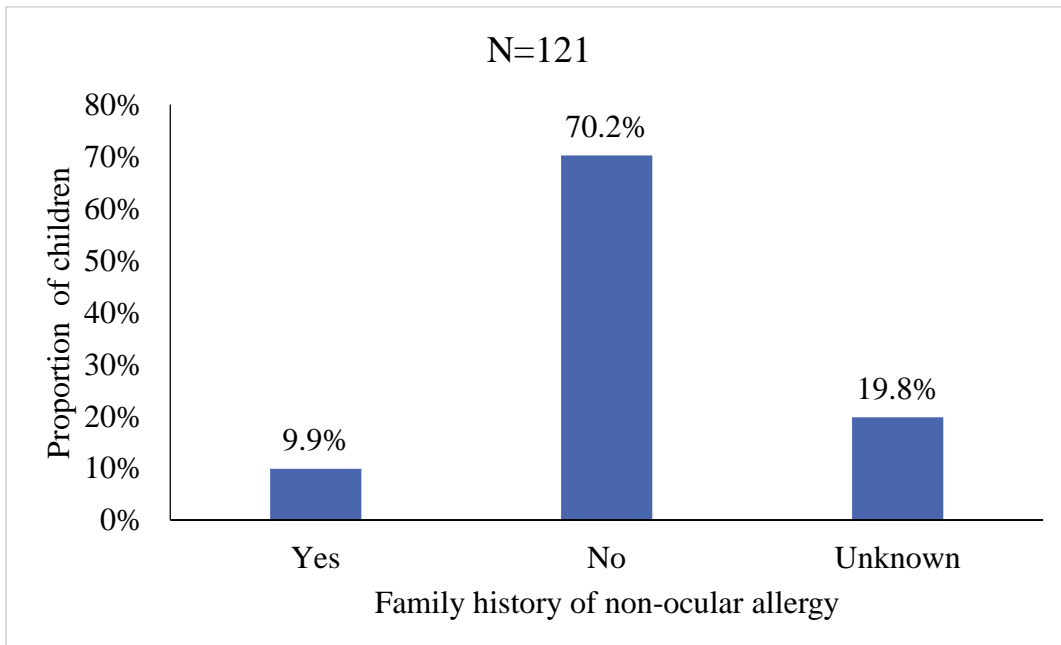


Table VII: Severity of Allergic Conjunctivitis and Family History Atopy

The severity of allergic conjunctivitis was analyzed with the presence positive and negative family history of both ocular and non-ocular allergy. Positive family history was not associated with higher grade of allergic conjunctivitis.

The patient with unknown family history were not included in this table

| Allergy grade | Family history | | p-value |
|----------------------------------|-----------------------|---------------------|----------------|
| | Yes n (%) | No n (%) | |
| Mild allergic conjunctivitis | 6 (22.2) | 22 (31.4) | 0.352 |
| Moderate allergic conjunctivitis | 13 (48.1) | 36 (51.4) | |
| Severe allergic conjunctivitis | 8 (29.8) | 12 (17.1) | |

5. DISCUSSION

Demographic Characteristics

The male: female ratio in this study is almost similar to a study done in KNH by Mugho et al, and other studies in Gambia and Nigeria which all found no sex predominance in allergic conjunctivitis.(20)(19)(34)

The mean age in this study is also similar to many studies in Gambia, Nigeria, Ghana and Brazil whereby this ranges from 8-13 years(20)(19)(30)(24). The peak ages were also similar ranging from 6-13years.These findings differed slightly from previous study at KNH where the mean age was 16 years which could have be due to inclusion of adults and different range in age.(34)

Severity of Allergic Conjunctivitis

The most prevalent grade of allergic conjunctivitis in this study is in contrast to a study in KNH by Mugho et al whereby the most common grade of allergy was mild allergic conjunctivitis(34). This may be attributed to the difference in age group of that study which also included adults and that allergic sensitization decreases with age.

Ocular Comorbidities

The ocular comorbidities found in this study showed that refractive error was the most common, with astigmatism being the highest. This is consistent with a study by Yangho et al who found association between astigmatism and allergic conjunctivitis, because the persistent eye rubbing in response to itchiness causes changes on the corneal surface(7). However, astigmatism was not associated with increase in severity of allergic conjunctivitis in this study, p-value 0.093 (table II). Refractive error was also the most common ocular comorbid condition in hospital-based studies done in Nigeria and Gambia. However, this study found a much higher prevalence compared to those studies done in Nigeria and Gambia whereby the refractive errors were 15% and 7.4% respectively(19). This difference may be due to large difference in sample sizes Nigeria; 972 and 7912 in Gambia in addition to the two studies including both adults and children.

