• Investigation •

# Referral patterns of children with glaucoma and their caretakers in Northern Tanzania

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## Abstract

● **AIM:** To describe the referral patterns of children with primary childhood glaucoma (PCG) or secondary childhood glaucoma (SCG) and their presenting symptoms in Northern Tanzania.

● **METHODS:** A retrospective observational study of children <17y with PCG or SCG who were referred to Kilimanjaro Christian Medical Centre (KCMC) Eye Department between 2000 and 2013 was conducted. Presenting symptoms, age at presentation, place of origin, distance to hospital, type of glaucoma, visual acuity, optic disc appearance (vertical cup-to-disc ratio) and type of referral were described.

● **RESULTS:** Seventy patients with PCG and 27 patients with SCG were included in the study. Median age at first presentation was 1y in the PCG group (range 0-16y) and 9y in the SCG group (range 1-15y). In both groups around 87% of the children presented already with low vision (logMAR>0.48, better eye). Most of the children (60%) and their caretakers presented on their own initiative, while 24% were sent by different general health cadres and 16% by eye care professionals. Buphthalmos was the main symptom mentioned as a trigger for presentation.

● **CONCLUSION:** The study shows that most of the children presented late resulting in advanced stages of glaucoma at the time of initiation of treatment. The majority attended the referral eye department on their own initiative with buphthalmos being the most commonly described symptom. Awareness creation among caretakers of children, general health and eye care providers, ideally embedded in general child health promotion activities, is needed to increase and accelerate referrals.

● **KEYWORDS:** primary childhood glaucoma; secondary childhood glaucoma; referral; Africa
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## INTRODUCTION

The impact of childhood blindness is particularly tragic because children might live 40y longer without vision compared to those with adult-onset vision loss[1]. One of the highest rates of blind children worldwide are found in Africa[2-3]. Childhood glaucoma is one of the causes with an incidence of 2.29 per 100 000 residents younger than 20y in the United States[4].

Childhood glaucoma can be categorized into primary congenital glaucoma, which is caused by trabeculodysgenesis alone and juvenile open angle glaucoma as well as into secondary childhood glaucoma (SCG), where an outflow obstruction exists resulting from a different ocular or systemic condition[5-8]. Causes of SCG include congenital anomalies such as aniridia, Sturge-Weber syndrome, Axenfeld-Rieger syndrome, Peter's anomaly and acquired glaucomas including glaucoma due to previous surgery, aphakia, or ocular trauma[6,9-10]. The prognosis of children with primary[11] and secondary childhood[4,9] glaucoma is often very limited and therapy challenging. Furthermore, there is only little data available from low resource-settings with their distinctive challenges regarding health-seeking behavior and referral patterns for children with paediatric glaucoma. It is a rare disease but considering the number of 'blind years' makes it an important cause of childhood blindness in Africa[12].

A key factor is to detect the affected children early enough, which is a challenge particularly in low-resource settings. They can be characterized by a low awareness of the disease, limited access to and large travel distances to eye care services. Consequently, children present with already advanced disease and therefore limited prognosis even when treated.

A better understanding of health-seeking behavior, referral pattern and presenting symptoms is important to meet this key challenge. This study presents characteristics of the referral pathway and symptoms reported at presentation by affected children and their caretakers in Northern Tanzania.

## SUBJECTS AND METHODS

**Ethical Approval** Ethical approval was obtained from the College Research Ethics Review Committee of Kilimanjaro Christian Medical University College, Moshi, Tanzania, and the study was conducted in accordance with the Declaration of Helsinki. Because this study is a retrospective study no informed consent could be obtained by the patients.

A retrospective chart review of all patients with primary childhood glaucoma (PCG) or SCG who received a glaucomatous surgical intervention at the Department of Ophthalmology of Kilimanjaro Christian Medical Centre (KCMC) in Moshi, Tanzania was conducted. The Department provides paediatric eye care as one of few tertiary eye centres in Tanzania and serves a population of around 12 million people[13].

