Original Research Article

Assessment of risk factors for primary open-angle glaucoma: About 100 cases.

Abstract:

Introduction: primary open-angle glaucoma (POAG) is a chronic and progressive anterior optic neuropathy characterized by perimetric alterations and pathological excavation of the optic disc in the absence of other ocular pathologies or congenital anomalies. It is usually accompanied by an increase in intraocular pressure. Gonioscopic examination confirms that the iridocorneal angle is open. The term "risk factor" is defined as a condition statistically leading to an increased risk of occurrence of an event. The purpose of our work is to list the main risk factors of POAG.
Patients et methods: This is a retrospective study carried out in our ophthalmology department over a period of 4 years between January 2018 and December 2021, involving one hundred patients with POAG followed in glaucoma consultation.
Results: These are 100 cases, with an average age of 64.27, with a male predominance. The most found risk factors in our series are: age, intraocular hypertension (IOH), thin cornea, arterial hypertension, diabetes and family history of glaucoma.
Conclusion: The identification of the main risk factors of POAG at the individual level is a major data of the management. Knowing these factors helps to monitor patients at risk more carefully and to adjust the treatment more appropriately in patients likely to develop glaucoma or to aggravate already known glaucoma.

Key words: Glaucoma, primary open-angle glaucoma, intraocular hypertension, risk factors, heredity, arterial hypertension, diabetes.

Introduction:

Primary open-angle glaucoma (POAG) is a chronic and progressive anterior optic neuropathy characterized by perimetric alterations and pathological excavation of the optic disc, in the absence of other ocular pathologies or congenital anomalies **[1]**.
It is generally accompanied by an increase in intraocular pressure (IOP), the importance of which increases the relative risk of POAG.
Gonioscopic examination confirms that the iridocorneal angle is open. The term "risk factor" is defined as a condition statistically leading to an increased risk of occurrence of an event.
The aim of our work is to enumerate the main risk factors of POAG in patients followed in specialist consultation in glaucoma.

Patients and methods:

This is a descriptive retrospective study carried out in the ophthalmology department of the Moulay Ismail military hospital in Meknes. We included in our study 100 patients with primary open-angle glaucoma who were followed on an outpatient basis in a specialized glaucoma consultation, over a period of 4 years between January 2018 and December 2021.

We excluded patients with secondary open-angle glaucoma, closed-angle glaucoma, and patients with lost records or missing information.
All patients underwent a complete and bilateral ophthalmological examination
Data collection is carried out using an exploitation sheet. Data analysis is done in EXCEL.

Results:

Age: The average age of the hundred followed patients is 64.27 +/- 21 with age extremes of 14 to 89 years. Patients over the age of sixty represent the most affected age group (61.7%) (**figure 1**).
The gender: The distribution of patients by gender shows a male predominance with: 71% of men (71 cases) and 29% of women (29 cases) (**Figure 2**).
Intraocular pressure (IOP): The IOP is measured in all our patients by the Goldmann applanation tonometer. Corrected IOP values vary between 16 mmHg and 57 mmHg, with an average of 26.74 mmHg ± 5.76. Most eyes (85%) have corrected IOP between 22mmHg and 30mmHg.
Pachymetry: The central corneal thickness is measured with contact using an ultrasonic pachymeter, this measurement allows us to correct the value of the measured IOP.
The average pachymetry is 532.24 +/- 36.45 um (**table 1**) and 55% of patients have a corneal thickness less than 530 um (**figure 3**).
Other risk factors (Figure 4):
- Melanoderma is found in 11% (11 cases).
- 34 patients with diabetes (34%).
- 47% of patients are monitored for arterial hypertension (AHT) (47 cases).
- Myopia is found in 21 of the cases (between -1 and -8 spherical diopters) (21%).
- 7 patients are on corticosteroid therapy (7%).
- 18% of patients are smokers (18 cases).
- A family history of glaucoma is present in 32% (32 cases).

The most found risk factors in our series are: age, IOH, thin cornea, hypertension, diabetes and family history of glaucoma.