Dry eye syndrome was the second most common ocular comorbidity, in half of the patients (fig.V) and also in Nigeria and Ghana; although at much lower prevalence of less than 6%. (19)(24). Dry eye syndrome was associated with increase in severity of AC, p-value 0.001 (table I). This is similar to a study by Handan et al in Turkey which showed that higher ocular surface disease index was associated with DES in children with allergic conjunctivitis(8). Pflugfelder et al proposed that increase in inflammatory cytokines like

Interleukin 1, 8, and epidermal growth factor, damages the conjunctival epithelium and goblet cells, with resulting decrease in mucin production and tear break up time.(43)

Those patients with keratoconus were 7.4% (fig. V). This is higher than 3% prevalence found in KNH by Waweru et al in patient with VKC in 1991.(33) Findings in this study are also in contrast with those of a prospective study done by Mugho et al in 2016. The prevalence of keratoconus clinically was 10%, 20% with keratometry and 30.9% with corneal topography(34). This could be an indication that there has been increase in patient awareness and better health seeking behavior that has been able to prevent this condition by adequate management of allergic conjunctivitis. In contrast, it could mean that there has been a decline in surveillance by health care providers at KNH in diagnosing this condition, with early keratoconus not being detected. The findings in this study are comparable to a study in India whereby 6% of patients had keratoconus(37). The studies in Ghana and Gambia had much less prevalence of less than 1% (20) (24).Keratoconus was also associated with increase in severity of AC p-value <0.001 (table I).

Corneal pannus refers to corneal ingrowth of blood vessels from the limbus due to the inflammatory activity at the limbus that occurs in ocular inflammation conditions including AC(44). In this study, 7.6 % of the patients had pannus,(fig.V) which is comparable to the study in India with 7%(37). In Ghana it was much lower at 0.4%(24). Pannus was also associated with increase in severity of AC p-value <0.001(table I).

Shield ulcers were present in only 2 patients (fig. V), all of whom had severe allergic conjunctivitis. This was about half of the findings in the study in India which was 3%(37). The shield ulcers occur due to mechanical irritation of the cornea by giant papillae, in as well as toxic epitheliopathy from released mediators of inflammation by mast cells and eosinophils(45). The different findings in these two studies could be because the study in India only included patient with VKC which is more severe disease.

Bacterial conjunctivitis, clinically diagnosed, was found in 1.7% patients (fig.V), almost similar to findings by Malu et al in Nigeria(19). These could be secondary infections due scratching with dirty fingers, long duration of steroid use or dusty environment. There was however no association with increase in severity of AC p-value 0.465(table I). None of the patients in this study had keratitis.

Corneal scars were 9.9% (fig. V), 2 were from healed shield ulcers, the cause for the other 10 non-traumatic corneal scars was unclear. However, they were associated with increased severity of AC p value 0.003 (table I), an indication of possibly being healed shield ulcers prior to starting follow-up at KNH. This was comparable to a study in India by Pradhnya

et al where 11% of patients with VKC had corneal opacities(37). However, studies in Ghana, Gambia and found much less prevalence of 1%. (24)(20)

Steroid Treatment Complications

Majority of the patients had history of treatment with topical steroids used in the management of allergic conjunctivitis (fig. VII). Despite this large number, only a few developed complications. Those that developed raised IOP, also known as steroid responders were 10.5% and 2.3% developed steroid induced cataracts (table III). None had steroid induced glaucoma. This may be an indicator of good follow-up and management of patients on topical steroids. This is different from a study in Singapore by Marcus et al where 28% of patient with VKC developed ocular hypertension and 5.5% developed glaucoma(35). In India Pradhnya et al found 3.3% had steroid induced glaucoma and 37.2% had steroid induced cataracts(37). The reason for these differences could be that these studies in India and Singapore included only patients with VKC, which being more severe disease, may require longer and more frequent steroid administration resulting in higher risk for complications. There could also be a genetic factor influencing steroid responsiveness.(46)

Systemic Comorbidities Associated with Allergic Conjunctivitis

In this study, about one third of the patients had systemic comorbidities (fig VIII.) and the most common was allergic rhinitis (fig. IX). All the food allergies were protein allergies. Some of the patients had more than 1 comorbidity (table IV). There was no sexual predilection on any of the comorbidities (table V).

These findings differ slightly from those by Waweru et al in KNH in 1991(33), allergic rhinitis and eczema was higher by 4.6% and 7.7% respectively, while asthma was lower by 3%. These are generally minor differences considering that the population in urban Nairobi has markedly increased along with increase in air pollution and climate change over the 28years duration, all of which are factors contributing to prevalence of allergic conditions(28).The other systemic conditions were not included in the study by Waweru et al.

