• Clinical Research •

# Etiology and clinical analysis of secondary glaucoma: a single-center study from northwest China

Ying Liu<sup>1</sup>, Jie Yang<sup>2</sup>, Rui–Xue Zhang <sup>1</sup>, Yao Lu<sup>1</sup>, Wei Sang<sup>1</sup>, Jin–Wei Xi<sup>1</sup>, Jun Jia<sup>1</sup>, Dan–Ping Guo<sup>3</sup>, Yuan He<sup>1</sup>

<sup>1</sup>Department of Ophthalmology, the Second Affiliated Hospital of Xi'an Medical University, Xi'an 710038, Shaanxi Province, China

<sup>2</sup>Xi'an Aier Eye Hospital, Xi'an 710001, Shaanxi Province, China

<sup>3</sup>Department of Ophthalmology, Shangluo Central Hospital, Shangluo 726000, Shaanxi Province, China

Co-first Authors: Ying Liu and Jie Yang

**Correspondence to:** Yuan He. Department of Ophthalmology, the Second Affiliated Hospital of Xi'an Medical University, Xi'an 710038, Shaanxi Province, China. heyuan@xiyi.edu.cn Received: 2025-04-30 Accepted: 2025-08-25

### **Abstract**

- AIM: To investigate the etiology and clinical characteristics of hospitalized secondary glaucoma (SG) patients in northwestern China.
- **METHODS:** A cross-sectional study was conducted involving SG patients hospitalized between July 2024 and January 2025. Clinical data were collected, including medical history, best-corrected visual acuity (BCVA), intraocular pressure (IOP), slit-lamp examination, gonioscopic findings, and fundus examination. Demographic characteristics, etiological factors, and treatment modalities were analyzed.
- **RESULTS:** A total of 67 patients (82 eyes) were enrolled, aged 7 to 90y. Males accounted for 54.0% (36/67), and 22.4% (15/67) of patients had bilateral involvement. The predominant etiologies of SG were neovascular glaucoma (NVG; 25.4%), traumatic glaucoma (23.9%), uveitic glaucoma (20.9%), and lens-induced glaucoma (14.9%), collectively accounting for 85.1% of all cases. The peak age-specific incidence occurred in the 50-59 years age group (32.8%, 22/67), while NVG was prevalent across the 40-79 years age range. IOP of the 82 affected eyes was stratified into five severity tiers: 22-29 mm Hg (15 eyes, 18.3%), 30-39 mm Hg (14 eyes, 17.1%), 40-49 mm Hg (13 eyes, 15.9%), 50-59 mm Hg (20 eyes, 24.4%), and ≥60 mm Hg (20 eyes, 24.4%). The overall mean IOP was 45.2±12.3 mm Hg, indicating a significant pathological elevation. Surgical intervention was required in 46.3% of cases, predominantly for NVG, lens-

induced glaucoma, and traumatic glaucoma—conditions prone to rapid IOP elevation. The etiologies with the highest surgical intervention rates were malignant glaucoma, pigmentary glaucoma, lens-induced glaucoma, and NVG. In contrast, uveitic glaucoma cases were primarily managed with targeted anti-inflammatory therapy, which effectively controlled IOP in the early disease stages and potentially obviated the need for surgery.

- **CONCLUSION:** This study identifies NVG, traumatic glaucoma, uveitic glaucoma, and lens-induced glaucoma as the four leading etiologies of SG in Northwestern China. These findings emphasize the critical need for targeted prevention strategies and evidence-based health education programs among high-risk populations. Implementation of such initiatives will improve early detection, enable ophthalmologists to deliver timely therapeutic interventions, and ultimately reduce preventable vision loss in this region.
- **KEYWORDS:** secondary glaucoma; epidemiological; northwestern China; etiology

DOI:10.18240/ijo.2026.01.09

Citation: Liu Y, Yang J, Zhang RX, Lu Y, Sang W, Xi JW, Jia J, Guo DP, He Y. Etiology and clinical analysis of secondary glaucoma: a single-center study from northwest China. *Int J Ophthalmol* 2026;19(1):69-76

#### INTRODUCTION

laucoma is a leading cause of irreversible blindness worldwide, characterized by progressive optic nerve damage that results in vision loss and visual field deterioration. The estimated prevalence of glaucoma among individuals aged 40 to 80 is approximately 3.5%<sup>[1]</sup>. With the growing aging population worldwide, the number of glaucoma cases is expected to reach 111.8 million by 2040<sup>[1]</sup>. Although primary glaucoma is more prevalent, secondary glaucoma (SG) is also relatively common. Since glaucoma treatments vary based on underlying pathophysiological mechanisms, identifying the causes of SG is crucial for effective management<sup>[2]</sup>.

