ISSN: 2377-3634

Godfrey E et al. Int J Diabetes Clin Res 2025, 12:184
DOI: 10.23937/2377-3634/1410184
Volume 12 | Issue 1
Open Access

International Journal of Diabetes and Clinical Research

RESEARCH ARTICLE

Non Retinal Visual Impairement in Children with Type 1 Diabetes Mellitus in Dar Es Salaam Tanzania

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Abstract

Introduction: Global increase in incidence of type 1 diabetic mellitus, is linkage to increase in complications of type 1 diabetes. Non retinopathy visual impairment are common and among the leading cause of visual loss in people with diabetes. Despite all of this there is a dearth of data on magnitude of non-retinopathy visual impairment in T1DM. We aimed to assess the burden of non-retinopathy visual impairment in T1DM so that appropriate intervention can be instituted.

Methods: A cross sectional study among children and youth aged 1 to 26 years, attending diabetes clinic in 5 centers in Dar es Salaam-Tanzania. A structured questionnaire was used to collect demographics and clinical data. Visual acuity examination was done using Snellen's chart, with one standing at 6 meters away. The results were classified as normal or abnormal, fundopictures were done and all those with visual acuity as a result of retinopathy and cataract were removed from the analysis of visual acuity abnormalities. Blood sample were collected for checking fasting/random blood sugar and glycated hemoglobin.

Results were summarized using mean ± standard deviation for continuous variables and percentage/proportion for categorical variables. Pearson Chi-square χ^2 test was used to compare differences between the categorical variables. In the inferential analysis, a bivariate logistic regression was done. Adjusted odds ratio (AOR) was used in multivariate analysis.

Result: there were 281 participants with 50% of them aged less than 10 years, 7.5% were having obesity, one in every 3 children were having elevated systolic hypertension. Majority of participants 94% were having poor glycemic control, and nearly 21% having abnormal visual acuity while 11.2% had retinopathy and 9.2% had cataracts. Risk factors identified for reduced visual acuity and cataract were lower age at diagnosis (AOR 9.626087 CI (1.267388 - 7.311224) male sex (AOR 2.087694 CI (1.146803 - 3.800537) and duration of diabetes for more than 5 years AOR 1.94 CI 1.067597 - 3.53569).

Conclusion: Non retinopathy ocular complication in T1DM are not uncommon in our setting leading to impaired visual acuity. Lower age at diagnosis and duration of diabetes were associated with impaired visual acuity.

Background

Globally there is increase in type 1 Diabetes Mellitus (T1DM) up to 8.4 million cases in 2021 and each year there are about 500,000 new cases. It is expected that this number will double to 17.4 Million by 2040 year. Significant difference in life expectancy exist whereby on average a person with type 1 diabetes in Sub-Sarahan Africa will have a life expectance of 13 years after diagnosis compared to 65 years in high income countries [1,2]. An increase in incidence of DM

Citation: Godfrey E, Muze K, Mfinanga SG, et al. (2025) Non Retinal Visual Impairement in Children with Type 1 Diabetes Mellitus in Dar Es Salaam Tanzania. Int J Diabetes Clin Res 12:184. doi.org/10.23937/2377-3634/1410184

Accepted: April 15, 2025: **Published:** April 17, 2025

implies increase in DM complications including ocular complications such as retinopathy , cataracts, optic neuropathy, keratopathy, and refractive eye disorders like hyperopia myopia, and strabismus (Non ocular complication) [3,4]. These disorders later lead to visual impairment and blindness. Among 2.2 billion people with vision impairment or blindness globally, 1 billion are due to unaddressed refractive errors, and this is the leading cause of visual impairment and blindness [5].