Some of the systemic comorbidities are only comparable to findings of study in Ghana by Abokyi et al whereby allergic Rhinitis(AR) was found in a fifth of the patients while asthma and eczema were much lower below 3%(24). In Nigeria and Gambia, less than 1%

had any of the systemic comorbidities(19)(20). These show much lower prevalence of these comorbidities in West Africa. There are also differences between the countries despite them being African, within the same geographical region in West Africa with similar climate, diet, socioeconomic status.

Studies done in countries within Europe, Asia and southeast Asia have shown much higher prevalence of these systemic comorbidities in children with allergic conjunctivitis compared to those in Africa(29)(4)(30)(15). Despite these countries being in different latitudes with different climate, some of these differences may be due to genetic susceptibility among the different races, since all the children studied had allergic conjunctivitis as the common factor. This is an area that needs further studies to ascertain the genetic susceptibility to allergic conditions among different races.

Food allergies were present in 7.4% and drug allergies in 2.5% (fig. IX). This was similar to drug allergies found in a study by Kim H.Y et al in Korea in, but differed in food allergies in the same study which was higher in a fifth of children with allergic conjunctivitis. This was the only study found in literature that included food and drug allergies.(15)

The studies above did not include adenoid hypertrophy, which was an incidental finding in the records of 8.3% (fig. IX) of the children, all of whom had allergic rhinitis and had undergone adenoidectomy. Therefore, this may be an indirect systemic comorbidity in allergic conjunctivitis.

The presence of systemic comorbidities was associated with higher grade in severity of allergic conjunctivitis, p-value 0.007(table VI)

Family History of Atopy

Family history of ocular and non- ocular allergy was found in about a tenth of the patients (fig. X, XI). These findings differ from those found in Ethiopia whereby family history of ocular and non-ocular allergy was found in a third of the patients with VKC(47). These also differ markedly from a study by Olusanya et al in Nigeria whereby more than two thirds had family history of atopy. This may have been attributed to the fact that it was a small sample of 28 patients with atopic keratoconjunctivitis and VKC(48). In another study half the patients with VKC had positive family history of atopy(26). The severity of ocular allergy was not affected by positive family history of atopy, p-value 0.352. (table VII). Information on family history of atopy was missing from records of a fifth of patients, which could have resulted in underreporting.

6. STUDY LIMITATIONS

This study was a review of records therefore there may be some incomplete or missing data leading to underreporting. To mitigate this, patient files from other departments and those with different volumes of files were retrieved in an attempt to fill in the gaps.

7. CONCLUSION

1. Ocular comorbidities were found in more than two thirds of the children while only about one third had systemic comorbidities
2. The most common ocular comorbidities were refractive errors and dry eye syndrome. Dry eye syndrome was associated with higher grade of allergic conjunctivitis.
3. The complications of treatment with steroids were very few.
4. The most common systemic comorbidity was allergic rhinitis and there was no sex predominance in any of the comorbidities.
5. Family history of atopy was low and did not influence the severity of allergic conjunctivitis, although this may have been impacted by missing data.

8. RECOMMENDATIONS

- Emphasis should be made on holistic approach on evaluation and management of ocular comorbidities especially refractive errors and dry eye syndrome.
- Regular refraction should be part of evaluation for all children with allergic conjunctivitis and corneal topography done for those with irregular astigmatism, in order to ensure early detection of keratoconus.
- Systemic comorbidities should be evaluated in all patients with allergic conjunctivitis and referred appropriately for multidisciplinary management.

REFERENCES

1. Katelaris C, Pete S. World Allergy Organization - Ocular Allergy [Internet]. Westmead Australia; 2020 [cited 2021 Nov 10]. Available from: © 2021 World Allergy Organization.
2. Bowling B. Kanski's clinical ophthalmology, a systematic approach-8th edition. In: Chapter 5. 2016. p. 144–51.
3. Wing JO. There's More to Ocular Allergy Than Meets the Eye. *Rev Optom* [Internet]. 2005;142(4). Available from: <https://www.reviewofoptometry.com>.
4. Yanqing F, Xiangning W, Fang W, Rongming L, Lu C, Shuqin W, Xia Y, Miaoying C, Yu-Qing R, Jing Li. The Prevalence of Ocular Allergy and Comorbidities in Chinese School Children in Shanghai. *Hindawi, Biomed Res Int* [Internet]. 2017;2017(Article ID 7190987):11 pages. Available from: <https://doi.org/10.1155/2017/7190987>
5. Dartt D, Reza D, D'amore P, Niederkorn J. Immunology, Inflammation and diseases of the eye. In: Dartt DA, editor. 1st ed. San Diego, USA: Elsevier; 2011. p. 114–20.
6. Ono SJ, Abelson MB. Allergic conjunctivitis: Update on pathophysiology and prospects for future treatment. *J Allergy Clin Immunol*. 2005;115(1):118–22.
7. Yangho K, Inbo O, Jiho L, Chang SS, Yeon SO, Ju-Hyang L. Astigmatism Associated with Allergic Conjunctivitis in Urban School Children. *J Ophthalmol* [Internet]. 2019;2019(Article ID 9453872):8 pages. Available from: <https://doi.org/10.1155/2019/9453872>
8. Akil H, Celik F, Ulas F, Iknur SK, Akil H, Celik F, Ulas F, Iknur SK. Dry Eye Syndrome and Allergic Conjunctivitis in the Pediatric Population. *Middle East Afr J Ophthalmol*. 2015;22(4):467–71.
9. Pascale D, Prokopich CL, Alexander H, Harold K. A contemporary look at allergic conjunctivitis. *Allergy, Asthma Clin Immunol* [Internet]. 2020;16(5):1–18.