SG encompasses a diverse group of glaucoma caused by ocular or systemic conditions. A defining characteristic of

SG is elevated intraocular pressure (IOP), which can lead to optic nerve damage<sup>[3]</sup>. The etiology of SG is multifaceted, encompassing various conditions such as pigmentary glaucoma (PG), neovascular glaucoma (NVG), lens-induced glaucoma, steroid-induced IOP elevation, drug-related glaucoma, tumorassociated glaucoma, and caused by viral infections<sup>[1-2,4-5]</sup>.

In previous epidemiological studies, the leading cause of SG in India has been identified as NVG<sup>[6]</sup>, while drug-induced glaucoma is predominant in Indonesia<sup>[7]</sup>. In Japan, PG is the most common trigger<sup>[8]</sup>, and in countries such as Nigeria, Saudi Arabia, and Paraguay, syndrome-associated SG is frequently reported<sup>[9]</sup>. Several syndromes associated with SG include Peter's anomaly, PG, exfoliation syndrome, Sturge-Weber syndrome, iridocorneal endothelial (ICE) syndrome, and Axenfeld-Rieger syndrome. The etiology of SG varies across countries, likely shaped by factors such as ethnicity, geography, socioeconomic conditions, healthcare access, and regional medical practices<sup>[9]</sup>.

In China, epidemiological studies on SG indicate that 60% of cases occur in individuals aged 30 to 70y, with males accounting for 66.94% and females for 33.06%<sup>[9]</sup>. A study conducted in Southern China from 2010 to 2019 found that traumatic causes accounted for 28% of SG cases, followed by vascular diseases (18%), lens-induced glaucoma (9%), inflammatory factors (11%), drug-induced glaucoma (2%), anterior segment surgery (7%), posterior segment surgery (11%), syndrome-associated glaucoma (4%), and tumors (1%). Notably, from 2015 to 2019, trauma-related glaucoma declined significantly, while surgery-related and drug-induced cases increased<sup>[9-10]</sup>.

Research on the causes and clinical characteristics of SG in China remains limited, particularly regarding its etiology in the Northwest region. This knowledge gap highlights the need for more comprehensive studies. Given the challenges of data collection, regional variations, and technical demands, expanding research in this field is essential. Future investigations are expected to improve diagnostic accuracy and treatment strategies by uncovering underlying mechanisms while also providing clinically relevant data to guide personalized glaucoma management and public health prevention efforts.

This cross-sectional study systematically analyzed the epidemiological characteristics and clinical profiles of consecutive SG cases treated at the Second Affiliated Hospital of Xi'an Medical University between July 2024 and January 2025. Through standardized data extraction from electronic medical records of hospitalized patients, this study seeks to establish a comprehensive clinical database for understanding disease progression patterns and treatment outcomes in SG. This study aims to systematically analyze the etiological

spectrum and clinical manifestations of SG within a tertiary ophthalmic center in Northwestern China. Tailoring evidence-based clinical guidelines for Northwestern China requires a robust epidemiological foundation. Through comprehensive analysis of demographic characteristics, disease progression patterns, and treatment responses, we aim to establish this critical data groundwork. Ultimately, the collected dataset will serve as a foundation for developing stratified intervention protocols and optimizing multidisciplinary management approaches for glaucoma patients in resource-limited settings. The findings are expected to enhance medical service quality and improve the overall quality of life for patients.

#### PARTICIPANTS AND METHODS

Ethical Approval This study adopted a cross-sectional research method to analyze the clinical data of hospitalized SG patients from July 2024 to January 2025. The ethical approval for this study was obtained from the Medical Ethics Committee of the Second Affiliated Hospital of Xi'an Medical University on June 30, 2022, with a validity period of three years (No. X2Y202212). Participant recruitment and data collection began on the date after ethical approval and conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from all participants and their guardians when applicable.