**Patient Selection** Paediatric glaucoma was defined if at least two of the following aspects were present: intraocular pressure (IOP) >21 mm Hg; an optic nerve cupping with increasing cup/disc ratio or asymmetry of cup/disc ratio or focal thinning; a cornea with Haab striae or increased diameter; myopic shift or visual field defects in older children. Because paediatric glaucoma treatment in rural areas is primarily surgical we were able to identify this children from manual theatre registries or the computer-based patient registry system of the eye department and included all children <17y who underwent a surgical intervention for primary or SCG between the years 2000 and 2013. PCG was defined as glaucoma caused by trabeculodysgenesis alone and SCG, where an outflow obstruction exists resulting from a different ocular or systemic condition or due to previous ocular surgery such as cataract surgery.

**Patient Examination** Visual acuity (VA) was typically measured with different methods depending on age. Fixation tests or testing the ability to follow light was used below one year; Cardiff VA charts from 1-3y, LEA Symbols from 4- to 6-years, Sheridan Gardiner charts between 6- to 7-years, and Snellen charts were used for children 7y and above. Low vision was defined as a VA of >0.48 logMAR in the better eye of children aged ≥4y. IOP was measured using a Schiötz tonometer in operating theatre, and since 2010 using an Icare tonometer (Icare, Finland) in theatre and in clinic. A short general anaesthesia using halothane for induction followed by isoflurane as the maintenance agent was performed for measurement of IOP as well as for handheld slit lamp examination and fundoscopy [including vertical cup/disc ratio (VCDR)]. At first presentation the child and accompanying caretakers were usually asked about the main symptoms which lead to presenting at KCMC Eye Department and if they have been referred. Main presenting symptoms were analysed and categorized as buphthalmos, epiphora/glare/corneal opacity, painful eye and loss of vision.

**Data Collection and Main Outcome Measures** Data collection included age at presentation, gender, place of origin, presenting symptoms and signs, type of referral, type of glaucoma, surgical intervention, IOP, total duration of follow-up and preoperative vertical cup/disc ratio if available. Distance to the hospital was estimated by the distance of the respective region of origin to the Kilimanjaro Christian Medical Center.

**Statistical Analysis** Proportions for the total group stratified by type of childhood glaucoma were calculated. The presence of normal distribution was tested with the Kolmogorov-Smirnov test. Mean and standard deviation, median and 25%-/75%-percentiles (Q1, Q3) and range were calculated and nonparametric statistics were used when applicable. Nominal parameters were compared by the Chi-square test. The unit of analysis were patients and two-sided tests were performed using $P \leq 0.05$ as statistically significant threshold. Statistical analyses were performed using SPSS 20.0 (SPSS Inc., Chicago, USA).

## RESULTS

Seventy patients (116 eyes) with PCG and 27 patients (36 eyes) with SCG were included in this study. Forty-six children (65.7%) with PCG and 21 children (77.8%) with SCG were male.

**Causes of Secondary Childhood Glaucoma** SCG was associated in 13 eyes (13 children) with ocular trauma, in 12 eyes (7 children) with cataract surgery, in 5 eyes (3 children) with congenital aniridia, in two eyes (one child) with Sturge-Weber syndrome, 2 eyes (1 child) with corticosteroid treatment, one eye with unspecified leucoma and one eye with uveitis. The results of the surgical interventions of our cohort (for PCG: goniotomy, trabeculotomy, transscleral cyclophotocoagulation, and trabeculectomy; for SCG: transscleral cyclophotocoagulation and trabeculectomy) were reported previously[14-15]. Types of glaucoma surgeries are presented in Tables 1 and 2.

**Age at Presentation** Median age at presentation of the 70 patients with PCG was 15mo (Q1, Q3: 4, 135mo). Patients with bilateral PCG (46 children) presented at an age of 10mo (Q1, Q3: 3.25, 24mo) compared to 115.5mo (Q1, Q3: 6.25, 177.5mo) in unilateral PCG (24 children) ($P$<0.001). Bilateral SCG presented at an age of 108mo (9 children) (Q1, Q3: 56, 160mo) compared to unilateral SCG (18) at 136mo (Q1, Q3: 99.75, 179.0mo; $P$=0.030; Figure 1). Patients with PCG were significantly younger than patients affected by SCG ($P$<0.001).