10. Bawazeer AM, Hodge GW, Lorimer B. Atopy and Keratoconus: a multivariate analysis. *Br J Ophthalmol*. 2000;84(8):834–6.
11. Chin T. GPC: Don't call it an allergic reaction. *Rev Optom [Internet]*. 2006;143(10). Available from: <https://www.reviewofoptometry.com/article/gpc-dont-call-it-an-allergic-reaction>
12. Toda I, Shimazaki J, Tsubota K. Dry Eye with Only Decreased Tear Break-up Time is Sometimes Associated with Allergic Conjunctivitis. *Ophthalmology*. 1995 Feb 1;102(2):302–9.
13. Bore M, Ilako D, Kariuki M, Nzinga JM. Clinical evaluation criteria of ocular allergy by ophthalmologists in Kenya and suggested grading systems. *J Ophthalmol Eastern, Cent South Africa*. 2014;18(1):35–43.
14. Arabkhazaeli A. The association between a genetic risk score for allergy and the risk of developing allergies in childhood. *Paediatric Allergy Immunol*. 2018;29:72–7.
15. Kim H Y, Kwon EB, Baek JH, Shin YH, Yum H, Jee HM, Yoon JW, Han K. Prevalence and comorbidity of allergic diseases in preschool children. *Korean J Paediatr [Internet]*. 2013;56(8):338–42. Available from: <https://doi.org/10.3345/kjp.2013.56.8.338>
16. Tamar M, Tanaka S, Hirota T. Genome-wide association studies of allergic diseases - PubMed. *Allergol Int*. 2013;62(1):21–8.
17. Bonini S, Lambiase A, Sergio B. Genetics of Ocular Allergy. *Acta Ophthalmol*. 1999;77(s228):31–2.
18. Rosario N, Bielory L. Epidemiology of Allergic Conjunctivitis. *Curr Opin Allergy Clin Immunol*. 2011;11(5):471–6.
19. Malu KN. Allergic Conjunctivitis in Jos Nigeria. *Niger Med J*. 2014;55(2):166–70.
20. Wade P, Iwuora A, Lopez L, Muhammad M. Allergic Conjunctivitis at Sheikh Zayed Regional Eye Care Center, Gambia. *J Ophthalmic Vis Res*. 2012;7(1):24–8.
21. Stefan S, Nkurikiye J, Yannick F. Vernal keratoconjunctivitis in School Children in Rwanda and its Association with Socio-economic Status: A population based survey. *Am J Trop Med Hyg*. 2011;85(4):711–7.

