

# Prevalence and Factors Associated with Dry Eyes Syndrome in Glaucomatous Patients on Anti-Glaucoma Eye Drops Followed up at the Garoua Regional Hospital-Northern Cameroon

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## Abstract

**Background:** Dry eye and glaucoma are two common pathologies in the elderly, and are very often associated. This association suggests a link between them and between their treatments. Our purpose for this study is to determine the prevalence of dry eye in our glaucoma patients treated with eye drops and deduce the factors associated with it. **Patients and Methods:** We conducted a cross-sectional, analytical study from October 2022 to September 2023 in the ophthalmology department of Garoua Regional Hospital in glaucoma patients aged over 15 years able to answer the Ocular Surface Disease Index (OSDI) questionnaires and treated with antiglaucoma eye drops for more than 3 months. These patients underwent a complete ophthalmological examination and a tear film break-up time test. **Results:** A total of 73 patients (146 eyes) were examined. The average age of the patients was  $47.2 \pm 16.5$  years, with a male predominance of 54.8%. The prevalence of dry eye syndrome in our patients according to the OSDI score was 56.2% (95% CI) (44.8; 67.6). The prevalence of dry eye syndrome on clinical examination of the BUT in the right eye was 83.7% (95% CI) (75.1; 92.1) and 79.4% (70.2; 88.7) in the left eye. The duration of antiglaucoma treatment was the factor associated with dry eye syndrome ( $p < 0.05$ ) in glaucoma patients in our setting. **Conclusion:** Dry Eye Syndrome is common in glaucoma patients on drops in our setting. Treatment duration of more than 1 year seems to be associated with dry eyes.

## Keywords

Dry Eyes, Glaucoma, Conservative Eye Drops Médications, Garoua-Cameroon

## 1. Introduction

Dry Eye syndrome (DES) is a multifactorial disorder of the eye characterized by the inability to produce tears of high quality or sufficient quantity to hydrate the ocular surface [1]. It is responsible for discomfort, visual disturbance and tear film instability, with potential damage to the ocular surface [2]. Its prevalence varies from 5% to 50% worldwide. It is 75.9% in patients aged 40 or over followed up at the Yaoundé Central Hospital [3]. DES is more frequent in the elderly and in women [1]. Glaucoma is a blinding disease. It mainly affects people aged 40 and over, and is generally treated with hypotensive single- or multiple-application eye drops [4]. Some studies have identified advanced age, duration of glaucoma treatment, multiple therapies and the preservative Benzalkonium Chloride as the main risk factors for DES in glaucoma patients [5]. DES has an impact on medication compliance and quality of life in glaucoma patients [6]. Few studies have been carried out in Cameroon on DES in glaucoma patients. The aim of our study is therefore to determine the prevalence of dry eye syndrome in glaucoma patients taking hypotonizing eye drops, and to deduce the associated factors in our environment.

## 2. Materials and Method

We conducted a cross-sectional, analytical study from October 2022 to September 2023 in the ophthalmology department of the Garoua Regional Hospital (GRH) after obtaining research authorization and ethical clearance. The sample size was calculated using Open Epi software, taking into account the hospital prevalence of glaucoma of 5.5% according to Ellong *et al.* in 2006 [7], the number of patients admitted to the outpatient department of the HRG ophthalmology service at 22,000, we considered a minimum sample of 73 patients for a confidence interval of 95% and a precision threshold of 1%.