**Table 1 Type of referral depending on type of glaucoma, gender, distance to the hospital, age, preoperative IOP at presentation** *n* (%)

| Items | Ophthalmologist | General health cadres | Eye outreach | Self-referral | Total | *P* |
|---|---|---|---|---|---|---|
| Total number of patients | 13 (13) | 23 (24) | 3 (3) | 58 (60) | 97 | 0.68 |
| PCG | 9 (13) | 19 (27) | 2 (3) | 40 (57) | 70 | |
| SCG | 4 (15) | 4 (15) | 1 (4) | 18 (67) | 27 | |
| Gender | | | | | | 0.08 |
| Male | 6 (9) | 20 (30)[a] | 2 (3) | 39 (58) | 67 | |
| Female | 7 (23) | 3 (10)[a] | 1 (3) | 19 (63) | 30 | |
| Distance to hospital | | | | | | 0.12 |
| <100 km | 4 (8) | 10 (20) | 1 (2) | 36 (71)[a] | 51 | |
| ≥100 km | 9 (17) | 13 (28) | 2 (4) | 22 (48)[a] | 46 | |
| Age | | | | | | |
| <3y | 6 (14) | 15 (34)[a] | 0 | 23 (52) | 44 | 0.15 |
| 3 to 8y | 2 (13) | 2 (13)[a] | 0 | 11 (73) | 15 | |
| >8y | 5 (13) | 6 (16)[a] | 3 (8) | 24 (63) | 38 | |
| IOP, mm Hg | | | | | | 0.33 |
| 21 to 30 | 3 (9) | 12 (34) | 2 (6) | 18 (51) | 35 | |
| 31 to 40 | 4 (12) | 8 (24) | 0 | 22 (65) | 34 | |
| 41 to 50 | 3 (16) | 2 (11) | 1 (5) | 13 (68) | 19 | |
| >50 mm Hg | 3 (33) | 1 (11) | 0 (0) | 5 (56) | 9 | |
| Cup-disc ratio | | | | | | 0.32 |
| ≤0.5 | 5 (24) | 6 (29) | 1 (5) | 9 (43) | 21 | |
| 0.6 to 0.8 | 3 (14) | 3 (14) | 0 | 15 (71) | 21 | |
| ≥0.9 | 1 (4) | 5 (21) | 1 (4) | 17 (71) | 24 | |
| No measurement documented | 4 (13) | 9 (29) | 1 (3) | 17 (55) | 31 | |
| Corneal diameter | | | | | | 0.35 |
| <12 mm | 0 | 0 | 0 | 2 (100) | 2 | |
| 12 to 13 mm | 1 (25) | 0 | 0 | 3 (75) | 4 | |
| >13 mm | 0 | 2 (40) | 0 | 3 (60) | 5 | |
| No measurement documented | 12 (14) | 21 (24) | 3 (4) | 50 (58) | 86 | |
| Type of surgery | | | | | | 0.23 |
| Goniotomy | 7 (21) | 10 (29) | 0 | 17 (50) | 34 | |
| Trabeculotomy | 0 | 0 | 0 | 5 (100) | 5 | |
| Transscleral cyclophotocoagualtion | 3 (14) | 2 (9) | 1 (5) | 16 (73) | 22 | |
| Trabeculectomy | 3 (8) | 11 (31) | 2 (6) | 20 (56) | 36 | |

IOP: Intraocular pressure; PCG: Primary childhood glaucoma; SCG: Secondary childhood glaucoma. [a]Significant difference between the two groups ($P \leq 0.05$).

**Visual Acuity, Intraocular Pressure and Cup-to-disc Ratio** Overall, low vision (logMAR>0.48) was observed in children with documented best corrected visual acuity at first presentation (age ≥4y) in 87% (20/23) and 87.5% (21/24) of the PCG and SCG group, respectively.

IOP was higher in SCG patients compared to PCG patients [PCG median IOP 31 (Q1, Q3: 24, 39.7) mm Hg *vs* SCG 38 (Q1, Q3: 29.3, 47.8) mm Hg; $P$=0.002]. VCDR was significantly larger in PCG patients than in SCG patients [VCDR PCG median 0.8 (Q1, Q3: 0.5, 0.9) *vs* SCG median 0.6 (Q1, Q3: 0.4, 0.8); $P$=0.007].