Discussion:

- ✓ **Heredity and genetic factors:**

The last decade of the 20th century saw the emergence of several molecular supports to explain glaucomatous heredity, suspected and then recognized for a long time.
A first gene involved in a form of juvenile chronic glaucoma was identified in 1993 by Sheffield **[2]**, carried by chromosome 1 (GLC1A).
The corresponding protein was identified in 1997, and named TIGR (trabecular meshwork induced glucocorticoid response).
It leads to the formation of dimers and oligomers in the trabecular structures increasing resistance to aqueous flow.
Since then, many other genes have been implicated in different familial forms of open-angle glaucoma, located on various chromosomes (2,3,7,8...).
Other researchers have identified two loci for normal pressure glaucoma: GLC1B, located on chromosome 2, and GLC1E located on chromosome 10.
Since most individuals with the GLC1B and GLC1E genes appear to develop a lower pressure type of glaucoma, these mutations may render the optic nerve abnormally sensitive to IOP, or facilitate IOP-independent damage to the optical nerve.

Mutations in OPTN, the gene that encodes the optineurin protein, have been identified in patients carrying the GLC1E gene. The characterization of the protein(s) encoded by these genes can lead to a better potential knowledge of these elements **[3]**. GLC1F and GLC1G, other POAG loci, have been located. The relationship with another family was also used to localize the pigment dispersion syndrome to a chromosome distal to GLC1F.
Their transmission is each time dominant. Their expressiveness is however very variable, and the same mutation can simply lead to mild non-glaucoma High IOP as well as severe glaucoma with very strong High IOP.
The corresponding proteins (myocilin (MYOC), optineurin (OPTN), etc.) are gradually identified, and some can also be expressed simultaneously at the trabecular and papillary levels. These findings give hope for genetic screening for glaucoma.
The routine is however far from being acquired in this field, because this screening comes up against strong economic contingencies, whereas only a small percentage of glaucoma would be concerned by a genetic mutation currently recognized and identifiable.

- ✓ **Known POAG risk factors:**

Glaucoma is known to have a multifactorial origin, including genetic and biological risk factors **[4]**. However, the root causes remain unknown today for many types of glaucoma. Recent epidemiological studies have identified risk factors that may promote the onset of glaucoma in a healthy individual. Some of these factors are:
Intraocular hypertension (IOH): An IOH is defined by an intraocular pressure greater than 21mmHg. This is the main risk factor for the onset of POAG according to various studies, including the OHTS study (Ocular Hypertension Treatment Study) and the EGPS study (European Glaucoma Prevention Study) **[5 - 6]**.
Thus, the risk of onset of glaucoma increases with the elevation of IOP **[7]**. However, even if most glaucoma is related to an OHI, the appearance of the latter does not directly mean glaucoma **[8]**. This risk factor can be modified, in particular by drug treatment when the diagnosis is early.
Myopia: Moderate to severe myopia would favor variations in IOP through damage to the optic nerve head, thus leading to the appearance of glaucomatous neuropathy **[9]**.
Age: Studies have shown that advanced age is a risk factor for the onset of glaucoma in a healthy individual **[7]**. Indeed, the risk of onset of POAG increases after the age of 40, and this risk is even higher from the age of 70 **[10]**. More specifically, an analysis of 8 studies conducted in a general Caucasian population was carried out: the authors found a frequency of glaucoma of 0.2% in people over 40 and a frequency of 4.3% in people over 80 years old. The incidence increases by 0.11% per year in people between 55 and 77 years old **[7]**.
Ethnic origin: Work carried out has highlighted the strong variation in the prevalence of glaucoma according to ethnic origin. Indeed, studies have shown that a person of Caribbean, African-American origin has a greater risk of developing glaucoma compared to a Caucasian **[7]**. The onset of glaucoma in a person with melanoderma occurs in most cases early and has a very aggressive course. This high prevalence in this population could be explained by two observed anatomical factors **[11]**:

- A thinner cornea which would give an erroneous result of the IOP: an underestimation of 1 to 2mmHg which could lead to a delay in diagnosis and therefore a more marked aggressiveness of the disease. The OHTS study **[12]** found an increased risk of onset of glaucoma with decreasing corneal thickness: compared to a group of patients with a corneal thickness greater than 588 µm, patients with a corneal thickness between 555 and 588 µm presented a 1.7-fold increased risk of developing glaucoma, and patients with corneal thickness less than 555 µm presented a 3.4-fold increased risk.
- A large optic papilla which would favor under the effect of the pressure a greater deformation leading to a more consequent crushing of the optical fibers.