### 2.1. Sampling Procedure

We recruited all patients presenting to our consultation during the study period who had been diagnosed with glaucoma. Patients being monitored for glaucoma in our department were also invited by telephone to be examined and complete the OSDI questionnaire. Once present, they were selected according to defined criteria. Each patient completed a questionnaire to assess the OSDI score, and underwent a complete ophthalmological examination and tear film break-up time test. The Ocular Surface Disease Index (OSDI), developed by the Outcomes Research Group at Allergan Inc (Irvine, Calif), is a 12-item questionnaire designed to provide a rapid assessment of the symptoms of ocular irritation consistent with dry eye disease and their impact on vision-related functioning. The 12 items of the OSDI questionnaire were graded on a scale of 0 to 4, where 0 indicates none of the time; 1, some of the time; 2, half of the time; 3, most of the time; and 4, all of the time [8]. The total OSDI score was then calculated on the basis of the following formula:  $OSDI = [(sum\ of\ scores\ for\ all\ questions\ an-$

swered)  $\times$  100]/[(total number of questions answered)  $\times$  4] [8]. The questionnaire consisted of 12 questions divided into three sections: frequency of symptoms, effects of symptoms on daily tasks and effect of environmental factors such as wind and air conditioning [8]. The total score was classified for severity as follows: normal ( $\leq 12$ ), mild (13 - 22), moderate (23 - 32) or severe ( $> 32$ ) [8].

All glaucoma patients over 15 years of age who gave oral and/or written consent and were able to answer the OSDI questionnaires, and who had been treated with hypotensive eye drops for more than 3 months, were included.

Patients with palpebral abnormalities and/or recent infection (less than 3 months), recent palpebral trauma, ocular surface trauma, cataract surgery or glaucoma of the eye were excluded. Patients answered a French version of the questionnaire to assess the OSDI score through an interview conducted by us. For patients who did not understand French, the questions asked were translated by a senior ophthalmology nurse into the local Fulfulde language. Patients reported the type and number of eye drops used for glaucoma treatment. Each patient received the following examinations:

- Eyelid examination was performed to look for blepharitis, Meibomian gland dysfunction, palpebral telangiectasia, palpebral malposition or eczema,
- Conjunctival examination Conjunctival hyperemia was noted. Conjunctival folds were noted before and after fluorescein testing of the bulbar conjunctiva in the area perpendicular to the temporal and nasal limbus above the lower eyelid.

## 2.2. Fluorescein Test

The ocular surface was assessed by imbibing a single-use fluorescein strip in the conjunctival cul-de-sac after instillation of a drop of anesthetic (propacaine) to detect conjunctival and corneal lesions. The BUT was also the time (in seconds) between a blink and the appearance of a dark spot in the in fluorescein. The BUT was classified as normal ( $> 10$  mm), minimal to moderate (6 to 10 mm) and severe ( $< 5$  mm).

We investigated factors that might influence OSDI score, Dry Eye signs and ocular surface alteration. These factors were age and gender, duration of glaucoma treatment, number of molecules (we noted fixed or separate combination in case of multiple therapies), types of molecules and the presence of Benzalkonium chloride).

## 2.3. Statistic Analysis

Collected data were entered into a statistical software and analyzed using the IBM SPSS (Statistical Package for Social Sciences) version 23.0. The qualitative data were presented in the form of numbers or proportions, the quantitative data on average or median. The qualitative variables were compared with the exact Fischers test and the qualitative variables using the Student's test or the non-parametric Mann-Whitney test. The factors associated with Dry Eye Syn-

drom found in our glaucomatous patients after the univariate analysis was put into the same logistic regression model to determine the independent factors associated with sickle cell retinopathy. The threshold of significance was set at  $p$  value  $\leq 0.05$ .

### 3. Results

We examined 73 patients (146 eyes) (See **Table 1**).

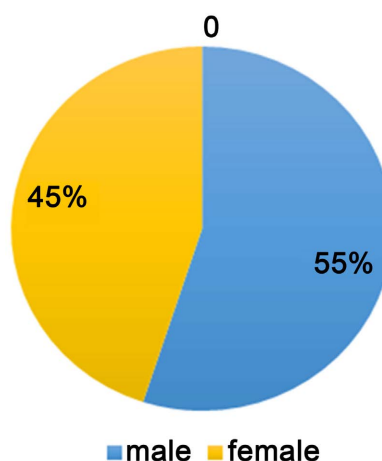
**Table 1.** Distribution of patients by profession.

| Patient professions | Frequency | Percentage% |
|---------------------|-----------|-------------|
| Pupil/student       | 11        | 15.1        |
| Informal            | 25        | 34.2        |
| Civil servant       | 14        | 19.2        |
| Retired             | 08        | 11.0        |
| No profession       | 15        | 20.5        |

#### 3.1. Sociodemographic Data

The average age of glaucoma patients followed at the GRH is  $47.2 \pm 16.5$  years.