**Type of Referral** Totally 60% of patients with childhood glaucoma came without being referred by a clinician (self-referral), 24% were sent by a general health cadres and 13% by an ophthalmologist, and 3 patients were detected during an outreach clinic (3%). Data on referral pattern stratified for PCG/SCG, sex, distance to the hospital, age at examination, preoperative IOP, preoperative VCDR, corneal diameter and type of surgery are presented in Table 1. Infants with a travel distance less than 100 km presented more frequently following the initiative of their parents (self-referral).

**Symptoms at Presentation** Buphthalmos was the most common reason followed by loss of vision and corneal opacity observed by parents. A painful eye was reported by 12 children (12%) as reason for referral. Buphthalmos was significantly more often reported as reason for presentation in children with

**Table 2 Main symptoms at first presentation as reported by parents or children** *n* (%)

| Items | Buphthalmos | Corneal opacity | Painful eye | Visual loss | Total | *P* |
|---|---|---|---|---|---|---|
| Total number of patients | 31 (32) | 25 (26) | 12 (12) | 29 (30) | 97 | 0.001 |
| PCG | 29 (42)[b] | 16 (23) | 4 (6)[b] | 21 (30) | 70 | |
| SCG | 2 (7)[b] | 9 (33) | 8 (30)[b] | 8 (30) | 27 | |
| Gender | | | | | | 0.16 |
| Male | 21 (31) | 13 (19)[a] | 9 (13) | 24 (36) | 67 | |
| Female | 10 (33) | 12 (40)[a] | 3 (10) | 5 (17) | 30 | |
| Distance to hospital | | | | | | 0.23 |
| <100 km | 15 (29) | 10 (20) | 9 (18) | 17 (3%) | 51 | |
| ≥100 km | 16 (35) | 15 (33) | 3 (7) | 12 (26) | 46 | |
| Age | | | | | | <0.001 |
| <3y | 26 (59)[c] | 14 (32) | 0[b] | 4 (9)[c] | 44 | |
| 3 to 8y | 3 (20)[c] | 4 (27) | 2(13)[b] | 6 (40)[c] | 15 | |
| >8y | 2 (5)[c] | 7 (18) | 10 (26)[b] | 19 (50)[c] | 38 | |
| IOP, mm Hg | | | | | | 0.73 |
| 21 to 30 | 13 (37) | 9 (26) | 3 (9) | 10 (28) | 35 | |
| 31 to 40 | 8 (24) | 11 (32) | 4 (12) | 11 (32) | 34 | |
| 41 to 50 | 8 (42) | 3 (16) | 4 (21) | 4 (21) | 19 | |
| >50 | 2 (22) | 2 (22) | 1 (11) | 4 (45) | 9 | |
| Cup-disc ratio | | | | | | 0.16 |
| ≤0.5 | 10 (48) | 6 (29) | 1 (5) | 4 (19) | 21 | |
| 0.6 to 0.8 | 7 (33) | 5 (24) | 5 (24) | 4 (19) | 21 | |
| ≥0.9 | 7 (29) | 4 (17) | 2 (8) | 11 (46) | 24 | |
| No measurement documented | 7 (23) | 10 (32) | 4 (13) | 10 (32) | 31 | |
| Corneal diameter | | | | | | 0.55 |
| <12 mm | 2 (100) | 0 | 0 | 0 | 2 | |
| 12 to 13 mm | 3 (75) | 1 (25) | 0 | 0 | 4 | |
| ≥13 mm | 2 (40) | 1 (20) | 1 (20) | 1 (20) | 5 | |
| No measurement documented | 24 (28) | 23 (27) | 11 (13) | 28 (33) | 86 | |
| Type of surgery | | | | | | <0.001 |
| Goniotomy | 20 (59)[c] | 10 (29) | 0[a] | 4 (12)[b] | 34 | |
| Trabeculotomy | 4 (80)[c] | 1 (20) | 0[a] | 0[b] | 5 | |
| Transscleral cyclophotocoagualtion | 3 (14)[c] | 5 (23) | 6 (27)[a] | 8 (36)[b] | 22 | |
| Trabeculectomy | 4 (11)[c] | 9 (25) | 6 (17)[a] | 17 (47)[b] | 36 | |

At first presentation all patients or parents were asked about the one main symptom leading to presentation like buphthalmos, cornea haziness, painful eye, and visual loss. PCG: Primary childhood glaucoma; SCG: Secondary childhood glaucoma. IOP: Intraocular pressure. [a]*P*<0.05; [b]*P*<0.01; [c]*P*<0.001.

