THE PREVALENCE, SPECTRUM AND RISK FACTORS ASSOCIATED WITH OCULAR DISEASES IN CHILDREN AND YOUTH WITH TYPE 1 DIABETES SEEN AT THE PAEDIATRIC ENDOCRINOLOGY CLINIC INKENYATTA NATIONAL HOSPITAL FROM 2008-2021 (A RETROSPECTIVE CROSS-SECTIONAL STUDY)

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DECLARATION

This dissertation is my original work and has not been presented for the award of a degree in any other university.

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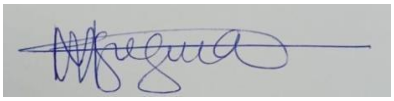
Signature:  **Date:**5th May 2023

COLLABORATING INSTITUTIONS

1. University of Nairobi
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ABBREVIATIONS

DM- Diabetes Mellitus

T1DM- Type 1 Diabetes mellitus

HIF-1- Hypoxia Inducible Factor 1

NPDR- Non-Proliferative Diabetic Retinopathy

PDR-Proliferative Diabetic Retinopathy

BMI- Body mass index

IL-6- Interleukin 6

AIC- Akaike Information Criterion

OR- Odds ratio

CI- Confidence Interval

ABSTRACT

Introduction: The most prevalent endocrine condition among young people around the world is type 1 diabetes mellitus. Chronic and acute complications of poorly controlled diabetes include diabetic ketoacidosis, hypoglycemia, cardiovascular and renal complications, neuropathy, and ocular complications. Diabetes-related retinopathy, macular oedema, cataracts, and glaucoma are examples of ocular complications. The main causes of vision loss in children and adolescents with T1DM are proliferative diabetic retinopathy and diabetic macular oedema.

To identify and treat any potential ocular complications, the Kenya Ministry of Health advises routine screening for diabetic retinopathy in children with diabetes. Within five years of T1DM diagnosis and then annually after that, children with T1DM should have their eyes examined by an ophthalmologist or optometrist.

Objectives: On the spectrum and risk factors of ocular problems in children and youth with T1DM in Kenya, there are no locally available data published.

Methodology: This was a retrospective cross-sectional study of children and youth with T1DM who were seen in the Paediatric Endocrinology clinic between 2008 and 2021. Demographic and clinical data were extracted from patient records and transcribed onto a data collection tool for statistical analysis.

Data analysis: This was done with R version 4.2.2 statistical analysis software. Categorical variables were summarized using proportions and percentages, continuous variables were summarized using means to make inferences and draw conclusions.

Results: The prevalence of all ocular complications among children and youth with T1DM was 12.5%. The most common complication identified was diabetic retinopathy with a prevalence of 5.7%, glaucoma and cataracts had a prevalence of 2.8% while optic atrophy had a prevalence of 1.9%. The risk of developing ocular complications increased with an increase in the duration of T1DM.

Conclusion: The prevalence of ocular disease in T1DM children and youth was comparable to those found elsewhere. Diabetic retinopathy was the most prevalent complication in the study population. Duration of T1DM was a risk factor for the development of ocular complications.

CHAPTER 1: INTRODUCTION

Type 1 diabetes mellitus, which results in insulin insufficiency, is brought on by the autoimmune destruction of the pancreatic beta cells that make insulin. Hyperglycemia occurs from a lack of insulin, which is necessary for glucose to enter cells.

A plasma glucose concentration of 11.1 mmol/l or higher or fasting plasma glucose of 7 mmol/l or higher is required for the diagnosis of type 1 diabetes mellitus. Other diagnostic criteria include the presence of the characteristic signs of diabetes (polydipsia, polyuria, weight loss, or hyperglycemic crises). (1)

The most frequent endocrine disorder in young people worldwide is diabetes mellitus type 1. The global burden of diabetes is increasing with an estimated 1.2 million children and adolescents diagnosed with Type 1 diabetes worldwide, and an estimated 5300 children living with T1DM in Kenya in the year 2021. (2) An estimated 96,000 children develop diabetes annually worldwide. (2)

Untreated type 1 diabetes mellitus could result in both acute and/or chronic complications. Acute complications present as life-threatening diabetic ketoacidosis, and chronic complications involve the cardiovascular system, the kidney, nerves, and the eye.

Patients and their families, health systems, and national economies are all impacted by type 1 DM and its complications, which result in high treatment expenses and missed work or school days. (3) A national health survey carried out in South Africa in 2011-2012 listed diabetes as one of the major risk factors for vision loss in the area. (3) Type 1 DM and its complications impact patients and their families, health systems and national economies through heavy costs of treatment and loss of work or school days. (3) A national health survey carried out in South Africa in 2011-2012 listed diabetes as one of the major risk factors for vision loss in the area.

Screening for ocular pathology in children with T1DM is recommended within 5 years of diagnosis of diabetes or upon attaining puberty, whichever comes first (American Diabetes Association). (4) The main causes of visual loss in diabetics are macula oedema and proliferative diabetic retinopathy. (5)

Signs and symptoms of ocular diseases in diabetes include; spots floating across the patient's vision, blurry vision, dark or empty patches in the centre of vision, trouble seeing at night and blindness. (6)

Diabetic Retinopathy

Of the ocular complications caused by diabetes mellitus type 1, retinopathy is the most severe. It carries with it a risk of blindness. (6) Prevention of diabetic retinopathy requires strict control of blood glucose and overall good management of the condition. Risk factors for developing retinopathy in T1DM include hyperglycaemia, diabetes duration, obesity, puberty, high blood pressure, hyperlipidemia and genetic predisposition. (7)

Diabetic retinopathy is classified into two:

- Non- proliferative diabetic retinopathy
- Proliferative diabetic retinopathy.

Non-proliferative diabetic retinopathy(NPDR) is classified into mild, moderate and severe. In mild NPDR, only microaneurysms are present in the retina. In moderate NPDR there are both microaneurysms and intraretinal haemorrhages, but less severe than in the severe non-proliferative type. In severe non-proliferative diabetic retinopathy, in addition to microaneurysms, the retinal haemorrhages are more than 20 in each retinal quadrant and there is venous beading in at least 2 retinal quadrants and prominent microvascular abnormalities within the retina in at least 1 quadrant, but no signs of proliferative retinopathy. (8) The signs of proliferative retinopathy are neovascularization and/ or vitreous or pre-retinal haemorrhages. (8) Proliferative retinopathy can cause blindness through recurrent haemorrhage from the new vessels that have formed, through retinal detachment that can complicate neovascularization or through glaucoma that can occur due to neovascularization. (9)

The pathophysiology of diabetic retinopathy involves multiple metabolic pathways. Hyperglycaemia causes dilation of retinal blood vessels and an increase in blood flow via autoregulatory mechanisms to increase glucose metabolism in the eye. Hyperglycaemia causes the death of pericytes, the cells that support retinal capillary walls, resulting in an outpouching of the capillary walls and microaneurysm formation. Hyperglycaemia also causes apoptosis of the retinal capillary endothelial cells and thickening of the basement membrane which are also changes

in diabetic retinopathy. Death of pericytes and endothelial cells causes occlusion of retinal capillaries and results in retinal hypoxia and ischaemia. Retinal hypoxia causes the release of HIF-1(Hypoxia-inducible factor 1) which causes increased levels of vascular endothelial growth factor (VEGF), causing vessel proliferation in diabetic retinopathy, and increasing vessel permeability. Diabetic patients also have raised levels of phospholipase A2, an enzyme that triggers the upregulation of VEGF. VEGF results in the development of proliferative diabetic retinopathy (PDR) and also macula oedema. (9) In T1DM there is chronic low-grade inflammation causing increased adhesion of leucocytes to vessel walls and leukostasis, mediated via chemokines and cell adhesion molecules, this contributes to vessel occlusion that occurs in diabetic retinopathy. Raised serum interleukin 6 (IL-6) levels have been demonstrated in the vitreous humor of patients with T1DM. (9) Hyperglycaemia also causes retinal neurodegeneration in diabetic retinopathy. (9)

In a retrospective consecutive cohort study carried out in children under 18 years both with type 1 and 2 diabetes mellitus at the Children's Hospital of Philadelphia and the Scheie eye institute whose objective was to study the prevalence and onset of ocular complications in diabetes, the authors found no association between duration and control of diabetes and diabetic ocular complications. They recommended screening for retinopathy to commence at the age of 15 years, or after 5 years of diagnosis of diabetes, whichever comes first, or screening if the paediatric endocrinologist judges the child as high risk. (10) These findings are challenged by a different study done by MohdIlam et al, published in the Korean Journal of Ophthalmology in 2021 that showed that macula thinning was observed in children, who had no retinopathy. (11)

Furthermore, a study done by Sasha Strul et al in 2020 on paediatric retinopathy telescreening in children with diabetes found that screening using fundus photography picked out more cases of retinopathy than the standard wide-field fundoscopy. (9) This suggests that the mode of screening for retinopathy determines the prevalence of retinopathy.