Sex ratio was 1.2 in favor of women (See **Figure 1**).



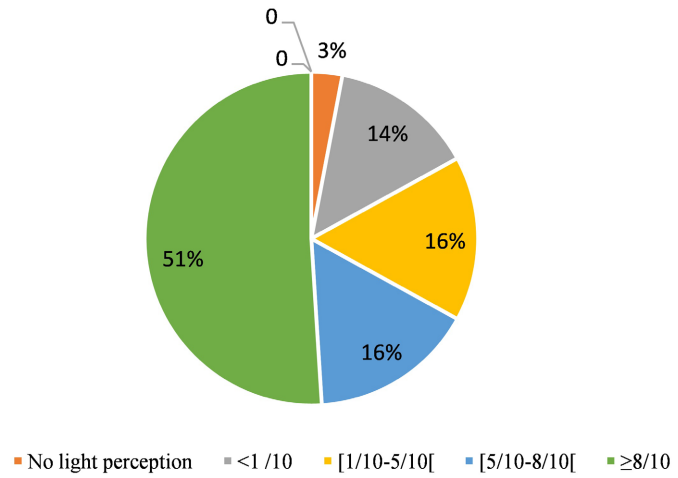
**Figure 1.** Distribution of patients by gender.

#### 3.2. Clinical Data

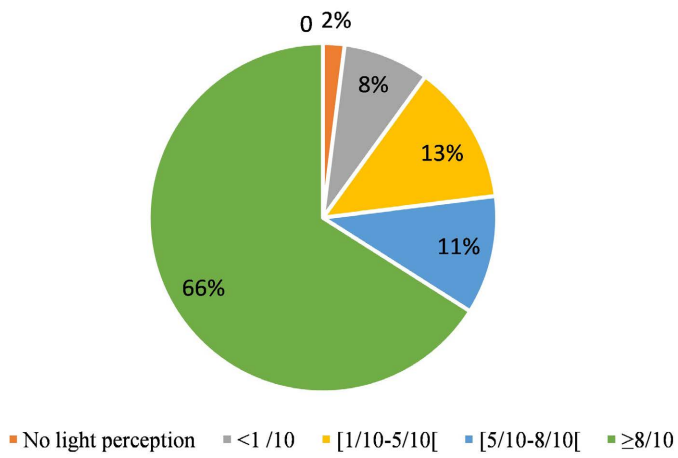
In our series, most of our glaucomatous patients has central visual acuity conserved: more than 8/10 (55% at the right eye and 66% at the left eye) (See **Figure 2** and **Figure 3**).

Glaucoma patients with subjective signs of dry eye according to the OSDI score accounted for 56.1% of cases (See **Table 2**).

In the right eye, we observed ocular dryness in our glaucoma patients through BUT examination in 83.5% of cases (See **Table 3**).



**Figure 2.** Distribution of patients' visual acuity in the right eye.



**Figure 3.** Distribution of patients' visual acuity in the left eye.

**Table 2.** Distribution of patients according to their OSDI score.

| OSDI Score                      | Frequency | Percentage % |
|---------------------------------|-----------|--------------|
| Normal                          | 32        | 43.8         |
| Light (score between 13 and 22) | 15        | 20.1         |
| Moderate (between 23 and 32)    | 15        | 20.1         |
| Severe ≥ 33                     | 11        | 15.1         |
| Total                           | 73        | 100          |

**Table 3.** Distribution of patients according to BUT evaluation in the right eye.

| BUT of right eye                   | Frequency | Percentage % |
|------------------------------------|-----------|--------------|
| Normal ≥ 10                        | 12        | 16.4         |
| Light to moderate between 5 and 10 | 45        | 61.6         |
| Severe < 5                         | 16        | 21.9         |
| Total                              | 73        | 100          |

In the left eye, we observed ocular dryness in our glaucoma patients through BUT examination in 79.5% of cases (See **Table 4**).