Diabetes related visual impairment remains a significant public health concern with 4 time higher in low income countries [6,7].Studies done in adults have shown that non-retina ocular complications of diabetes are among the leading cause of visual loss and morbidity ranging from 16.63% in lower middle income countries to as high as 58.5% in sub-Saharan Africa[8,9]. Visual impairment in Africa ranges from12.4% to as high as 43% in various African setting [7,10,11]. Different factors have been associated with the risk of developing visual impairment like uncontrolled long duration of diabetes, male and hypertension as a risk factor for developing visual impairment[10 - 12].On the other hand the prevalence of cataract which is another form of non-retinal ocular complication of diabetes, ranges from 3.3% to 8.3% in different studies [4,13,14] .Its prevalence increases with age, severity of retinopathy if present and proteinuria.

To mitigate this complication appropriate screening program needs to be established. The American Academy of pediatrics suggest retinopathy screening from 3 years of age and American Academy of ophthalmology recommends screening 5 years from diagnosis of Type 1 DM,[15,16] however there is a dearth of literature on screening for non-retinal ocular complication of diabetes. Age of onset, and screening programs studied are based on retinopathy screening alone, however, there is variations and risk factor for non-retinopathy ocular complications of T1DM, worldwide but also in our setting where dearth of data is common. So this survey aimed at assessing the burden of visual impairment caused by non-retinal eye complications of diabetes and its associated factors in our setting.

Methods

Study design

This was hospital based cross sectional study among children and youth (age 0-26 years) attending diabetes clinics in Dar es Salaam Tanzania, between Jan 2021 – March and March 2022. This included five pediatric diabetes clinics in Dar es Salaam under the collaboration of Life for a Child, Changing Diabetes in Children and the Ministry of Health, with one private diabetes clinic. These clinics are Muhimbili National Hospital (MNH) in Ilala Municipal, Mwananyamala in Kinondoni Municipal, Temeke in Temeke Municipal, Vijibweni in Kigamboni Municipal, and one private clinic Hindu Mandal Hospital. Each Centre can attend up to 300 diabetes children and youth per month.

Inclusion and exclusion criteria: All children that are confirmed type 1 DM on insulin and given consent and / or assent were enrolled.

Data collection: Structured questionnaire was used to collect demographic and clinical characteristics, information collected includes age gender social economic status, and duration of diabetes mellitus, and we also collected blood for glycated hemoglobin (HbAIc).

Eye examination

A well-trained nurse performed eye examinations and took fundal pictures which were analyzed by the same ophthalmologist. At the start of the examination, the child was examined for visual acuity using Snellen's chart and standing at 6 meters. The eye measurement read between 6/6 and 6/25, where by between 6/6-6/9 classified as normal, and above that it is referred as abnormal. These children and youth also had a fundal picture to rule out retinopathy detailed of examination is published elsewhere [17].

Laboratory investigations

Under aseptic technique blood samples were collected from the anterior cubital fossa (3mls) following standard procedures. This was preceded by overnight fasting. We immediately used one drop of blood on the glucostick for determination of fasting blood glucose, using a glucometer (Gluconavii, home health, (UK) LTD Unit A, Greatham Road, industrial estate Greatham Road, Bushey, Hertfordshire WD23 2NZ, United Kingdom), another drop was put on Hemocue® HbA1c 501, (full automated point of care machine (Radiometer group, Angelholm-Sweden) for HbA1c determination. Both machines were validated to be used for point-of-care tests. The machines were calibrated on a daily basis.

Statistical analysis

Statistical analysis was performed using SPSS version 22 (IBM In., Chicago) and Stata 14 (Stata Corp, College Station, TX). SPSS was used for preliminary analysis and to examine the co linearity between variables of interest. The final analyses were done using Stata 14. In the descriptive analysis, the results were summarized using frequency/counts and mean ± standard deviation for continuous variables while percentage/proportion was used for categorical variables. Pearson Chi-square χ^2 test was used to compare differences between the categorical variables of interest. In the inferential analysis, a bivariate logistic regression was done to find the association between complications of diabetes mellitus (visual impairment or/and cataract) and each of the independent factors, separately. Adjusted odds ratio (AOR) was used to present the results of the multivariate analysis.