Diabetic retinopathy screening can be effectively done through retinal photography. (12)

Treatment modalities for diabetic retinopathy include antiangiogenic drugs that counter the action of VEGF and anti-inflammatory medication to counter the effect of chronic inflammation which includes intravitreal steroid injections, anti-IL-6 antibodies, and IL-6 receptor antibodies (tocilizumab), laser photocoagulation among other modalities which are underway. (9)

Diabetic cataracts

Cataracts are a major cause of blindness in patients with diabetes in 3rd world countries, as well as in developed countries. (10) Cataracts are a major cause of blindness in children in Sub-Saharan Africa. (11)

The prevalence of cataracts in children of African descent and Haitians is increased according to a study done by Robinson et al which showed a prevalence of 16% of children examined. (13) A study done by Marco Simunovic et al showed that initial screening upon diagnosis of type 1 DM and continued follow-up with regular eye examination as a measure of prevention of cataracts is required in the paediatric population. They also found that long-term control of blood sugar and insulin therapy reduced the prevalence of early diabetic cataracts in children and adolescents. (12) Diabetic cataracts form in the lens of patients with diabetes via a pathway called the polyol pathway. In the eye, the enzyme aldol reductase reduces glucose to sorbitol. Sorbitol is osmotically active and results in the formation of hydropic lens fibres leading to the formation of sugar cataracts if sorbitol is not eliminated in time. Sorbitol diffuses slowly and hence is poorly eliminated once generated. The elimination is via the enzyme sorbitol dehydrogenase. In patients with T1DM with poorly controlled diabetes, more sorbitol is produced due to hyperglycaemia than can effectively be removed by sorbitol dehydrogenase, predisposing them to cataract formation. (10)

Treatment of diabetic cataracts is by surgery (phacoemulsification), however, cataract surgery in patients with diabetes has poorer outcomes than in individuals without diabetes. (10)

Diabetic macula oedema

Diabetic macula oedema is characterized by the accumulation of exudate in the macula. It occurs due to the elevation of vascular endothelial growth factor (VEGF), and its levels are increased in the eyes of individuals with T1DM. VEGF causes a breakdown in the blood-retinal barrier by affecting endothelial junctional proteins. This results in the extravasation of fluid from the capillaries and into the macula. (14)

Poor glycaemic and blood pressure control are associated with macula oedema. It is diagnosed via optical coherence tomography. Treatment involves focal or grid laser photocoagulation, but the standard of care is intraocular anti-VEGF agents.

Diabetic glaucoma

Diabetic glaucoma is a disease of the eye caused by raised intraocular pressure resulting in retinal ganglion cell damage and subsequent optic nerve damage. It is progressive and results in irreversible blindness. In patients with diabetes, the most common type of glaucoma is the primary open-angle glaucoma, in which the angle of the anterior chamber remains open. It develops due to hyperglycaemia-induced damage to the microvasculature of the eye, and nutritional deprivation to retinal ganglion cells due to interference of blood supply in the region of the head of the optic nerve. The death of retinal ganglion cells induces glaucomatous changes. (15)

The presence of type 1 diabetes mellitus together with raised fasting glucose levels results in raised intraocular pressures. Glaucoma is defined as central visual acuity of less than 3/60 after correction, or a visual field of fewer than ten degrees in the better-seeing eye. (16)

Diagnosis of glaucoma requires two or more of the following;

- Elevated intraocular pressure
- Optic nerve damage
- Enlarged cornea
- Descemet's membrane raptures
- Enlarged eye

Treatment involves surgery to control intraocular pressure, lifelong monitoring, and treatment to prevent amblyopia. (17)

CHAPTER 2: LITERATURE REVIEW

To prevent ocular complications and preserve visual health in children and young people with T1DM, strict glycemic control needs to be upheld and managing comorbid conditions such as hypertension. A retrospective chart review was conducted in an ophthalmologic referral centre in the USA by Mark Porter et al and published in the Journal of paediatric diabetes in 2020 that aimed at evaluating the diabetic retinopathy prevalence and determining the risk factors among youth with diabetes found a prevalence of 3.8%. Patients with HbA1c of more than 8% were more at risk of developing diabetic retinopathy. The presence of hypertension had a positive correlation with retinopathy occurrence. (18) A study conducted by Marco Simunovic et al in Croatia in 2017 on cataracts as an early manifestation in young patients with T1DM found that the prevalence of early diabetic cataracts in T1DM patients aged less than 18 years with type 1 diabetes varied between 0.7 and 3.4% and that its occurrence in most paediatric patients is the first manifestation of T1DM and it can occur within 6 months of diagnosis of T1DM. In this study, a patient as young as 5 years old had cataracts, but most were adolescents. The study also demonstrates 2 cases of reversible cataracts with good glycemic control. This study highlights the importance of aggressive screening for ocular complications in children and young people with T1DM and the need for strict glycemic control. (12)

An observational cross-sectional study carried out in India in 2016 by Handan Akil et al that compared intraocular pressures of T1DM patients against healthy age and sex-matched controls revealed that the type 1 DM group exhibited raised intraocular pressure and reduced retinal thickness compared to their age-matched controls, thus T1DM children and young people are at risk of developing glaucoma. (19)

A retrospective consecutive cohort study carried out in children with T1DM aged less than 18 years over a 4-year period in Philadelphia USA that aimed to study the prevalence and onset of ocular complications in children with T1DM and the risk factors for ocular disease found that diabetic retinopathy was a rare finding in children regardless of duration and control of diabetes. (10) These findings have been contradicted by a cross-sectional retrospective study carried out in Haiti in 2016 by Marie E. Robinson et al that found a high prevalence of diabetic retinopathy among children and adolescents with T1DM at 18% and cataracts at a prevalence of 16%.

A cross-sectional hospital-based study carried out in China by Tao Li et al and published in 2019 in which the eyes of children both with type 1 diabetes and those without found that microvascular abnormalities of the retina occurred in T1DM patients who neither had diabetic retinopathy nor visual impairment. (20)

A cross-sectional hospital-based descriptive study carried out in Ethiopia in 2016 by Mulugeta et al to study the prevalence of diabetic retinopathy in children and adolescents with T1DM found that it was difficult to establish good glycaemic control in the study subjects and 4.7% had diabetic retinopathy, the mean age of these children was 14.25%. The prevalence of maculopathy was 2.3%. (21)

In the year 2013, Marion Muhia conducted a study at Kenyatta National Hospital and published in the University of Nairobi repository on glycaemic control and its association with diabetic retinopathy, out of the 80 children who participated in the study whose mean age was 11.3 years and average duration of T1DM was 2.9 years and none of the examined children had diabetic retinopathy despite 25% of them having been admitted within 3 months of the study with hyperglycaemia, indicating poor control. This study however had few subjects, and the study period was 3 months. (22)

In a cross-sectional clinic-based study of 100 patients with T1DM patients aged 10-18 years carried out in Sudan by Hana Ahmed et al and published in 2020, the frequency of diabetic retinopathy was 33%. Individuals with T1DM with retinopathy were found to have higher HbA1c levels and longer diabetes duration than patients without diabetic retinopathy. The patient's age, ethnicity, the length they had suffered type 1 diabetes, and the presence of nephropathy were all independent risk factors for the development of retinopathy. (23)

A retrospective chart review was conducted of children and young people less than 21 years old with type 1 diabetes to identify factors associated with diabetic retinopathy and diabetic macula oedema and found that both diabetic retinopathy and macula oedema were associated with modifiable risk factors which were HbA1c levels, BMI and blood pressure. (24)

A cross-sectional study carried out in a hospital in Bangladesh by Zabeen et al over 1 year between October 2016 to October 2012 that included children, adolescents and young adults who had T1DM for over 2 years set to examine the prevalence of retinopathy and its risk factors found a

6.6% prevalence in these patients. Higher age, longer T1DM duration and elevated HbA1c had a positive correlation with retinopathy. (25)

A systematic review of studies carried out in Australia published in the year 2016 in the Journal of Clinical and Experimental Ophthalmology whose aim was to study the risk factors associated with the progression of retinopathy during pregnancy among pregnant T1DM patients established that pregnancy as an independent risk factor for worsening of retinopathy. The authors also concluded that poor glycaemic control and hypertension had a positive correlation with retinopathy in pregnant patients with T1DM. (26)

Based on these studies, risk factors for developing ocular disease in children and young adults with T1DM include higher BMI, higher systolic blood pressure, longer duration of diabetes mellitus and poorer glycaemic control. The prevalence of ocular disease varies with some studies finding very low/ non-existent prevalence and some studies finding a prevalence of up to 33%.