22. Abiy MA, Betelhem TY, Sofonias AF, Abiy MA, Betelhem TY SA. Prevalence of vernal keratoconjunctivitis and its associated factors among children in Gambella town, southwest Ethiopia,. PLoS One [Internet]. 2019;14(4):e0215528. Available from: <https://doi.org/10.1371/journal.pone.0215528>
23. Mpairwe H, Nkurunungi G, Tumwesige P. Risk factors associated with rhinitis, allergic conjunctivitis and eczema among school children in Uganda. *Clin Exp Allergy*. 2020;50(10):1111.
24. Abokyi S , Koffuor GA, Ntodie M, Kyei S, Gyanfosu L, Abokyi S , Koffuor GA, Ntodie M, Kyei S, Gyanfosu L. Epidemiological profile and pharmacological management of allergic conjunctivitis: A study in Ghana. *Int J Pharm Biomed Res*. 2012;3(4):195–201.
25. Ministry of Health. Kenya. National Eye Health Strategic Plan 2020-2025 [Internet]. 2020 [cited 2021 Sep 11]. Available from: <https://www.health.go.ke>
26. Bonini S, A. Lambiase, Juhas T, Sergio B. Allergic Conjunctivitis. *Immunology Dev Ophthalmol*. 1999;30:54–61.
27. Bantz SK, Zhu Z, Zheng T. The Atopic March: Progression from Atopic Dermatitis to Allergic Rhinitis and Asthma. *J Clin Cell Immunol*. 2014;5(2):202.
28. Miyazaki D, Kazumi F, Shigeki O, Fukushima A , Eiichi U, Nobuyuki E, Jun- Shoji J , Kenichi N, Yumiko S. Epidemiological aspects of allergic conjunctivitis. *Allergol Int*. 2020;69:487–95.
29. Gradman J, Wolthers OD,. Allergic conjunctivitis in children with asthma, rhinitis and eczema in a secondary outpatient clinic. *Paediatr Allergy Immunol*. 2006;17(7):524–6.
30. Bezerra HD, Capriglione MD, Zorilla JR, Sarmiento JF. Trachoma in Patients with Allergic Conjunctivitis. *Investig Ophthalmol Vis Sci*. 2008;49(13):415.
31. Ahmed S, Ahmed K, Morsy OA, Soliman SS, Ahmed S, Ahmed K, Morsy OA, Soliman SS. Epidemiology of Vernal Keratoconjunctivitis (VKC) among children aged (12–15) years - Menofia Governorate, Egypt. *Delta J Ophthalmol*. 2019;20(1):1–6.
32. Chen L, Pi L, Fang J, Chen X, Ke N, Liu Q. High incidence of dry eye in young children with allergic conjunctivitis in Southwest China. *Acta Ophthalmol*. 2016;94(8):727–30.

33. Waweru F. Vernal Keratoconjunctivitis as seen at Kenyatta National Hospital. University of Nairobi; 1991.
34. Mugho S, Ilako D, Nyenze E. Prevalence of Keratoconus in patients with allergic conjunctivitis, attending Kenyatta National Hospital eye clinic. *J Ophthalmol Eastern, Cent South Africa*, [Internet]. 2020;22(1). Available from: <https://joecsa.coecsa.org/index.php/joecsa/article/view/67>
35. Marcus A, Seng-Ei T, Farzavandi S, Rongli Z. Steroid-induced ocular hypertension in Asian children with severe vernal keratoconjunctivitis. *Clin Ophthalmol*. 2012;6:1253–8.
36. Bonini S, Lambiase A, Marchi S, Pasqualetti P, Zuccaro O, Rama P, Magrini L, Juhas T, Bucci MG. Vernal keratoconjunctivitis revisited: a case series of 195 patients with long-term followup. *Ophthalmology*. 2000;107(6):1157–63.
37. Pradhnya S, Swapnil J, Amit M, Chintan S, Alok S, Elesh J. Pattern of steroid misuse in vernal keratoconjunctivitis resulting in steroid induced glaucoma and visual disability in Indian rural population: An important public health problem in pediatric age group. *Indian J Ophthalmol*. 2019;67(10):1650–5.
38. Al-Akily S, Bamashmus MA, Al-Akily S, Bamashmus MA. Ocular complications of severe vernal keratoconjunctivitis (VKC) in Yemen. *Saudi J Ophthalmol*. 2011;25(3):291–4.
39. Laws of Kenya. Children Act. Kenya: Kenya Law Reports; www.kenyalaw.org; 2010.
40. Brien H, Timothy F, Kovin N, Hasan M, Gerhard S, Sonja C, Phil H, Hannah F, Jerry V, Clare G, Anthea B, David W.,. Strategy for The Elimination of Vision Impairment from Uncorrected Refractive Error. In: IAPB Refractive Error Program Committee [Internet]. Bangladesh: International Centre for Eyecare Education; 2008. Available from: <https://www.iapb.org>
41. Russell J, Courage ML, Drover JR CJ. Refractive error in 2-6year old children: Normative Data Obtained With The Welch Allyn Suresight non-Cycloplegic Autorefractor. *Investig Ophthalmol Vis Sci*. 2011;52(14):2826.
42. Zadnik K, Manny RE, Yu JA, Mitchell GL, Cotter SA, Quiralte JC, Shipp M, Friedman NE, Kleinstein R, Walker TW, Jones LA. Ocular Component Data in Schoolchildren as a Function of Age and Gender. *Optom Vis Sci*. 2003;80(3):226–