**Table 4.** Distribution of patients according to BUT evaluation in the left eye.

| BUT of left eye                    | Frequency | Percentage % |
|------------------------------------|-----------|--------------|
| Normal $\geq 10$                   | 15        | 20.5         |
| Light to moderate between 5 and 10 | 43        | 58.9         |
| Severe $< 5$                       | 15        | 20.5         |
| <b>Total</b>                       | <b>73</b> | <b>100</b>   |

In both eyes frequent corneal lesions were punctuated superficial keratitis (**Table 5**).

**Table 5.** Distribution of patients according to corneal lesions in each eye.

|                                  |                                 | Corneal lesions of the left eye |            |                       | Total     |
|----------------------------------|---------------------------------|---------------------------------|------------|-----------------------|-----------|
|                                  |                                 | Punctuate superficial keratitis | No lesions | Filamentous keratitis |           |
| Corneal lesions of the right eye | No lesions                      | 3                               | 32         | 0                     | 35        |
|                                  | Punctuate superficial keratitis | 30                              | 3          | 1                     | 34        |
|                                  | Filamentous keratitis           | 1                               | 0          | 3                     | 4         |
|                                  | <b>Total</b>                    | <b>34</b>                       | <b>35</b>  | <b>4</b>              | <b>73</b> |

**Table 6.** Factors associated with dry eye in glaucoma patients.

| Associated factors                              | Ocular dryness |        | P value |
|---|----------------|--------|---------|
|   | Present        | Absent |         |
| Age more than 40 years                          | 27             | 23     | 0.84    |
| <b>Sex</b>                                      |                |        | 0.66    |
| <b>Female</b>                                   | 19             | 14     |         |
| <b>Male</b>                                     | 21             | 19     |         |
| <b>Antiglaucomatous eye drop</b>                |                |        | 0.06    |
| <b>Conservative eye drop</b>                    | 33             | 21     |         |
| <b>Non conservative eye drop</b>                | 07             | 12     |         |
| <b>Treatment duration of more than one year</b> | 29             | 11     | 0.001   |
| <b>Good therapeutic compliance</b>              | 22             | 20     | 0.63    |
| <b>Number of instillations drops per day</b>    |                |        | 0.75    |
| <b>One instillation per day</b>                 | 29             | 25     |         |
| <b>More than one instillation per day</b>       | 11             | 8      |         |
| <b>Presence of meibomitis/blepharitis</b>       | 21             | 14     | 0.39    |

Meibomian gland dysfunction was found in 35 (47.9%) patients. Compliance was found in 55.7% of patients. The average duration of antiglaucoma treatment was 2.9 years, with a minimum of 01 year and a maximum of 13 years. Patients with a treatment duration of more than one year accounted for 83.5% of cases.

### 3.3. Prevalence of DES

The prevalence of dry eye in our patients according to the OSDI score was 69.8 (59.3; 80.4)% (95% CI) (**Table 1**). The prevalence (95% CI) of dry eye on clinical examination of the BUT in the right eye was 83.7% (75.1; 92.1) and 79.4% (70.2; 88.7)% in the left eye (**Table 2** and **Table 3**).

## 4. Discussion

The limitation of our study is that we didn't know the previous state of our patients' ocular surface before they were put on antiglaucoma eye drops.