Participants This single-center study enrolled 67 patients (82 eyes) with SG at the Second Affiliated Hospital of Xi'an Medical University between July 2024 and January 2025. All enrolled participants met the inclusion criteria, provided written informed consent after comprehensive study disclosure. Sociodemographic and clinical data, including patient history, best-corrected visual acuity (BCVA), IOP (icare ic100, Finland), slit-lamp (Topcon SL-D7, Japan), gonioscopic (VOLK G-4 Goniolaser, USA), and fundus findings (Carl Zeiss FF450PLUS, Germany), were systematically collected and documented.

Inclusion and Exclusion Criteria Inclusion criteria: 1) Diagnosis of SG based on discharge records; 2) Elevated IOP with glaucomatous optic nerve damage and corresponding visual field loss; 3) A history of factors associated with SG, such as ocular trauma, intraocular surgery, uveitis, lens-related disorders, or systemic diseases that may contribute to its development. Exclusion criteria: 1) A prior diagnosis of primary glaucoma, including primary open angle glaucoma, angle-closure glaucoma, or other primary glaucomatous conditions; 2) The presence of other ocular diseases, such as non-glaucomatous optic neuropathies, that may interfere with the diagnosis of SG; 3) Patients with incomplete clinical records or those not meeting the established diagnostic criteria for SG; 4) Individuals unable or unwilling to provide informed consent.

Research Methods Patient records, including medical history, imaging findings, and treatment plans, were systematically reviewed using the hospital's electronic medical record system to ensure data accuracy and completeness. Demographic characteristics, etiological factors, treatment modalities, and clinical outcomes were systematically categorized and analyzed using descriptive statistics.

Statistical Analysis Demographic characteristics, etiological subtypes, diagnostic classifications, and treatment modalities of secondary glaucoma patients underwent comprehensive statistical analysis. Data processing and graphical visualization were performed using Microsoft Excel® (Version 2021). Descriptive statistics, including frequency, percentage, mean, and standard deviation, were calculated. Visualizations such as histograms and pie charts were used to clearly depict the distribution of demographic features and etiological classifications.

#### **RESULTS**

Sex and Laterality Distribution This study analyzed 67 SG patients. The cohort comprised 54% males and 46% females, demonstrating a male predominance in this hospital-based sample. This observed male predominance (54%) aligns with established epidemiological trends in glaucoma susceptibility, though the precise mechanisms warrant further investigation. Regarding laterality patterns, unilateral involvement predominated (77.6%, 52/67), affecting the left eye marginally more frequently than the right [40.3% (27/67) vs 37.3% (25/67)]; bilateral presentation occurred in 22.4% (15/67). Unilateral cases were more common, with a slightly higher prevalence in the left eye. Characterizing laterality patterns informs etiology-specific diagnostic protocols and guides targeted management strategies.

**Age Distribution** The cohort comprised 67 SG patients aged 7 to 90y. To optimize age-stratified analysis, participants were categorized into nine age strata: <10, 10-19, 20-29, 30-39, 40-49, 50-59, 60-69, 70-79, and  $\ge 80y$ .

Peak prevalence occurred in the 50–59y (32.8%, 22/67), followed by the 60–69y (17.9%, 12/67). The distribution across remaining age strata was: <10y (1.5%, 1/67), 10–19y (3.0%, 2/67), 20–29y (3.0%, 2/67), 30–39y (11.9%, 8/67), 40–49y (13.4%, 9/67), 70–79y (10.5%, 7/67), and  $\geq$ 80y (6.0%, 4/67; Figure 1).

These findings demonstrate a peak occurrence of SG in individuals aged 50–69y, comprising 50.7% (34/67) of cases. However, SG affected all age groups, confirming its panage pathophysiology. Pediatric presentations (<10y) were exceptionally rare (1.5%, 1/67), aligning with established epidemiological patterns. This age-specific distribution reflects the predominant association of SG with acquired etiologies–particularly vascular disease, lens-induced pathologies, and

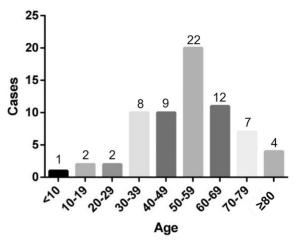


Figure 1 Age distribution of secondary glaucoma patients (n=67).

ocular trauma—which exhibit higher incidence in populations  $\geq$ 50y.