PCG (42%) versus SCG and in patients aged below 3y (59%). A painful eye was reported more commonly by children with SCG (30%) as well as in older children (over 2-year old patients). The main symptoms at presentation are shown in Table 2.

**Travel Distance to the Eye Hospital and Follow up of Children** Median travel distance to the eye unit of all patients was 80 km. Almost one third of the children and their caretakers had to travel more than 300 km (Figure 2). Median travel distance of PCG patients was 122 km (Q1, Q3: 47, 408 km) and for SCG 63.5 km (Q1, Q3: 36, 356 km).

Travel distance did not differ in terms of type of glaucoma (*P*=0.20) and sex (*P*=0.36). However, younger patients with age below 3y had a median travel distance of 260 km (Q1, Q3: 63.5, 584 km) compared to a travel distance of 80 km (Q1, Q3: 36, 260 km) for children with age of ≥3y (*P*=0.006).

Overall, 35/70 (50%; after one year) and 23/70 (32%; after two years) of the children with PCG and 18/27 (66%; after one year) and 10/27 (37%; after two years) of the children with SCG returned after their first visit for follow up examinations.

Mean overall follow up duration for patients with PCG was 25.8±37.8mo (Q1, Q3: 2, 39mo; range 0-169) and for SCG 23.3±25.9mo (Q1, Q3: 7, 28mo; range 0-100; *P*=0.30). No association was found between duration of follow up and sex,

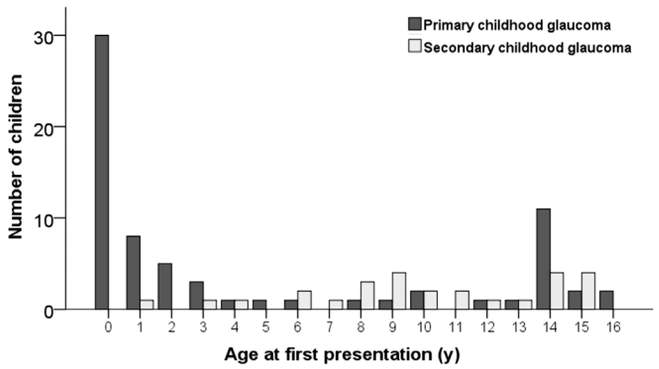


**Figure 1 Distribution of age at presentation stratified for patients with primary and SCG.**

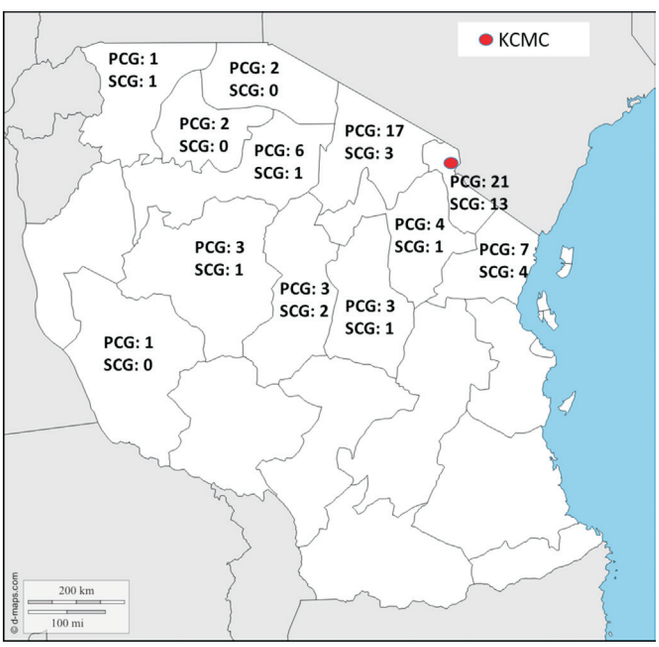


**Figure 2 Regions of origin in Tanzania for patients with primary and SCG who accessed KCMC.**

age, type of glaucoma, travel distance, IOP at first presentation and reasons for presentation. Children with more than 10mo of follow up predominantly had to travel less (300 km, 81%, 38/47) as opposed to 19% (9/47) who came from far (>300 km, $P$<0.05). The proportion of infants with follow up at 24mo was higher when they were referred by an ophthalmologist 69% (9/13) or by self-referral 60% (35/58) than when they were referred by general health cadres 39% (9/23).