At the end of our study, we can say that the average age of glaucoma patients followed at the GRH is  $47.2 \pm 16.5$  years, with a male predominance of 54.8% (**Figure 1**). Patients aged 40 and over account for 68.5% in our study population. The prevalence of dry eye in our patients according to the OSDI score was 69.8 % (**Table 1**) and 83.7% on clinical examination of the BUT in the right eye, 79.4% in the left eye (**Table 2** and **Table 3**). They mostly have retained central vision (**Table 4** and **Table 5**). These patients are treated with preserved antiglaucoma eye drops in 74% of cases and with non-preserved drops in 26% (**Table 6**). Our patients were compliant with treatment in 57.5% of cases (**Table 6**). Meibomitis or blepharitis was present in 47.9% of patients, and corneal lesions (KPS and filamentous keratitis) were present in 57.5% on slit-lamp examination. The frequency of dry eye in glaucoma patients is reflected in the literature, which notes that patients treated for chronic glaucoma or HTO frequently present with ocular surface damage [9]. Emmanuel Kobia-Acquah *et al.* in Ghana found a mean age of  $60.44 \pm 14.05$  years in 2021 in a hospital study in which dry eye in glaucoma patients was assessed [7]. In Ethiopia, the mean age for a similar study in 2021 was  $62.2 \pm 11.58$  years [10]. In these African studies, we find a higher mean age, probably because these are countries with a slightly larger sample size than ours. Miraf Shalu and Abeba T Giorgis in Ethiopia in 2021 [10] found similar proportions of men and women, but Emmanuel Kobia-Acquah and al in Ghana found that 60% were women [7]. The prevalence of dry eye in our patients according to the OSDI score is lower than that found in the BUT clinical examination. This is because the OSDI score is a subjective assessment of dry eye, and questions about vision can be confusing in elderly patients who also have cataracts. The corneal sensitivity of glaucoma patients treated with eye drops seems to be diminished [9]. This may explain why subjective dry eye symptoms may be less common than lesions on the ocular surface. Meibomian gland dysfunction is found in 47.9% of patients. In a hospital study carried out in Douala, Cameroon, in 2017 on patients aged 50 and over, Omgbwa and al found a prevalence of meibomian gland dysfunction of 71.8% [11], much higher

than ours due to the target population, which in this study was over 50 years of age and more likely to have dry eyes. Most of our patients, 51 (72.9%), used preserved eye drops. BAK is the most commonly used preservative. BAK is implicated in the initiation or aggravation of ocular surface disease, and is weakly allergenic, with both time- and dose-dependent toxicity on the conjunctiva and cornea [2] [12]. It can trigger or aggravate ocular surface disease by destabilizing calciform cells and, subsequently, the tear film, inducing squamous metaplasia of the conjunctival epithelium, disrupting the corneal epithelium by reducing epithelial cell density and increasing activation of stromal keratocytes [9]. Pisella *et al.*, in a study involving 249 ophthalmologists following 4017 glaucoma patients in 2002, showed that the exclusive use of preservative-free eye drops, or even a reduction in the number of preserved eye drops used, clearly reduced signs of ocular surface irritation in glaucoma [13].

In addition, adverse changes in tear film stability, tear osmolarity, conjunctival hyperemia and eyelid margins were observed in treated eyes. This suggests that inflammatory mechanisms may be involved in the development of dry eye in patients receiving long-term topical antiglaucoma therapy [14] [15]. The duration of antiglaucoma treatment (more than one year) and the type of eye drops (preserved or not) are factors associated with dry eye according to the OSDI score and the BUT. In a 2017 European study, Francisco Pérez-Bartholomé *et al.* also identified advanced age as a factor associated with dry eyes [16]. Emmanuel Kobia-Acquah *et al.* in Ghana found age, duration of antiglaucoma treatment, type of preservative used and number of ocular instillations to be associated factors [7]. More recently, in 2020, Nijm *et al.* noted that signs and symptoms of ocular surface disease were relatively frequent in elderly patients, but signs of ocular surface disease were significantly higher in people instilling topical glaucoma treatment [17]. In a Turkish study involving a survey of ophthalmologists, variable rates of ocular surface disease in glaucoma patients were found to be a function of chronic consumption of preservatives.