Family history of glaucoma or intraocular hypertension: Studies have shown a link between a family history of glaucoma and the onset of glaucoma: for a person the risk of onset of glaucoma increases if a member of the family is affected by this optic neuropathy **[7]**. Indeed, the study of families in which several people presented POAG revealed an autosomal dominant transmission. The analyzes carried out within these families made it possible to determine genes encoding proteins whose mutation involves them in the genesis of POAG. About twenty of these genes have been localized, three of which have been identified: the GLCIA gene coding for myocilin, the GLC1E gene coding for optineurin and the GLC1G gene coding for 36 proteins of the WD40 domain. The involvement of these many genes demonstrates the genetic heterogeneity of these cases. The identification of all of these genes involved will allow a better understanding of the genetic part in this pathology as well as a better therapeutic orientation **[13]**.

Arterial hypertension (AHT) [7]: Uncontrolled or untreated arterial hypertension is a risk factor for elevated IOP. Indeed, there is an increase in IOP of about 1mmHg simultaneously with a rise in blood pressure of 10mmHg. Thus, IOH can occur following hypertension, increasing the risk of developing glaucoma **[14, 15, 16, 17]**.

Diabetes: The presence of this chronic pathology in this list is controversial. Indeed, there is currently no proven scientific link between diabetes and the risk of developing glaucoma. Many studies have been conducted to analyze the possible prevalence of diabetes on the POAG. The results differ considerably: some writings expose the risk of onset of glaucoma in a diabetic patient, others establish a protective factor of diabetes on glaucoma **[18, 19, 20, 21]**. The high number of glaucomatous patients among diabetics could be explained by more regular consultation of diabetics with the ophthalmologist to monitor their disease and thus allow more frequent screening.

Smoking: Regarding the link between past or current smoking and ocular hypertension, the results of studies are contradictory, and, if smoking is a risk factor for elevated IOP, it is likely that its role is modest **[22]**. The relationship between smoking and the risk of glaucoma also shows opposite results **[23, 24]**; however, a Chinese study **[25]**, including admittedly few patients, found a risk of glaucoma multiplied by 10.8 (confidence interval $CI_{95\ \%}$: 1.85 to 63.0), ethnic or methodological differences that may explain this result.

Conclusion:

Primary open-angle glaucoma (POAG) is a chronic, long-asymptomatic optic neuropathy requiring lifelong treatment. The major risk of POAG is blindness, hence the importance of systematic screening, especially from the age of 40.

We conducted a retrospective study carried out in the ophthalmology department of the Moulay Ismail military hospital in Meknes over a period of 4 years between January 2018 and December 2021, involving one hundred cases.

The aim of our work is to enumerate the main risk factors for POAG, because their knowledge **[26]** makes it possible to monitor patients at risk more attentively and to adjust the treatment more appropriately in patients likely to develop glaucoma or to aggravate an already known glaucoma.

Figures:

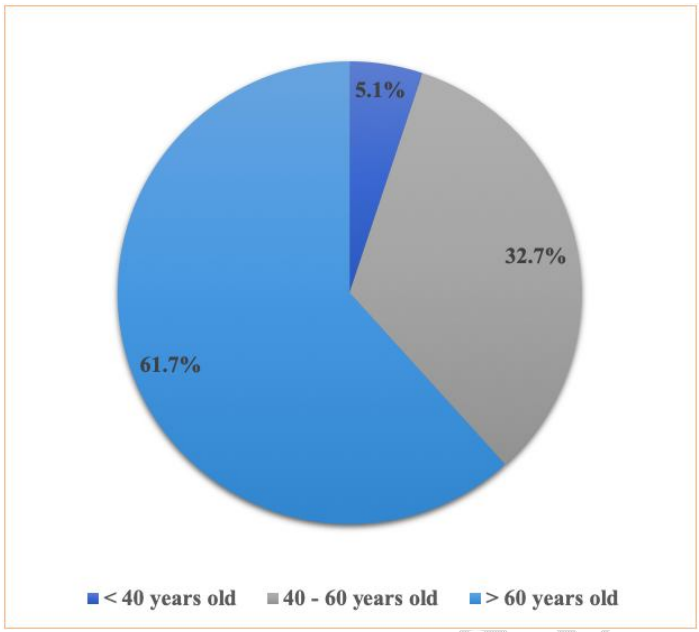

Figure 1: Percentage of patients according to age group.