Table 1: Literature review summary

Reference	Study Design	Study aim	Findings	Recommendations	Limitations
Cataract as Early Ocular Complication in Children and Adolescents with Type 1 Diabetes Mellitus- Marko Simunovic, Martina Paradzik et al- 2018, International Journal of Endocrinology. (12)	Review of publications	To review research on diabetic cataracts, one of the earliest visual side effects of T1DM diagnosed in children, and stress the value of early detection	Prevalence of early diabetic cataracts depending on the authors varied between 0.7% and 3.4% The youngest cataract patients described were 5 years old, while the majority were adolescents. One author reported equal incidence among the sexes, the rest reported a higher incidence in females. Significant variability was demonstrated in HbA1C levels at the time of onset of cataracts. Multiple morphologies of early diabetic cataracts were reported- posterior subcapsular, lamellar,	Recognition of T1DM early signs like polyuria, polydipsia, polyphagia, and weight loss can help to prevent cataract development in T1DM by lowering the lens' exposure to hyperglycemia. Initial screening for cataracts in T1DM, and continuous surveillance to prevent cataracts as it is the leading cause of blindness in T1DM. Inclusion of cataract screening in guidelines of major paediatric diabetic societies.	The majority of studies were conducted in industrialized nations and it was impossible to completely rule out the impact of numerous environmental factors and patient socioeconomic level on the prevalence of cataracts in T1DM. Lack of guidelines on screening of cataracts in the paediatric population.

			cortical, snowflake, and milky white, with posterior subcapsular being the most common type in childhood. Demonstration of 2 cases of reversible cataracts with good glycaemic control. The occurrence of cataracts in most patients occurred within 6 months of diagnosis.		
Ocular manifestations of Type 1 diabetes mellitus in pediatric population- Handan Akil, Ayse Derya, Nesibe Andiran, Mehmet Numan Alp, 2016, Indian Journal of Ophthalmology. (19)	Observational cross-sectional study	To study the ocular findings of T1DM in relation to the HbA1C level and the length of diabetes and compare the ocular findings to those of healthy children who do not have diabetes.	Compared to the age-matched control group, the Type 1 DM group showed significantly reduced tear production on the Schirmer test, higher IOP, and decreased retinal thickness.	Additional research should be conducted using bigger sample sizes and incorporating more DM-related parameters. Increased screening to detect diabetic ocular problems early	Small sample size. In a cross-sectional study therefore difficult to determine the effects of time on measurements. Selection bias could have affected the results.
Retinal Microvascular Abnormalities in Children with Type 1 Diabetes Mellitus Without Visual Impairment or Diabetic Retinopathy- Tao Li, Yan Jia, Shansan Wang, Anken Wang, Lu Gao, Chenhao Yang, Haidong Zou- Journal of Investigative Ophthalmology and visual science 2019. (20)	Case-control hospital-based study including children with or without DM	To study the characteristics and associated factors of retinal microvascular abnormalities of children with T1DM who do not have visual impairment and diabetic retinopathy.	Retinal microvascular complications had already occurred in the parafoveal area of children with T1DM without visual impairment or diabetic retinopathy. Serum creatinine level(p=0.009) and mother's excessive weight gain during pregnancy (p =0.004) were independent risk factors	Recommended early screening and close follow-up of children with high-risk factors.	A small number of individuals were included in a single-centre study that was based on a single population (the Chinese Han population). The study excluded data on deep retinal capillaries as the software employed couldn't examine those, and studies in adults revealed deep retinal capillary changes occurring earlier than the superficial capillary changes.
Ocular complications in children with diabetes mellitus-Megan M. Galoneck, Brian J. Forbes, James Shaffer, Guishuang Ying, Gil Binenbaum- Pubmed 2016. (6)	A retrospective consecutive cohort study	To identify risk factors for ocular disease, the prevalence and timing of ocular	Diabetic retinopathy- 0 children. Cataract- 12 children	Screening could begin later based upon the study, then the recommended 5 years after T1DM diagnosis by ADA, and 3-	Lack of inclusion of fluorescein angiographic analysis to identify occult

		pathology in children with diabetes mellitus, and to recommend a screening schedule for asymptomatic children.	Strabismus- 19 High refractive error- 42 children There was no correlation between these factors and the length of DM control. Regardless of the severity and control of T1DM, children rarely developed diabetic retinopathy.	5 years after diagnosis of T1DM by AAP. Collaborative consensus groups should consider revising their screening guidelines.	DR- not routinely done in children. Lack of performance of ocular colour fundus photography to screen for DR, which is more sensitive than ophthalmoscopy to screen for mild DR. The limited ethnic and racial profile of the study cohort.
Pediatric diabetic retinopathy: experience of a tertiary hospital in Ethiopia-Mulugeta Sitot Shibeshi, Bereket Fantahun, Tedla Kebede, birkneh Tilahun- BMC journal 2016. (21)	A cross-sectional hospital-based descriptive study of children between 9-17 years attending the follow-up clinic of Tikur Specialised Hospital.	To study the prevalence of diabetic retinopathy	With a mean age of 14.25 years (S.D. 1.89), 2 of the 4 children (4.7%) who had retinopathy at the time of T1DM onset also had maculopathy.	Systematic screening for all microvascular complications of diabetes. Improvement of quality of care of children with T1DM in Ethiopia. Follow-up of children with diabetes, for complications, with standard guidelines like IPSAD 2014. Prospective follow-up of children with retinopathy to evaluate the progression of retinopathy. More research is needed to evaluate the prevalence and contributing factors of developing diabetic retinopathy in Ethiopia as well as the level of glycemic control and its contributing factors.	Inability to assess the study subjects' long-term glycemic control. Due to a lengthy waiting list, patients with maculopathy were unable to see an ophthalmologist for an evaluation, hence the cause of their decreased visual acuity was unknown. The study could not be taken into account as typical of Ethiopia's pediatric diabetic community.
Prevalence of diabetic retinopathy in children and adolescents at an urban tertiary eye care centre-	Retrospective chart review	To assess the incidence of diabetic retinopathy in young people with diabetes at a	3.4% of type 1 DM patients had diabetic retinopathy (9 had mild DR, 3 had severe DR and 1 had proliferative DR).		

Mark Porter, Roomasa Channa, Jessica Wagner, Laura Prichett, Tin Yan, Alvin Liu, Risa M. Wolf 2020, (International Society for Paediatric and adolescent diabetes. (18)		significant ophthalmologic referral center.	Patients with HbA1c > 8% were more likely to experience DR (P =.049). In this group, there were no individuals with DR who had an HbA1c below 8%. Higher systolic blood pressure had a marginal association with risk for DR in the multivariate analysis (P =.07).		
Pediatric Diabetic Retinopathy: Updates in Prevalence, Risk Factors, Screening, and Management- Lin Tyger et Al. (27)		To highlight risk factors, offer an update on the prevalence of diabetic retinopathy in young people, and evaluate current developments in diabetic retinopathy screening	Several risk factors for diabetic retinopathy were identified, including glycemic control, T1DM duration, hypertension, and hyperlipidemia.		

2.1 STUDY JUSTIFICATION

There has been a rise in T1DM cases among children and youth globally. Diabetes mellitus is a lifelong condition and is associated with chronic complications such as diabetic retinopathy. These complications are preventable with early diagnosis and appropriate management. Diabetes is a lifelong condition, and the burden of diabetic ocular complications needs to be known to help curb the associated factors, however, the prevalence, spectrum, and risk factors of diabetic ocular complications among children and youth in our set-up remain largely undocumented.

Data generated from this study would serve to highlight the prevalence of these complications and related risk factors. This would contribute to the formulation of policies on early diagnosis and appropriate management and enhance risk reduction strategies.

CONCEPTUAL FRAMEWORK

The conceptual framework around ocular complications in diabetes is outlined in the diagram below.

This framework puts into perspective the various factors and variables that may influence the prevalence, spectrum and risk factors of diabetic ocular complications.