- 36.
43. Adolfo A, Dagoberto M, Pflugfelder S, David J, Zhonghua J. Altered cytokine balance in the tear fluid and conjunctiva of patients with Sjögren's syndrome keratoconjunctivitis sicca. *Curr Eye Res.* 2009;19(3):201–11.
 44. Chih-Wei W, Jin-Hong C, David E. Corneal angiogenesis and lymphangiogenesis. In: Leonard A. Levin DMA, editor. *Ocular Disease.* Elsevier; 2010. p. 74–82.
 45. Jain AK, Sukhija J, Chopra I. Keratic precipitates in bilateral vernal corneal ulcer. *Asian J Ophthalmol.* 2006;(8):159–60.
 46. Fini ME, Schwartz SG, Gao X, Jeong S, Patel N, Itakura T, Price MO, Price FW, Varma R, Stamer WD. Steroid-induced ocular hypertension/glaucoma: Focus on pharmacogenomics and implications for precision medicine. *Prog Retin Eye Res.* 2017;56:58–83.
 47. Hayilu D, Legesse K, Lakachew N, Aspheraw M. Prevalence and associated factors of vernal keratoconjunctivitis among children in Gondar city, Northwest Ethiopia. *BMC Ophthalmol* [Internet]. 2016;16(167). Available from: <https://doi.org/10.1186/s12886-016-0345-7>
 48. Olusanya BA, Bekibele CO. Chronic allergic conjunctivitis: an evaluation of the role of family history and atopy. *Ann Ibadan Postgrad Med.* 2006;4(1):37–41.

APPENDIX A: BUDGET

| Item | Quantity | | Total cost (ksh) |
|--|----------------------|-----------------|------------------|
| Proposal/Ethical approval | | | |
| Proposal printing (30 pages) | 3 copies | | 600 |
| Binding of proposal | 3 copies | | 300 |
| Ethics proposal cost | | | 2000 |
| Internet | | | 2400 |
| | | Subtotal | 5300 |
| Collection of data | | | |
| Questionnaire printing | 2 pages | | 20 |
| Photocopying of questionnaires | 2 pages (130 copies) | | 400 |
| Stationery | | | 200 |
| Box file for questionnaires | 5 | | 825 |
| Flash disc (16gb) | 1 | | 1500 |
| | | Subtotal | 2945 |
| Transport | | Subtotal | 1500 |
| Contracted services | | | |
| Statistician | | Subtotal | 30000 |
| Dissemination | | | |
| Printing of final book (Approximately 50 pages) | 3 copies | | 1500 |
| Binding of finished book | 3 copies | | 800 |
| | | Subtotal | 2300 |
| KNH research permission letter | | | 1500 |
| | | Total | 43545 |

APPENDIX B: Questionnaire

CODE.....

Please tick as appropriate

1. Demographics

Age.....

Sex: Male Female

2. Diagnosis

(a)

| | | |
|----------------------------------|--|--|
| Mild allergic conjunctivitis | | |
| Moderate allergic conjunctivitis | | |
| Severe allergic conjunctivitis | | |

(b)Any other ocular condition

Yes No

If yes, proceed to (c).....

(c)Co-morbid ocular pathology

Refractive error

| | |
|-------------|--|
| Myopia | |
| Hyperopia | |
| Astigmatism | |

| | |
|--|--|
| Dry eye syndrome | |
| Shield ulcer | |
| Pannus | |
| Corneal scar | |
| Keratoconus | |
| Herpes simplex keratitis | |
| Bacterial keratitis | |
| Fungal keratitis | |
| Raised intraocular pressure (steroid responder) | |
| Steroid induced glaucoma | |
| Steroid induced Cataract | |

Other, specify.....

d) History of steroid use

Yes

No

d) Any systemic illness associated with allergic conjunctivitis

Yes

No

If yes, proceed to (e)

(e) Please tick as appropriate

| | |
|----------------------------|--|
| Allergic Rhinitis | |
| Atopic dermatitis (eczema) | |
| Asthma | |
| Food allergy | |
| Drug allergy | |

Others, specify.....

Family history of ocular allergy Yes









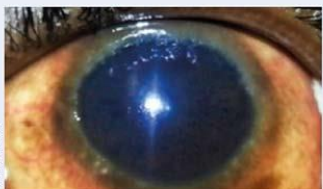

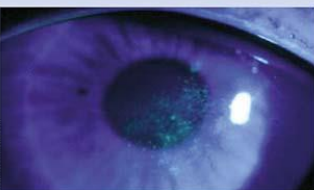

No

Family history of another allergy Yes

No

APPENDIX C: Allergic Conjunctivitis Grading Guide







Table 1. A grading guide based on the Ocular Allergy Clinical Grading Guide developed for use in Kenya. The grading is determined by the most severe sign present in the most severely affected eye