Ethical clearance

Ethical clearance to conduct this study was obtained from the Kilimanjaro Christian Medical University College (KCMUCo) Ethical Clearance Committee and given a certificate No 2478.

Permission to conduct the study was sought from specific participating hospitals. Informed written consent was obtained from youth and parents/ guardians of the children. In addition, children between 12 -18 years provided assent.

The patients' information and results were kept strictly confident.

Result

Demographic characteristics of the enrolled participants

There were 281 enrolled participants with nearly equal numbers of males and females. Most of them 55.5% aged less than 10 years, about half 46.3% were in secondary school with few 17% that had attained university level of education. About two third 64% of parents were divorced and most of them were either having no formal or have attained primary education level. The main source of the income for both parents, (mother and father) were business. Regarding the duration of DM there was equal distribution whereby 50% had symptoms for less than 5 years similarly 50% had a duration of DM for more than 5 years. Based on BMI 47 % had normal nutritional status, 18.5% underweight and 7.5% were obese, and 98 (30%) had elevated mean systolic and diastolic blood pressures. The majority of study participants 94% had poor blood sugar control based on HbAIc with few 1.4% having good glycemic control, nearly 21% of the participants had an abnormal visual acuity of both eyes, and a proportion of children with cataract were 9.2% (as shown in table 1).

Ocular manifestations in relation to HbA1C

The majority of participants with cataracts and abnormal visual acuity had poor glycemic control but this was not statistically significant as shown in (table 2 below).

Table 1: Demographics and clinical characteristics of the enrolled participants.

S/N	Variable (n)	Response	Percentages
1	AGE (years) N = 281	< 10 = 156 11-18 = 28 > 18 = 97	55.52% 9.96% 34.52%
2	SEX N = 281	MALE = 137 FEMALE = 144	48.75% 51.25%
3	Children's education level N = 281	NO FORMAL ED = 50 PRIMARY = 101 SECONDARY and above = 130	17.79% 35.94% 46.26%
4	PARENT'S marital status N = 281	SINGLE = 53 MARRIED = 24 DIVORCED = 182 CO-HABITING = 22	18.86% 8.54% 64.77% 7.83%
5	MOTHER' s level of Education N = 281	NO FORMAL = 56 PRIMARY = 105 SECONDARY = 68 UNIVERSITY = 52	19.93% 37.37% 24.20% 18.51%
6	FATHER' s level of Education N = 281	NO FORMAL = 100 PRIMARY = 72 SECONDARY = 60 UNIVERSITY = 49	35.59% 25.62% 21.35% 17.44%
7	DURATION OF DM N = 281	< 5 YEARS = 141 > 5YEARS = 140	50.18% 49.82%
8	BMI N = 281	UNDEWEIGHT = 52 NORMAL = 133 OVERWEIGHT = 75 OBESE = 21	18.51% 47.33% 26.69% 7.47%
9	BLOOD PRESSURE MEAN SBP N = 281	LOWERED = 16 NORMAL = 167 ELEVATED = 98	5.69% 59.43% 34.88%
10	GLYCEMIC CONTROL (HbC1) N = 281	GOOD = 4 MODERATE = 13 POOR = 264	1.42% 4.63% 93.95%
11	VISUAL ACUITY LEFT N = 281	NORMAL = 222 ABNORMAL = 59	79.00% 21.00%
12	VISUAL ACUITY RIGHT N = 281	NORMAL = 224 ABNORMAL = 57	79.72% 20.28%
13	CATARACT N = 281	YES = 26 NO = 255	9.25% 90.75%

Table 2: Ocular manifestations in relation to HbA1C.