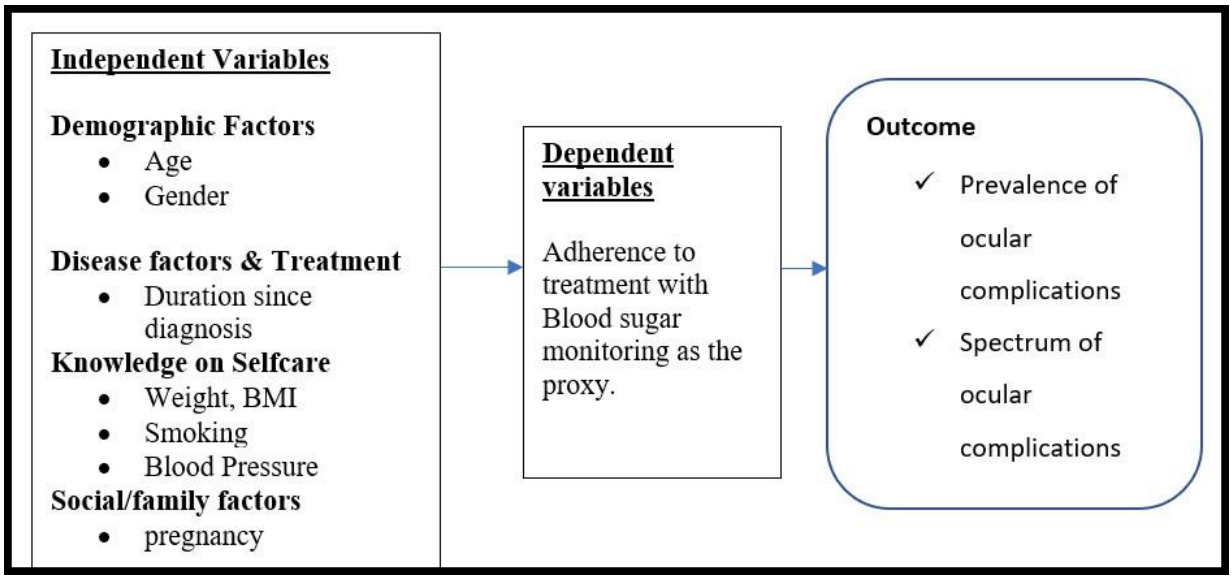

Figure 1: Conceptual framework

The independent variables for this study are the induvial level factors as listed in the schema above.

Literature postulates that diabetic complications including ocular complications are a function of adherence to treatment and other control measures. In this study, we used the level of glycaemic control (through HBA1c) as the proxy measure for treatment adherence.

These are taken as the dependent variables. Finally, the outcomes of interest are the prevalence and spectrum of ocular complications.

2.2 STUDY QUESTION

What are the prevalence, spectrum and risk factors associated with ocular complications in children and youth with type 1 diabetes mellitus at the paediatric endocrinology clinic in Kenyatta national hospital?

STUDY OBJECTIVES

Primary Objective

To determine the prevalence and spectrum of ocular disease in children and youth with T1DM seen at the paediatric endocrinology clinic, Kenyatta National Hospital from 2008 to 2021.

Secondary objective

To determine the risk factors associated with ocular disease in children and youth with T1DM seen at the paediatric endocrinology clinic, Kenyatta National Hospital from 2008 to 2021.

CHAPTER 3: METHODOLOGY

3.1 STUDY DESIGN

The study was a hospital-based retrospective cross-sectional study. This study design was chosen because it was feasible, conducting a prospective study of this kind would require follow-up of the study population over a longer duration. Obtaining records from the KNH registry was cost-effective since the records were available. The design enabled us to study the participants over a 10-year duration.

3.2 *STUDY LOCATION*

This was a hospital-based study that was conducted at Kenyatta National Hospital (KNH) health records department and diabetic eye clinic.

KNH is an 1800-bed capacity facility situated in Nairobi County. It serves as both the University of Nairobi College of Health Sciences' teaching hospital and a public tertiary referral centre. The biggest hospital in both the nation and East Africa. The hospital has various specialist clinics including Paediatric Endocrinology and Opthalmology clinics. The ophthalmology clinic is run by specialists, subspecialists and resident doctors.

The paediatric endocrinology clinic is run by Subspecialists (Paediatric Endocrinologists), Specialists (Paediatricians) and resident doctors in Paediatrics. The clinic sees T1DM children and youth up to 25-year-olds who are then transferred to the adult endocrinology clinic after their 25th birthday. The catchment population is about 1,050 in number. The clinic runs on Tuesdays from 8 am to 2 pm. Children and youth with T1DM are reviewed and sent for lab investigations and treatment is case-based. They are then sent to the ophthalmology clinic for an eye examination if they meet the screening criteria. Paediatric Endocrinology clinic patient records are kept at the hospital's central registry.

The ophthalmology department has a special room designated for the ocular examination of patients with diabetes. Here the patients have their retinal photographs taken by an optometrist

and sent to the consultant ophthalmologists for interpretation. The eye clinic has a records department where patient data is kept and this department is part of the hospital's central registry.

3.3 *STUDY POPULATION*

Children and young adults with T1DM who underwent an eye examination between January 1, 2008, and December 31, 2021, at the paediatric endocrinology clinic at Kenyatta National Hospital comprised the study population.

3.4 *SAMPLE SIZE*

The study was a whole population census study of records from January 2008 when the endocrinology clinic was started to December 2021.

Our sample size of 104 study participants was sensitive enough to pick the occurrence of common ocular complications of T1DM, as depicted in the table below:

Table 2: Apriori Sensitivity analysis of Power based on different possible sample sizes

Sample Size	Effect size (Cohen's D)	Interpretation
25	0.75	Can only pick a large effect size
50	0.40	Can only pick a large or medium size
100	**0.28**	**Can only pick a large or medium size**
150	0.23	Can only pick a large or medium size
200	0.20	Can pick any effect size- large, medium or small
300	0.16	Can pick any effect size- large, medium or small
400	0.14	Can pick any effect size- large, medium or small
500	0.13	Can pick any effect size- large, medium or small
750	0.10	Can pick any effect size- large, medium or small
1000	0.09	Can pick any effect size- large, medium or small

3.5 *STUDY PERIOD*

The study period was from January 2008 to December 2021. Data collection occurred in 2022 and 2023.

3.6 *STUDY PROCEDURES*

The study procedure involved the identification of all type 1 diabetes mellitus patients aged between 6 months and 25 years seen at the paediatric endocrinology clinic at Kenyatta National Hospital between 1st January 2008 and 31st December 2021. This was done at the central registry by filtering the files by diagnostic codes and by age. The files were then examined to confirm the right diagnosis of T1DM. Identification of the patients who had eye exams was done from the files. Data on the eye examinations of these patients were obtained from the ophthalmology department and entered into the data collection tool. Demographic and clinical characteristics of these patients were collected using the data collection tool. The hospital number for each study participant was anonymized to identifiers for the final dataset to be used for analysis. This ensured confidentiality and protected the privacy of the study participants. Data were analyzed after compilation and conclusions were drawn.

Study procedure flowchart:

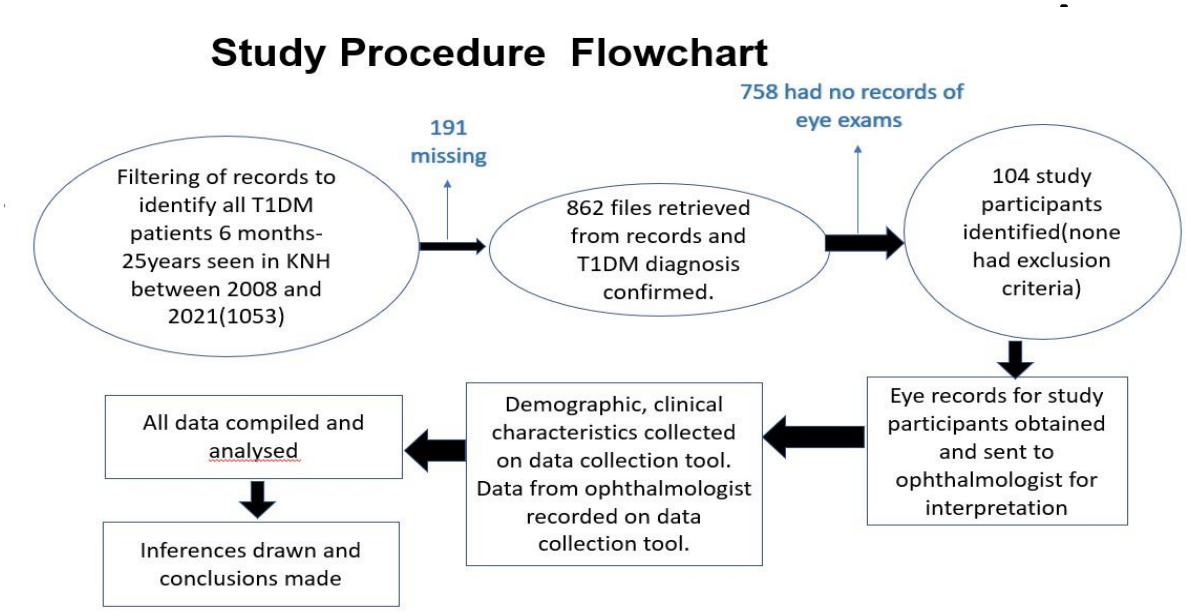

Figure 2: Study procedure flowchart

3.7 *CASE DEFINITIONS/ DEFINITIONS OF KEY EXPOSURES AND OUTCOMES*

The specific disease of interest in this study was Type 1 diabetes mellitus, which is defined as random blood sugar equal to or more than 11.1 mmol/l.