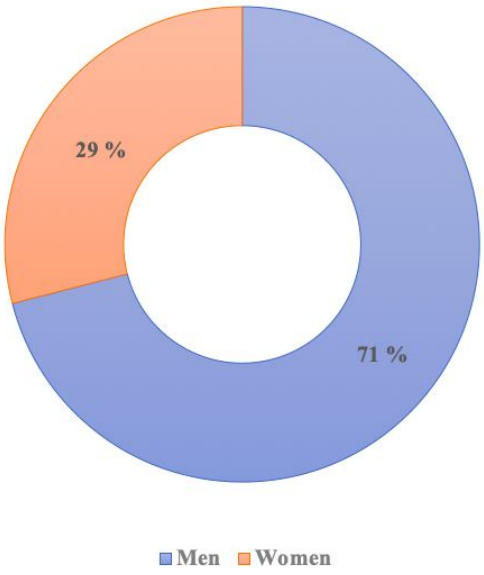

Figure 2: The distribution of patients according to gender.

Table 1: Medium central corneal thickness (CCT) by eye.

	Medium CCT	Extremes (Min – Max)
Right Eye	529,97 +/- 34.76	432 - 655
Left Eye	534.51 +/- 38.14	419 - 660

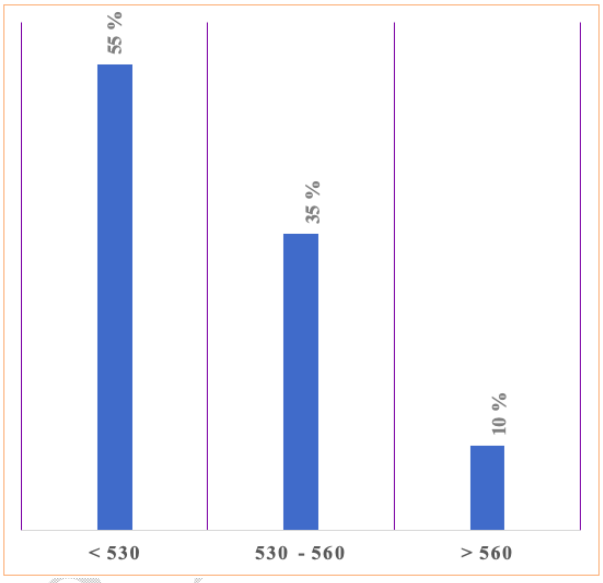

Figure 3: Distribution of patients according to the central corneal thickness.

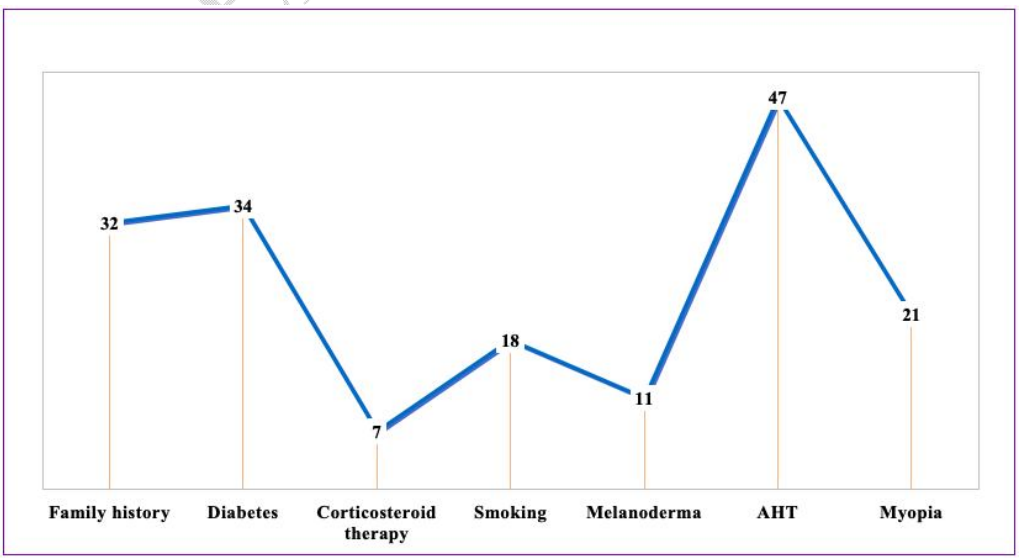

Figure 4: Other POAG risk factors.

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