## DISCUSSION

This study presents data on referral patterns of children with primary or SCG in Tanzania. About 60% of all children and their caretakers came on their own initiative, 16% were referred by an ophthalmologist or from eye outreaches, while 24% were sent by general health cadres. This might be due to the fact that around 38 ophthalmologist serve 48 million people in Tanzania[16], while about 2300 general health physicians work in the country[17].

There are several reports of late presentation and treatment which lead to advanced glaucoma in low-resource settings[18-19]. This was also shown by the advanced age at first presentation and the advanced stage of glaucoma in children with PCG and SCG in this study. Moreover, Li *et al*[20] reported a difference in time delay between boys and girls, and in outcomes after surgical intervention favouring males. Comparable to their findings, more than 2/3 of patients in this study were male, while epidemiological studies report comparable prevalence, at least for PCG, which might indicate less attendance of girls[3].

The main symptom recognized by relatives and leading to presentation was buphthalmos, which is a late symptom. PCG is a rare congenital disease and presentation at an age of 15mo is relatively late compared to high-income countries[21-23].

To overcome the problem of late diagnosis in general, broad-based community and national outreach programmes as well as awareness campaigns and reimbursements of travel expenses were performed in Tanzania to detect people in need of treatment[18]. However, despite these different efforts finding and following up affected children remains a challenging task in the region particularly in rural areas.

It may be beneficial to train general health care cadres such as community nurses on symptoms of paediatric eye diseases including paediatric glaucoma to detect and subsequently refer these children earlier.

In the present study, one third of the patients had travel distances of more than 300 km, which underpins the struggle of children and their caretakers to reach referral eye care centres. There are currently around three referral eye centres and more are planned offering comprehensive treatment of childhood glaucoma in Tanzania. Travel distance to the hospital was previously found to be the main reason for delay in presentation in patients with paediatric cataract[24], and may be a predisposing factor for children with glaucoma for advanced and/or irreversible stages of glaucoma at first presentation. This study showed a correlation between travel distance and duration of follow up. A distance of several hundred kilometres often means a travel time of several days. Overall, only one third of all patients returned for follow-up after two years. A previous study has shown that in 30 eyes of 16 patients progression of PCG can still occur in up 29% of the patients after 10y[25], which shows the importance of long term follow up in congruence to other reports[26-27].

Our study has several limitations including the retrospective hospital-based study design with a possible selection bias omitting all children who did not access the hospital. A large time interval was chosen to include a representative number of patients. In conclusion, children with childhood glaucoma and their caretakers presented predominantly on their own initiative for treatment with buphthalmos as the most common chief symptom. One of the key aims of the new WHO World Report on Vision is integrated people-centred eye care *e.g.* the

integration of eye care programs into national health plans, and there are moves in Tanzania to include eye assessment in training curricula of staff providing primary level child health services such as WHO's Integrated Management of Childhood Illness. Within this, awareness of signs and symptoms such as buphthalmos, glare or epiphora could help prevent needless childhood blindness and low vision from glaucoma.

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**Availability of Data and Material** The datasets generated and/or analysed during the current study are not publicly available due to internal regulations.

**Authors' contributions:** Fieß A and Philippin H designed the study. Fieß A did the data acquisition and Fieß A, Godfrey F, Schuster AK, Bowman R, Philippin H analyzed the data. Fieß A drafted the manuscript, all authors revised it critically and approved the final version. All authors agreed to be accountable for all aspects of the work.

**Conflicts of Interest: Fieß A,** None; **Godfrey F,** None; **Schuster AK,** None; **Bowman R,** None; **Philippin H,** None.

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