Key exposures/risk factors in this study include:

- Duration of diabetes
- Sex
- HbA1C levels
- Blood pressure
- Body mass index
- Serum lipid profile

Key outcomes of interest include:

- Mild NPDR; at least 1 micro aneurysm on examination.
- Moderate NPDR; haemorrhages, hard exudates and microaneurysms.

- Severe NPDR; haemorrhages, microaneurysms in 4 quadrants, venous beading in at least 2 quadrants, and microvascular intraretinal abnormalities in at least one quadrant.
- Proliferative diabetic retinopathy; diabetic retinopathy with neovascularization.
- Diabetic macula oedema; thickening of the retina at the centre of the macula, or thickening and/or adjacent hard exudates at or within 500 microns of the centre of the macula or an area of thickening greater than or equal to one disc area within 1 disc diameter of the centre of the macula.
- Diabetic glaucoma- Early-stage- normal or raised IOP with an open angle. Advanced stage- Elevated IOP >60mmHg with angle closure.
- Diabetic Cataract- a dense, cloudy area in the eye lens.

3.8 *INCLUSION CRITERIA*

- This included children and youth with T1DM who were between 6 months to 25 years old.
- Those who had eye examinations after T1DM diagnosis.

3.9 *EXCLUSION CRITERIA*

We excluded patients with co-morbid conditions alongside the diabetes mellitus which could cause eye disease including: -

- Hypertension
- Autoimmune conditions
- Thyroid disease
- Parathyroid disease
- Cushing's disease
- All neoplastic conditions
- Traumatic eye conditions
- Congenital eye diseases including inherited retinal diseases (retinitis pigmentosa, Stargardt disease, Cone-rod dystrophy and Leber congenital amaurosis, patients with primary congenital glaucoma and those with congenital cataracts).
- Addison's disease
- Sickle cell disease

- Asthma

We excluded those outside the study age bracket and any examinations done before the diagnosis of T1DM. T1DM is of rapid onset and any eye condition diagnosed before the diagnosis of Type 1 diabetes was deemed not to have been caused by it.

3.10 *DATA COLLECTION TOOL*

This was via a data collection form made to include the following details of each patient in the study:

- Patient demographics- age and sex
- Age at diagnosis of type 1 DM
- Duration of DM at ocular exam.
- HbA1C at ocular exam.
- Blood pressure
- Presence or absence of ocular disease
- Type of ocular disease
- The severity of ocular disease
- Tobacco smoking
- Cholesterol levels
- Body mass index
- Pregnancy

3.11 *DATA ANALYSIS*

Data were entered into a secure spreadsheet software where data cleaning was done. The data was then uploaded to R software Version 4.2.2. Descriptive and inferential analysis was done. Categorical data such as ocular disease were analyzed using frequencies and percentages while continuous data like age and body mass index were analyzed using appropriate measures of centrality (mean) and spread (SD).

The period prevalence was calculated using the cases of ocular disease in the worse eye. Subgroup period prevalence was calculated for each type of ocular disease e.g., Diabetic retinopathy using a similar formula as shown:

$$Period\ prevalence\ of\ ocular\ disease\ in\ Type\ 1\ DM(<25\ years) = \frac{No.\ of\ ocular\ disease\ diagnoses\ in\ worse\ eye\ during\ study\ period}{No.\ of\ Type\ 1\ DM(<25\ years) during\ study\ period}$$

The inferential analysis included an odds ratio calculation of different risk factors for those who developed ocular disease and those without.

To investigate the duration of T1DM as a risk factor for developing ocular disease, survival analysis/time-to-event analysis was done. The time-to-event analysis involved looking at the time from diabetes diagnosis to ocular disease diagnosis. Kaplan Meier survival analysis parameters included those at risk, failed cases, truncated cases and censored cases. Those at risk were all study participants with eye exams while failed cases were those with ocular diagnosis. Left truncated cases were those who experience the outcome (ocular disease) before DM diagnosis and right-censored participants were those lost to follow-up or with no recorded current eye exam.

ETHICAL CONSIDERATIONS

There were several issues for ethical consideration. First, this study utilized data collected from 2008 to 2021 period. Consent for use of this data was not sought prospectively from the guardians and retrospective consent was not feasible. Second, the physical files of each of the individual patient's data were accessed by the study team. Third, the patient identifiers were not anonymized or redacted. Finally, the age bracket 6 months to 25 years included minors, and therefore a vulnerable population.

The principal investigator and the study team put in place measures to mitigate the ethical issues. First, only the principal investigator of this study was initiated after approval to conduct the study and a waiver of informed consent was sought from and granted by KNH-UON Ethics and Review Committee. Further, institutional consent was sought from Kenyatta National Hospital. Third, to maintain confidentiality, only the study PI had access to the physical files to extract the data needed for analysis. Fourth, the final data for analysis did not include any parameters that could identify a given patient. Finally, during the study period, all the physical files were stored in secure cabinets and the final data for analysis was equally stored in a secure password-protected computer.

STUDY STRENGTHS AND LIMITATIONS

Strengths

We included all the children and youth with T1DM giving a large sample size. It was the first study on the spectrum of ocular complications done on children and youth with T1DM at a national referral hospital in Kenya.

Limitations

In our study, 191 files out of the total 1,053 study population could not be traced, at the central registry however the study population of 104 was enough to enable us to make valid conclusions.

The study could not look at tobacco exposure as a risk factor for ocular disease since the records of both passive and active smoking in the participants were not present in the files.

Some variables (some risk factors) had missing data. The missing data were handled through imputation, and inferences and conclusions were drawn for the variables whose missing numbers did not interfere with the result validity. This could not be done for LDL cholesterol levels as a risk factor for ocular disease since the numbers missing were high. There were risk factors that the study did not look at for example the presence of nephropathy as an independent risk factor for the development of retinopathy in children and youth with T1DM.

3.12 *STUDY MATERIALS*

These included file abstraction forms (data collection tool and stationery)

CHAPTER 4: STUDY RESULTS

During the study, out of the potential 1053 study participants that were identified, 850 files were extracted. 104 eligible participants were found. Records of a total of 104 study participants were collected for the study period.

4.1 Demographic characteristics of the study participants

i) Gender distribution of study participants

There were 68 male and 36 female participants.

There was a female predominance with 66% of the participants being female while 34% were male as depicted in the bar chart below.

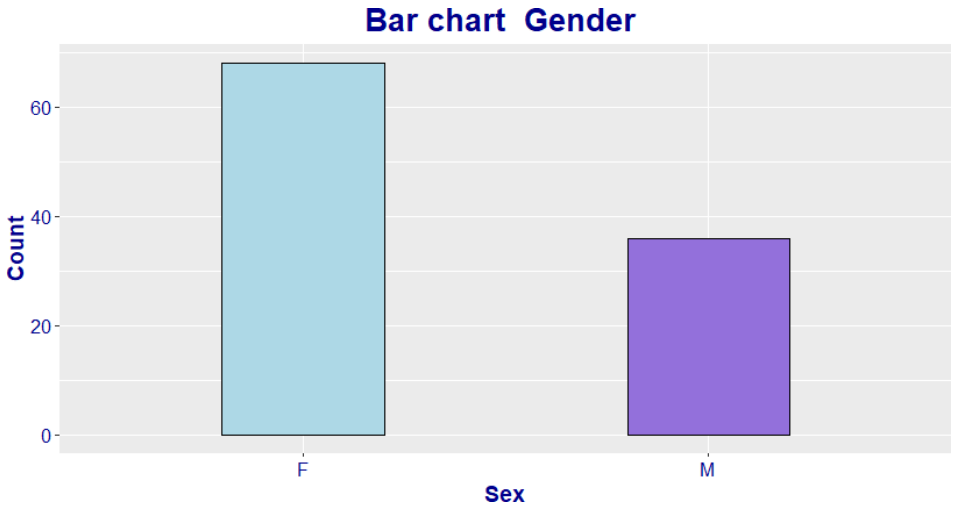

Figure 3: Bar chart of gender distribution

ii) Age distribution of study participants at ocular examination.