| Grade | Mild | Moderate | Severe |
|--|---|---|--|
| Papillae |  <p>Micro: <0.3mm</p> |  <ul style="list-style-type: none"> • Macro: between 0.3 and 0.5mm • +/- Fibrosis |  <ul style="list-style-type: none"> • Cobblestone papillae: >0.5 mm but smaller than 1.0 mm • Giant papillae: >1.0 mm |
| Conjunctiva |  <p>Hyperemia</p> |  <ul style="list-style-type: none"> • Hyperemia • Diffuse thin chemosis |  <ul style="list-style-type: none"> • Hyperemia • Cyst-like chemosis/scar • Conjunctivalisation of the cornea |
| Limbus (limbal oedema or Horner-Trantas dots) |  <p>No manifestations</p> |  <p><1/2 of limbal circumference affected</p> |  <p>1/2 or more of limbal circumference affected</p> |
| Cornea |  <p>Clear</p> |  <p>Superficial punctate keratitis</p> |  <ul style="list-style-type: none"> • Shield ulcer/epithelial erosion • Keratoconus +/- central leucoma |

Note that patients diagnosed with vernal or atopic keraconjunctivitis should be treated as 'severe' cases, whatever their presenting clinical signs.

APPENDIX D: Ocular Allergy Clinical Grading And Management Guidelines

Ocular Allergy Clinical Grading and Management Guide 2018

| Bore's Grading | Papillae | Conjunctiva | Limbus <small>(Lid margin/Tarsal folds)</small> | Cornea | Treatment | Follow up |
|-----------------|--|--|---|---|---|---|
| Mild |  <ul style="list-style-type: none"> - Micro: <0.3mm |  <ul style="list-style-type: none"> - Hyperaemia |  <ul style="list-style-type: none"> - No manifestation |  <ul style="list-style-type: none"> - Clear | <ol style="list-style-type: none"> 1. Topical antihistamine x 1 month 2. Or Multi-action drug x 1 month | <ol style="list-style-type: none"> 1. PRN* |
| Moderate |  <ul style="list-style-type: none"> - Macro: >0.3 <0.5mm - +/- Fibrosis |  <ul style="list-style-type: none"> - Hyperaemia - Diffuse thin chemosis |  <ul style="list-style-type: none"> - <1/2 of limbal circumference affected |  <ul style="list-style-type: none"> - Superficial punctate keratitis (SPKs) | <ol style="list-style-type: none"> 1. Mild topical steroid QID or <math>x</math> 2 Weeks 2. +/- Steroid ointment nocte x 2-4 Weeks 3. Mast cell stabiliser* / multi- action drug x 4-6 weeks or until stable | <ol style="list-style-type: none"> 2. Review after 4-6 weeks, then PRN* If stable |
| Severe |  <ul style="list-style-type: none"> - Cobblestone papillae: >0.5mm - Giant papillae: >1.0mm |  <ul style="list-style-type: none"> - Hyperaemia - Cyst like chemosis/scar - Conjunctivalisation of the cornea |  <ul style="list-style-type: none"> - 1/2 or > of limbal circumference affected - Keraticosis +/- central leucoma |  <ul style="list-style-type: none"> - Shield ulcer/ Epithelial erosion | <ol style="list-style-type: none"> 1. Pulsed topical steroid regimen (start frequently then taper) +/- Topical cyclosporine 0.5-2% till long remission then stop 2. Topical antihistamine + mast cell stabiliser/multiaction drug for 1 month then mast cell stabiliser for maintenance 3. Steroid ointment (nocte x 2-4 weeks 4. Cobblestone/giant papillae or refractory cases: Supratarsal steroid† (e.g. Triamcinolone) 5. Shield ulcer +/- Corneal Scraping/ superficial keratectomy + Topical steroid antibiotic + I - Mydriatic | <ol style="list-style-type: none"> 1. Review after 1-2 weeks then monthly while on steroids 2. Taper Steroids (check IOP) 3. Stagger reviews to 3 monthly once patient is stable |



NOTES

- Current UK guidance recommends avoidance of long-term use of topical steroids and use of preservative free artificial tears and oral antihistamines.
- Preserving the epithelial layer. Duration of steroids and tapering time should usually be 4-6 weeks.
- Timing of steroid taper: start taper 1 week commencing previous steroid maximum.
- Oral steroid guidelines and their practice to when steroid therapy commences depends on clinical and/or patients and should depend on clinical judgement.
- All patients with features of MCHC (High Prostaglandin, Elevated IOP, Severe keratitis) should benefit from steroid therapy. Steroid therapy should be avoided.
- Oral steroid instructions: start lowest oral steroid with the lowest possible dose.
- History of frequent changes in eye glasses when in use (especially contact lens) should be avoided.
- Long acting steroids may / sometimes 4-6 weeks.
- Make all patients who have steroid treatment aware of the risks and monitoring requirements.