S/N	variable	HbA1c	Chi2	P value
1	Cataract N = 26	GOOD = 1 MODERATE = 0 POOR = 25	2.5216	0.283
2	Abnormal visual acuity left N = 59	GOOD = 0 MODERATE = 1 POOR = 58	2.6010	0.272
3	Abnormal visual acuity right N = 57	GOOD = 0 MODERATE = 1 POOR = 56	2.4331	0.296

Table 3: Univariate /Multivariate Logistic Regression for Factors Associated with Diabetic Non-Retinal Visual Impairment.

PARAMETER	CATEGORY	COR (95%CI); p-value	AOR (95%CI); p-value
AGE	< 10 11-18 > 18	4.78 (1.08 - 21.06); 0.038 2.01(1.04 - 3.87); **0.036** Ref	9.63 (1.27 - 7.31); **0.029** 1.95 (1.01 - 3.75); **0.046** Ref
SEX	MALE FEMALE	1.72 (.96 - 3.07); **0.069** Ref	2.08 (1.146 - 3.80); **0.016** Ref
EDUCATION OF CHILD	PRIMARY LEVEL SECONDARY and above NO FORMAL ED	1.24 (.519 - 2.94); 0.633 0.765 (.344 - 1.703); 0.513 Ref	1.393 (.596 - 3.25); 0.443 0.982 (.447 - 2.156); 0.965 Ref
DURATION OF DM	> 5YEARS < 5 YEARS	1.461 (.8187 - 2.60); 0.199 Ref	1.941.067 - 3.53); **0.030** Ref
BMI	UNDEWEIGHT NORMAL OVERWEIGHT OBESE	0.556(.139 - 2.212); 0.405 0.4490(.1247 - 1.616); 0.221 1.3958 (.3356 5.805); 0.647 Ref	0.502924 (.0990 2.552); 0.407 0.2731 (.060 - 1.230); 0.091 0.771 (.153 - 3.880); 0.753 Ref
Hb1AC/ GLYCEMIC CONTROL	GOOD MODERATE POOR	1 3.378637 (.4303 - 26.52); 0.247 Ref	1 3.230768 (.411 - 25.37); 0.265 Ref
BLOOD PRESSURE MEAN SBP	LOWERED NORMAL ELEVATED	0.9735 (.2618 - 3.619); 0.968 0.711 (.186 - 2.709); 0.618 Ref	0.97355 (.262 - 3.62); 0.968 0.79720 (.2083 - 3.0508); 0.741 Ref
BLOOD PRESSURE MEAN DBP	LOWERED NORMAL ELEVATED	3.9230 (.2399 - 64.1287); 0.338 3.578947 (.2137 - 59.928); 0.375 Ref	1 3.35 (2.0330- 5.5199); **<0.01** Ref

Factors associated with T1DM abnormal visual acuity

The lower the age the higher the risk of developing DM ocular complications. Children under the age of 10 have a 4 to 9 times more likely hood and those between 11 - 18 are twice more likely to develop ocular manifestations as compared to those above 18 years which is protective. The male sex is more likely to develop ocular manifestations as compared to the females, with twice the odds. Those living with DM for more than 5 years are twice more likely to develop ocular manifestations compared to those with DM for less than 5 years. (As shown in table 3)

DISCUSION

In this study we aimed at assessing non-retina -ocular complication of type 1 diabetes. To our knowledge this is the first study in East Africa which assess non-retina ocular complication of DM, whereby there were equal number of male and female enrolment, 50% aged less than 10 years, more than 50% of parents were divorced, majority having no formal or primary level of education, the proportion of children with obesity were 7.5%, one in every 3 children with T1DM were having systolic hypertension, and 1 in every 5 children with T1DM were having abnormal visual acuity. The prevalence of cataract (one of the cause of non-retinal visual impairment) among children and youth with T1DM was 9.2%. Visual impairment caused by other non-retinal ocular manifestation grouped together were high 21% in this study, which was comparable to the study done by Klein et al.[18] Risk factors identified for progression of T1DM non-ocular complications include younger age at diagnosis, male gender, and longer duration of T1DM. These findings are similar to the findings by Klein et al and Kurawa et al which showed increase in visual impairment in patient with longer duration of diabetes,[11,18] however previous study showed gender to have no significant effect in visual acuity[11].