At the time of the eye examination, the study participants ages ranged from 8 to 25 years.

At the time of the ocular exam, the study participants' average age was 17.7 years. (SD +/- 3.42). This is depicted in the histogram below.

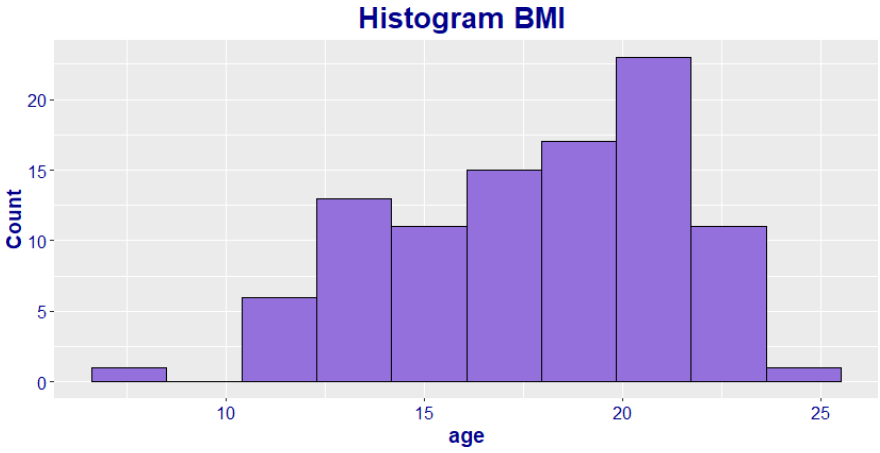

Figure 4: Histogram of age distribution at ocular exam in DM type 1

iii) Age at diagnosis of T1DM.

The mean age at diagnosis of T1DM of the study participants was 13.5±5.9 years with the youngest diagnosis occurring at 1 year and the oldest at 22 years.

This is depicted in the histogram below:

Variable		Total
Age in years (Mean(SD))		17.7(3.42)
Age at DM diagnosis in years(Mean(SD))		13.5(5.9)
Duration of DM in years (Mean(SD))		3.39(2.86)
Sex	Male	36(34.6%)
	Female	68(65.4%)

Table 3: Summary of Demographic Characteristics.

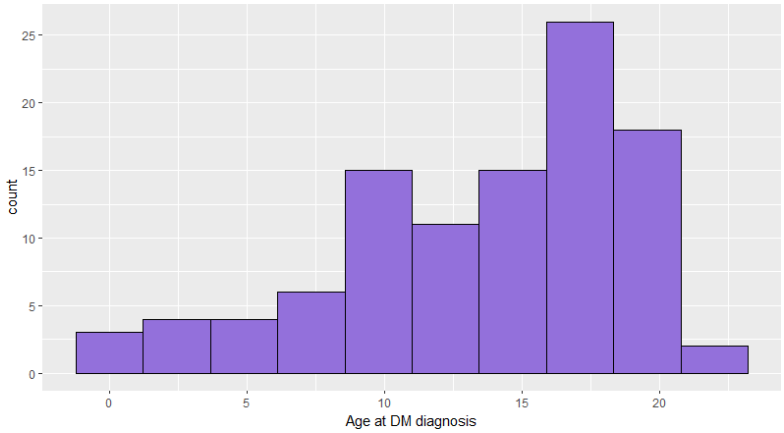

Figure 5: Histogram of age at diagnosis of DM type 1

4.2 Anthropometric characteristics of the study participants

i) Weight for age Z scores.

74 of the study participants had normal weight for age Z-scores, 3 had severe wasting and 2 were overweight.

A total of 88 participants had weight measurements, 16 had no weight measurements recorded in the files (missing data).

Table 4: Weight for age Z-score as per WHO criteria

Weight for Age Z Score	Grand Total	Percentage
Severe wasting (</= -3SD)	3	3%
Moderate wasting (-2 to -3SD)	2	2%
Mild wasting (-1to -2SD)	2	2%
Normal(-1to1SD)	74	71%
At risk of being overweight (+1 to +2SD)	5	5%
Overweight (+2 to +3SD)	2	2%
No readings	16	15%
Grand Total	104	100%

The number of participants (88) was enough to pick up a medium size effect (Apriori sensitivity testing), so the number was still adequate to analyse and draw valid conclusions.

ii) Height for age Z score.

56 study participants had normal height for age Z score, while 6 were severely stunted as depicted in the table below:

Table 5: Height for age Z-score as per WHO criteria

Height for Age Z Score	Grand Total	Percentage
Severe stunting (</= -3 SD)	6	6%
Moderate stunting (-2 to -3 SD)	8	8%
Mild stunting (-1to -2 SD)	17	16%
Normal(-1to1 SD)	56	54%
Tall (>1SD)	1	1%
No height reading	16	15%
Grand totals	104	100%

The number of study participants with recorded height was enough to pick up a medium-size effect (Apriori sensitivity testing which was adequate to draw valid conclusions from upon analysis).

iii) BMI

17 of the study participants were underweight, 23 were overweight, 48 had a healthy weight, and 16 did not have BMI calculated due to missing data in the files.

We couldn't calculate BMI for 16 individuals because of missing records, which represent 15% of the total sample. The available BMI values were sufficient to draw valid conclusions.

Table 6: BMI for age Z-score as per WHO criteria

BMI for Age Z Score	Grand Total	Percentage
Underweight (</= -2 SD)	17	16%
Healthy weight (-2 to 1SD)	48	27%
overweight (1 to 2 SD)	23	41%
Obese (>2SD)	0	0%
No recordings	16	15%
Grand totals	104	100%

4.3 Clinical characteristics of the study participants

i) Hypertension

28 of the participants had hypertension, while 55 did not have hypertension. 21 did not have blood pressure readings indicated in the records.

This is shown in the table below:

Table 7*:* BP status as per WHO criteria.

Variable	Count	Percentage
Hypertension	28	27%
No Hypertension	55	53%
Missing data	21	20%
Total	104	100%

ii) Cholesterol levels

We could only find LDL cholesterol levels for 46 out of the 104 study participants. 20 study participants had levels above 2.6 mmol/l (cut off for normal) representing 19% while 26 individuals had LDL cholesterol levels below 2.6 mmol/l translating to 25%. However, for the remaining 58 individuals (56%), LDLC levels were missing.

Table 8: Cholesterol levels

Variable	Total	Percentage
LDL Cholesterol > 2.6	20	19%
LDL Cholesterol < 2.6	26	25%
Missing	58	56%
Total	104	100%

iii) HbA1C

82 study participants had HbA1C levels recorded in the files, and 22 had missing records. Of those with available HbA1C levels, 45 participants had at the time of ocular exam values above 8% indicating poor glycaemic control, while 37 participants had HbA1C levels below 8% suggesting adequate glycaemic control.

Table 9*:* HbA1C levels

Variable	Total	Percentage
HbA1C > 8%	45	55%
HbA1C < 8%	37	45%
Total (n)	82	100%

4.4 Prevalence and Spectrum of ocular diseases

The spectrum of ocular diseases found in T1DM children and youth included diabetic retinopathy, glaucoma, cataracts and optic atrophy.

The period prevalence of ocular diseases, in general, was calculated using the formula below:

$$Period\ prevalence\ of\ ocular\ disease\ in\ Type\ 1\ DM(<25\ years) = \frac{No.\ of\ ocular\ disease\ diagnoses\ in\ worse\ eye\ during\ study\ period}{No.\ of\ Type\ 1\ DM(<25\ years)during\ study\ period}$$

The period prevalence of all ocular diseases was 106 cases per 1,000 population with type 1 DM (= 11/104*1000).

Diabetic retinopathy had a prevalence of 57.7 cases per 1000 DM type 1 population

(= 6/104*1000). Analysis of the severity of DR revealed that all the cases had mild diabetic retinopathy.

Glaucoma and cataracts had a similar prevalence of 28.8 cases per 1,000 population with DM1 each (= 3/104*1000).