- Examples:**
1. Excessive steroid use
 2. Overuse, excessive hyperaemia, chemosis, hyperaemia, swollen tarsus
 3. Hyperaemia
 4. Contact lens wear
 5. Avoid repeated use of the application to children aged less than 16 years (use of essential OTC PRN). Advised to come back when symptoms recur

This report guide is a production of the Ocular Allergy Services Unit, Ministry of Health. For everyday use in management of Ocular Allergy. No acknowledgment of experts and especially Technical Support from Dr H. Ebn. Dr H. Khatib and Prof. D. Ebn. All from the University of Marouf.

APPENDIX E: UoN Anterior Segment Assessment Tool – For Patients’ file

Patients Name: _____ **Sex:** _____

Date of Birth: _____ **Age:** _____ **OP/IP Number:** _____

Date: _____ **Contact:** _____

Chief Complaints:

History of Presenting Complaints:

Past Ophthalmic History:

Systemic Diseases: DM/HT/Asthma/Eczema/Arthritis/etc

Allergy to Drugs:

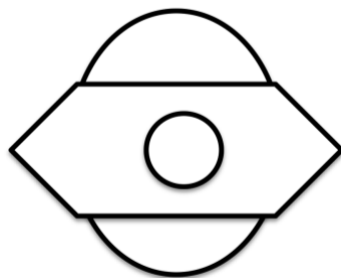
Family History: Glaucoma/RD/etc

| | Right Eye | Left Eye |
|--------------------------------|------------------|-----------------|
| VA Unaided: | | |
| VA with PH: | | |
| NV Unaided | | |
| VA with Own Correction: | | |

| | | |
|-------------------------------------|--|--|
| NV with Own Correction | | |
| Presenting Correction Power: | | |
| Auto Refraction: | | |
| Auto Keratometry: | | |
| Subjective Refraction: | | |
| VA with Refraction: | | |
| Duochrome: | | |
| IOP: | | |

| | Right Eye | Left Eye |
|------------------------------|------------------|-----------------|
| EOMM: | | |
| Orbit / Eye Lids: | | |

Conjunctiva:



Tear Film:

Cornea:



| | | |
|--------------|--|--|
| A/C: | | |
| Iris: | | |

| | | |
|---------------|--|--|
| Pupil: | | |
|---------------|--|--|

Lens:



| | | |
|--------------------------|--|--|
| Zonules: | | |
| Vitreous: | | |
| Fundus: | | |
| Impression: | | |
| Investigations: | | |
| Biometry: | | |
| Topography | | |
| Photograph | | |
| Others: BS/BP/etc | | |

Treatment/Plan:

-
-

Doctor's Name & Signature:

Name & Signature

APPENDIX F. Ethical Approval Certificate



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30th September, 2021

Dr. Emma Mukuku Nzioka
Reg. No. H58/8218/2017
Dept. of Ophthalmology
School of Medicine
College of Health Sciences
University of Nairobi



Dear Dr. Nzioka

RESEARCH PROPOSAL: PREVALENCE AND PATTERN OF COMORBIDITIES IN CHILDREN WITH ALLERGIC CONJUNCTIVITIS AT KENYATTA NATIONAL HOSPITAL, EYE CLINIC (P541/07/2021)

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH-UoN ERC) has reviewed and approved your above research proposal. The approval period is 30th September 2021 – 29th September 2022.

This approval is subject to compliance with the following requirements:

- i. Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
- ii. All changes (amendments, deviations, violations etc.) are submitted for review and approval by KNH-UoN ERC before implementation.
- iii. Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
- iv. Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
- v. Clearance for export of biological specimens must be obtained from KNH- UoNERC for each batch of shipment.
- vi. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (Attach a comprehensive progress report to support the renewal).
- vii. Submission of an executive summary report within 90 days upon completion of the study.

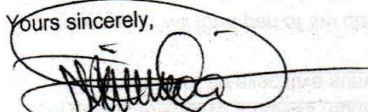
This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

Code: 1126915

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For more details consult the KNH- UoN ERC website <http://www.erc.uonbi.ac.ke>

Yours sincerely,



PROF. M.L CHINDIA
SECRETARY, KNH- UoN ERC

- c.c. The Principal, College of Health Sciences, UoN
The Senior Director, CS, KNH
The Chair, KNH- UoN ERC
The Assistant Director, Health Information, KNH
The Dean, School of Medicine, UoN
The Chair, Dept. of Ophthalmology, UoN
Supervisors: Dr. Stephen Gichuhi, Dept. of Ophthalmology, UoN
Dr. Lucy Njambi, Dept. of Ophthalmology, UoN

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