Duration of antiglaucoma treatment (longer than one year), type of eye drops (preserved or not) are factors associated with dry eye according to OSDI score and BUT. In a 2017 European study, Francisco Pérez-Bartholomé *et al.* also identified advanced age as a factor associated with dry eyes [16]. Emmanuel Kobia-Acquah *et al.* in Ghana found age, duration of antiglaucoma treatment, type of preservative used and number of ocular instillations to be associated factors [7]. More recently, in 2020, Nijm *et al.* noted that signs and symptoms of ocular surface disease are relatively frequent in elderly patients, but signs of ocular surface disease are significantly higher in people instilling topical glaucoma treatment [16]. In a Turkish study involving a survey of ophthalmologists, variable rates of ocular surface disease in glaucoma patients were found to be a function of chronic drug use and exposure to alcohol [18].

## 5. Conclusion

Dry eye is common in our setting in glaucoma patients on antiglaucoma drops,



according to the subjective criteria of the OSDI score and clinical examination of the cornea, and by the BUT test. Our patients presented with ocular surface lesions on ophthalmological examination mostly used eye drops preserved with BAK. Treatment duration of more than a year seems to be the factor that favors this dry eye. We therefore recommend that glaucoma patients undergo an ocular surface examination before starting antiglaucoma eye drops, and that non-preserved eye drops be used as much as possible for long-term follow-up.

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### Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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## Appendix

| Ocular Surface Disease Index <sup>®</sup> (OSDI-12) |   |                        |                         |                         |                         |                         |            |
|---|---|------------------------|-------------------------|-------------------------|-------------------------|-------------------------|------------|
| Item  | Have you experienced any of the following during the last week?                                   | All of the time        | Most of the time        | Half of the time        | Some of the time        | None of the time        |            |
| 1   | Eyes that are sensitive to light?   | 4                      | 3                       | 2                       | 1                       | 0                       |            |
| 2   | Eyes that feel gritty?  | 4                      | 3                       | 2                       | 1                       | 0                       |            |
| 3   | Painful or sore eyes?   | 4                      | 3                       | 2                       | 1                       | 0                       |            |
| 4   | Blurred vision?   | 4                      | 3                       | 2                       | 1                       | 0                       |            |
| 5   | Poor vision?  | 4                      | 3                       | 2                       | 1                       | 0                       |            |
|   | <b>Have your eyes felt uncomfortable in any of the following situations during the last week?</b> | <b>All of the time</b> | <b>Most of the time</b> | <b>Half of the time</b> | <b>Some of the time</b> | <b>None of the time</b> | <b>N/A</b> |
| 6   | Reading?  | 4                      | 3                       | 2                       | 1                       | 0                       | N/A        |
| 7   | Driving at night?   | 4                      | 3                       | 2                       | 1                       | 0                       | N/A        |
| 8   | Working with a computer or bank machine (ATM)?  | 4                      | 3                       | 2                       | 1                       | 0                       | N/A        |
| 9   | Watching TV?  | 4                      | 3                       | 2                       | 1                       | 0                       | N/A        |
|   | <b>Have your eyes felt uncomfortable in any of the following situations during the last week?</b> | <b>All of the time</b> | <b>Most of the time</b> | <b>Half of the time</b> | <b>Some of the time</b> | <b>None of the time</b> | <b>N/A</b> |
| 10  | Windy conditions?   | 4                      | 3                       | 2                       | 1                       | 0                       | N/A        |
| 11  | Places or areas with low humidity (very dry)?   | 4                      | 3                       | 2                       | 1                       | 0                       | N/A        |
| 12  | Areas that are air conditioned?   | 4                      | 3                       | 2                       | 1                       | 0                       | N/A        |