The prevalence of optic atrophy was 19.2 cases per 1,000 type 1 DM population. (= 2/104*1000)

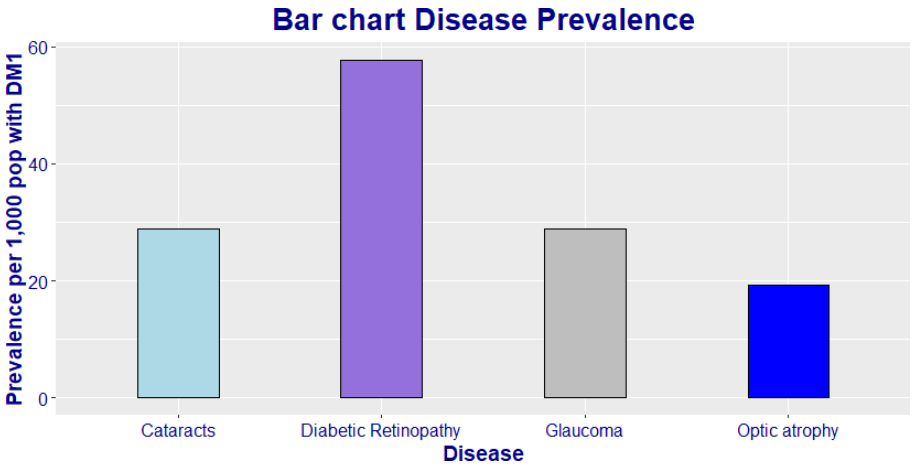

Figure 6: Prevalence of different ocular diseases per 1,000 population with DM1

4.5 Risk factors for ocular disease

i) Sex.

We looked at sex as a risk factor for developing ocular disease and we found that 8 males out of the 68 in the study had ocular disease, and 60 did not have ocular disease. 3 females had ocular disease while 33 out of the 36 females in the study did not have ocular disease. These differences were not statistically significant.

Our findings are depicted in the contingency table below.

Table 10: Contingency Table of Sex and ocular disease

Ocular disease	F	M	Grand Total
No	60	33	93
Yes	8 *(OR 1.47, 95%CI 0.36-5.9, p value=0.6)*	3	11
Grand Total	68	36	104

ii) Duration of T1DM at ocular examination.

In the subjects with ocular disease, the mean duration of T1DM at the time of the ocular exam was longer (4.80 (+/-3.47) years) compared to those without ocular disease (3.26

(+/-2.76) years). This difference was the difference was statistically significant on logistic regression.

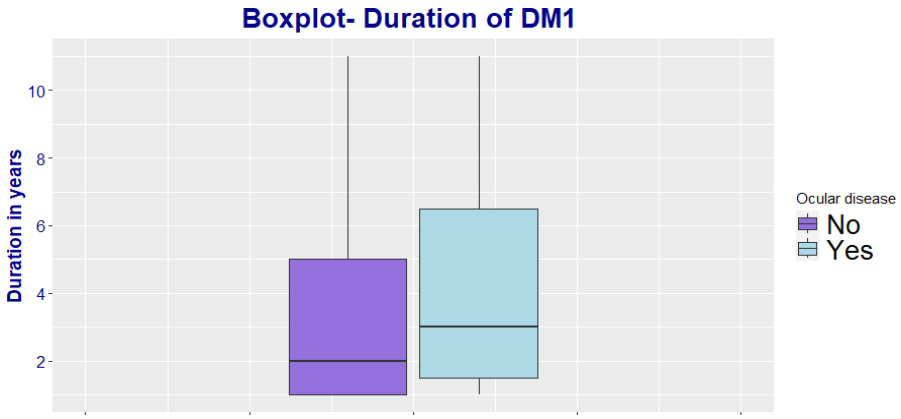

Figure 7: Box plot Duration of T1DM and ocular complications

The table below demonstrates the mean duration of diabetes at ocular exam among the participants who had ocular disease and those who did not have ocular disease.

Table 11: Mean duration of diabetes at ocular exam

Variable	With Ocular Disease	Without Ocular disease	Total	P value*
Duration of DM in years at ocular exam (Mean(SD))	4.80 (+/-3.47)	3.26 (+/-2.76)	3.39(+/-2.86)	0.3338

iii) Hypertension

Out of the 11 individuals with ocular disease, 2 (18.2%) were found to have systolic hypertension. In contrast, among the 74 individuals without ocular disease, 26 (35.1%) had systolic hypertension. A total of 9 (81.8%) participants with ocular disease had no hypertension, while 48 (64.9%) individuals without ocular disease were also free of hypertension. In our study, there was no correlation between hypertension and the onset of ocular illness in children and adolescents with T1DM. *(OR 0.41).*

Table 32: Contingency Table of Hypertension as per WHO criteria

	Ocular Disease	No Ocular Disease	P value	95 Confidence Interval
Hypertension	2	26	0.2765	0.08 to 2.04
No hypertension	9	48		
	11	74		

iv) BMI

Out of the 11 study participants with ocular disease, 10 had normal BMI, one was overweight. 59 of the participants without ocular disease had normal BMI, 3 were underweight, 15 were overweight and none were obese. The was no relationship between BMI and the development of ocular disease.

Table13: BMI for age z score

BMI for Age Z Score	No Ocular disease	Ocular disease	Chi-square + Yates(P value)
Underweight (</= -2 SD)	3	0	0.38
Healthy weight (-2 to 1SD)	59	10	
overweight (1 to 2 SD)	15	1	
Obese (>2SD)	0	0	
No recordings	16	0	
Grand totals	93	11	

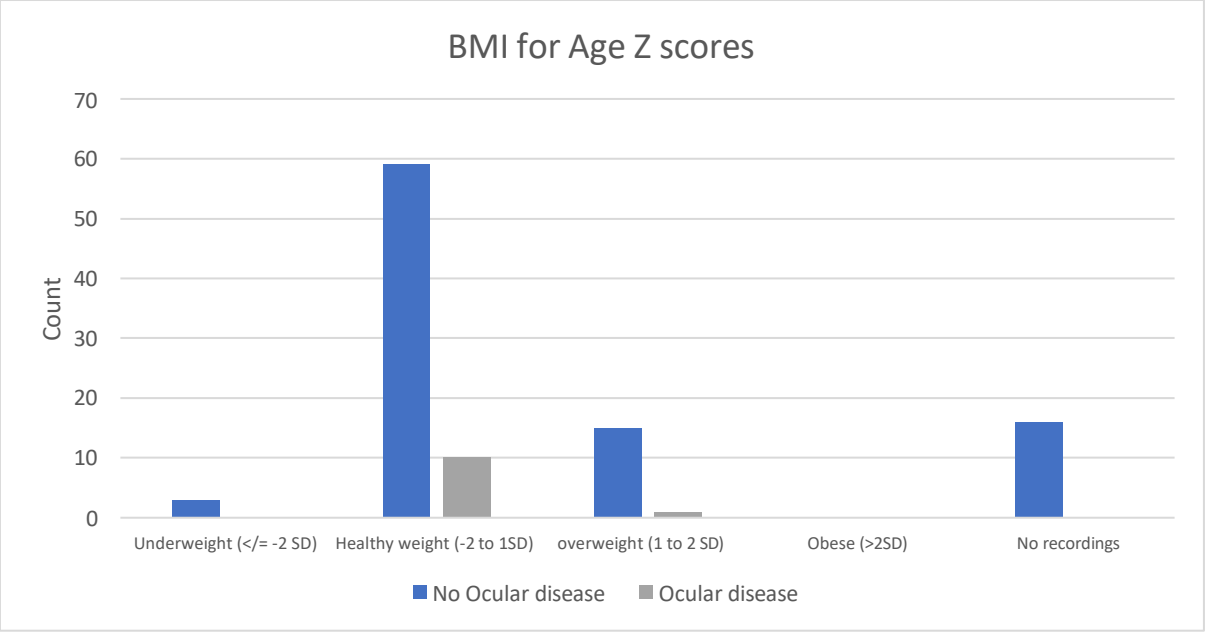

Figure 8: Histogram and bar chart of body mass index

v) HbA1C levels

The HbA1C levels among the study participants with ocular disease were found to be higher than that of the participants without ocular disease. However, the odds ratio, which measures the strength of the association between HbA1C level and ocular disease, was 2.69, making the differences between the two groups not statistically significant.

Table 14: Contingency table for HbA1C and ocular disease

	Ocular Disease	No Ocular Disease	Total	Odds ratio	95% CI	P value
HbA1C > 8%	6	39	45	2.69	0.51 – 14.2	0.2434
HbA1C < 8%	2	35	37			
Total	8	74	82			

vi) Cholesterol levels

We looked at the LDL levels of the study participants and found that the mean LDL levels in those with ocular disease were slightly higher than those without ocular disease. This difference lacked statistical significance. However, we were unable to compare this finding to studies done elsewhere as we had numbers of missing data large enough not to permit making any inferences or conclusions (56% of records were missing).