Children aged less than 10 years predominated this the study participants which is in keeping with previous studies,[19-21] that reported a global increase in T1DM in younger age group. Although autoimmune diseases disproportionately affect female and above 10 years [22] in this study we have equal number of male and female. The plausible reasons for this might be other multiple factors like virus infection, atopy, vitamin D deficiencies, and changes in microbiomes contributing

to the pathogenesis of T1DM [20,23,24] .One third of the participants have systolic hypertension; this is similar to other study finding [25] , however in this study it affect younger age compared to previous studies. The hypertension could have been attributed by poor glycemic control, obesity and overweight as it has been documented from various studies that these factors were associated with hypertension [23,25,26] and our study 94% had poor glycemic control 7.5% were obese and 26.7% were overweight. The frequently follow up, screening and treatment cannot be underestimate as microvascular and microvascular diseases have been implicated as the leading cause of long term mortality morbidity [25,27,28] . These findings highlight the advantage of checking the blood pressure even for children less than 10 years, as one of the strategies we can use to reduce morbidity and mortality is to address the hypertension by early screening and start treatment earlier in order to prevent progression to cardiovascular and renal disorder. This is also important as hypertension is also risk factors for visual impairment through increased risk of developing diabetic retinopathy,[25,29,30] .

In this study most of children were having poor glycemic control similar to previous studies done in Tanzania,[31-33] and other African countries,[34,35] but contrary to studies done in high income countries[28,36] .Difference in glycemic control could have been caused by methods of insulin administration and insulin storage as in low income countries some setting might not have enough facility to store insulin especially in tropical region where high temperature can impairs insulin function. This subsequently leads to increase in visual impairment in this cohort. According to DCCT trial glycemic control is important in prevention of development of microvascular and microvascular disease and visual impairment. Poor glycemic control, in cohort could have been contributed by poor psychosocial support as the majority of these children were living with divorced parents with low or no formal education which also increases the risk of glycemic control as it has been reported in some studies [32,34,37,38] . Risk factors identified for progression of visual impairment younger age at diagnosis male sex , duration of T1DM for less than 5 years contrary to other studies which reported no relationship between age at diagnosis and duration of T1DM, the of T1DM as risk factors for refractive eyes disorder[4] .

The prevalence of cataract 9.3% is higher than previous reported,[4,13,14] this could have been caused by poor glycemic control and duration of diabetes as has been showing to have influence on cataract formation, as most of children and youth in this cohort has poor glycemic control.

Study limitation

The interpretations of the findings should be in line with the observed limitations. In cross-sectional studies, it is difficult to establish the temporal association between exposure and outcome. For instance, it was not known when non-ocular manifestation set in and how the trend of glycemic control has been since diagnosis and initiation of treatment.

We did not check for refractive error which could explain the reduction in visual acuity.

Conclusion

Non retinopathy ocular complication in T1DM are not uncommon in our setting, there is increased in hypertension and obesity in our setting most of children has uncontrolled glycaemia, and the rate of visual impairment is high.

Recommendation

We recommend screening of vascular disease and screening of non-retinopathy eye disorder by doing visual acuity screening.

A prospective cohort study to establish the other risk factor for non-retinopathy ocular complication of T1DM.

Declaration

Competing Interest: There are no competing interests for any author.

Data availability statement: Data may be made available upon reasonable request to the corresponding author.

Ethics statements: Patient consent informed written consent was obtained from youth and parents/ guardians of the children.

Ethics approval: Ethical clearance to conduct this study was obtained from the Kilimanjaro Christian Medical University College (KCMUCo) Ethical Clearance Committee and given a certificate No 2478.

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