Table 15: LDL levels and ocular disease

Variable	With Ocular Disease	Without Ocular disease	Total	P value
Low Density Lipoprotein(LDL) Cholesterol in mmol/l (Mean(SD))	2.73 (0.76)	2.50 (0.63)	2.55(0.66)	0.3868
Percentage of Glycosylated Hemoglobin (HbA1C) (Mean(SD))	10.12 (4.18)	9.13 (3.94)	9.2 (4.02)	0.6148

CHAPTER 5: DISCUSSION, CONCLUSION AND RECOMMENDATIONS

5.1 Discussion

The most common endocrine disorder in children is T1DM. Untreated and poorly controlled T1DM results in complications of the cardiovascular and renal systems, ophthalmic complications, and neuropathy. Ocular complications of diabetes include diabetic retinopathy, macula oedema, cataracts, and glaucoma.

The prevalence of DR in this study was found to be 5.7% among children and youth with T1DM for the study period. This finding is comparable to findings in a previous study done by Mulugeta et al in a tertiary hospital in Ethiopia that showed the incidence of diabetic retinopathy among the studied population of children to be 4.7%. (21) In addition, all cases of diabetic retinopathy in our study were found to be mild, which is similar to the findings of previous studies that have reported a higher prevalence of mild diabetic retinopathy among children with T1DM. A retrospective chart review published in the International Journal of Endocrinology in

2018 found the prevalence of mild diabetic retinopathy to be higher than moderate and severe (9 children, 3 children and 1 child respectively). (18)

The prevalence of glaucoma in this study was found to be 2.8%. The prevalence of cataracts in this study was 2.8% a review of the previous study by Simunovic et al in 2018 showed that the prevalence of cataracts in children and youth with T1DM ranged between 0.7% to 3.4% findings consistent with findings in this study. (12)

The prevalence of optic atrophy was found to be 1.9%.

For every one-year increase in the duration of DM1, the log odds of developing ocular disease increased by 0.12. This corresponds to an odds ratio of 1.129, indicating that the odds of developing ocular disease increased by a factor of 1.129 for every one-year increase in the duration of DM1, after controlling for the other predictor variables in the model. Therefore, individuals with a longer duration of DM1 have a higher likelihood of developing ocular disease compared to those with a shorter duration of DM1. This is in line with similar findings from a cross-sectional clinic-based study of T1DM children and youth aged 10-18 years carried out in Sudan that found the frequency of retinopathy to be 33%, those with retinopathy were found to have higher HbA1c levels and longer diabetes duration than patients without diabetic retinopathy. (23) Our findings also relate to a study done in Bangladesh in 2020 to determine the risk factors associated with the development of ocular complications in young people which found duration of T1DM to be a significant risk factor for retinopathy development. (28) The length of T1DM and the degree of retinopathy among T1DM-affected children were found to be positively correlated in another study. (28)
The risk of ocular problems in children and adolescents with T1DM was not correlated with gender, according to our research. Other studies have not found a gender-specific risk for the emergence of ocular problems in kids with T1DM. (25)

Among those with hypertension, 3 (20%) had ocular disease, while 23 (80%) did not have ocular disease. The odds ratio of having an ocular disease with hypertension was not statistically significant. This differed from A study done by Wysocka et al demonstrated hypertension as one of the risk factors for developing ocular diseases. (8) Hypertension was identified as a major risk factor for the development of diabetic retinopathy in T1DM in a study to assess the prevalence of diabetic retinopathy in children. (8) A review of publications done in 2020 found that in a cohort

of young people, blood pressure above the 98th centile was more prevalent in those with abnormal diabetic retinopathy screening findings than those without. (29)

Our study found that individuals without ocular disease had a slightly lower mean HbA1c level (9.13%, SD 3.94) compared to those with ocular disease (10.12%, SD 4.56). However, the difference was not statistically significant at a 95% confidence level. While this difference is not statistically significant, it is important to note the mean HbA1c level for the population study crossed the 7% threshold. HbA1C was revealed to be a risk factor for the development of retinopathy in children and adults with T1DM in a population-based cohort research conducted in Sweden in 2019. (30) A retrospective chart review published in the Journal of paediatric diabetes in 2020 patients with HbA1c of more than 8% were more at risk of developing diabetic retinopathy. (18)

5.2 CONCLUSION

The prevalence of ocular complications among children and youth with T1DM attending the Paediatric endocrinology clinic was found to be 12.5% during the study period of 2008-2021.

The spectrum of ocular complications included diabetic retinopathy, cataracts, optic atrophy and glaucoma. The most prevalent condition was diabetic retinopathy. All cases of diabetic retinopathy were mild.

The length of diabetes was shown to be one of the risk factors for diabetic ocular complications, and it was proven to be positively correlated with the prevalence of ocular complications in children and adolescents with type 1 diabetes mellitus.

5.3 RECOMMENDATIONS

Children and youth with T1DM need to get eye examinations as per the recommendations of the Kenya Ministry of Health; at the time of diagnosis and then yearly after that, all children with T1DM need to have an eye exam.

STUDY TIMELINES

Study Timelines									
Months	1	2	3	4	5	6	7	9	10
Proposal writing									
Ethics approval									
Data collection									
Data analysis									
Report writing									

Figure 8: Study timelines.

Study budget

ITEM	**COST**
Printing cost	Kes. 10,000/-
Stationery	Kes. 10,000/-
Statistician	Kes. 50,000/-
KNH-UONEthics Committee fee	Kes. 2000/-
File retrieval fee at KNH records	Kes. 5000/-
Retinal photographs and ophthalmology resident fee	Kes. 65,000/-
TOTAL	Kes. 142,000/-

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APPENDICES

APPENDIX 1: DATA COLLECTION TOOL

DATA COLLECTION TOOL

THE PREVALENCE,SPECTRUM OF AND RISK FACTORS ASSOCIATED WITH OCULAR DISEASES IN CHILDREN AND YOUTH WITH TYPE 1 DIABETES SEEN AT THE PAEDIATRIC ENDOCRINOLOGY CLINIC IN KNH FROM 2008-2021

Client Biodata

File Number (last 4 digits)		Date of birth		Sex	
Date of DM diagnosis		Date of Last clinic visit		Smoking(Pack years)	
Number of recorded clinic visits		Number of recorded eye exams		Pregnancy status	

Clinic Visits with Eye exam

Date	Weight (kg)	Height (cm)	HbA1C	Systolic BP	Diastolic BP	LDL Cholesterol	RT Eye Diagnosis	LT Eye Diagnosis

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15th August, 2022

KENYATTA NATIONAL HOSPITAL APPROVED 15 AUG 2022

Dr. Belinda Chopdekar Narayan
Reg. No H58/37512/2020
Dept. of Paediatrics & Child Health
Faculty of Health Sciences
University of Nairobi

Dear Dr. Narayan,

RESEARCH PROPOSAL: THE PREVALENCE, SPECTRUM OF AND RISK ASSOCIATED WITH OCULAR DISEASE IN CHILDREN AND YOUTH WITH TYPE 1 DIABETES SEEN AT THE PAEDIATRIC ENDOCRINOLOGY CLINIC IN KENYATTA NATIONAL HOSPITAL FROM 2008-2021 (P163/03/2022)

This is to inform you that KNH-UoN ERC has reviewed and approved your above research proposal. Your application approval number is **P163/03/2022.** The approval period is 15th August 2022 – 14th August 2023.

This approval is subject to compliance with the following requirements;

i. Only approved documents including (informed consents, study instruments, MTA) will be used.
ii. All changes including (amendments, deviations, and violations) are submitted for review and approval by KNH-UoN ERC.
iii. Death and life threatening problems and serious adverse events or unexpected adverse events whether related or unrelated to the study must be reported to KNH-UoN ERC 72 hours of notification.
iv. Any changes, anticipated or otherwise that may increase the risks or affected 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 relevant institutions.
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 to KNH-UoN ERC.

- Prior to commencing your study, you will be expected to obtain a research license from National Commission for Science, Technology and Innovation (NACOSTI) https://research-portal.nacosti.go.ke and also obtain other clearances needed.

Yours sincerely,

DR. BEATRICE K.M. AMUGUNE
SECRETARY, KNH-UoN ERC

c.c. The Dean, Faculty of Health Sciences, UoN
The Senior Director, CS, KNH
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