Etiological Distribution Etiological analysis identified four predominant causes of SG: NVG (25.4%), traumatic glaucoma (23.9%), uveitic glaucoma (20.9%), and lens-induced glaucoma (14.9%), collectively accounting for 85.1% of cases. Less frequent etiologies comprised: Posner-Schlossman syndrome (PSS; 4.5%), malignant glaucoma (3.0%), post-surgical glaucoma (3.0%), ICE syndrome (1.5%), PG (1.5%), and steroid-induced glaucoma (1.5%; Figure 2).

These findings emphasize the multifactorial etiology of SG, with neovascular and inflammatory mechanisms representing predominant pathogenic drivers. Recognition of this etiological spectrum is crucial for developing region-specific diagnostic protocols and targeted therapeutic interventions.

Age Distribution of Predominant Etiologies NVG: Peak incidence at 40–79y, correlating with systemic vascular comorbidities. Traumatic glaucoma: Concentration in 50–59y, reflecting age-related trauma vulnerability. Uveitic glaucoma: Predominance in 40–59y, indicating middle-aged susceptibility. Lens-induced glaucoma: Highest burden in 50–80y, consistent with age-related lens pathology. This etiology-age interplay enables risk-stratified screening and targeted intervention strategies (Figure 3).

Intraocular Pressure Distribution IOP was stratified into five severity tiers across 82 affected eyes: 22–29 mm Hg: 15 eyes (18.3%), 30–39 mm Hg: 14 eyes (17.1%), 40–49 mm Hg: 13 eyes (15.9%), 50-59 mm Hg: 20 eyes (24.4%), and  $\geq$ 60 mm Hg: 20 eyes (24.4%). The overall mean IOP ( $\pm$ standard deviation) was 45.2 $\pm$ 12.3 mm Hg (n=82 eyes; 67 patients), reflecting significant pathological elevation (Figure 4).

IOP was stratified according to etiological subtypes: uveitic glaucoma, traumatic glaucoma, NVG, lens-induced glaucoma, and a composite other category. The latter comprised steroid-induced glaucoma, Posner-Schlossman syndrome, ICE syndrome, malignant glaucoma, PG, and

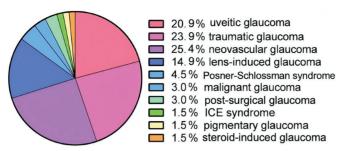


Figure 2 Etiological distribution of secondary glaucoma in northwestern China (*n*=67) ICE syndrome: Iridocorneal endothelial syndrome.

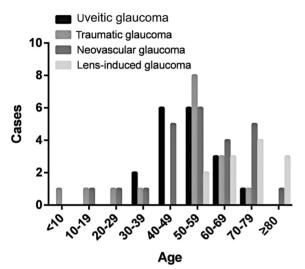


Figure 3 Age-stratified distribution of predominant secondary glaucoma etiologies in northwestern China (*n*=67).

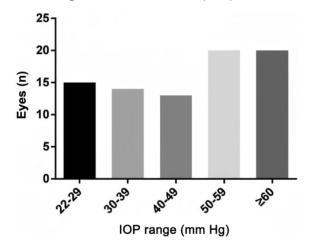
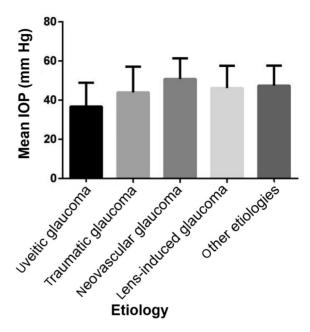


Figure 4 IOP distribution IOP: Intraocular pressure.

post-surgical glaucoma. Etiology-specific mean IOP values were: uveitic glaucoma 36.8±10.6 mm Hg, traumatic glaucoma 43.9±12.7 mm Hg, NVG 50.8±17.0 mm Hg, lensinduced glaucoma 46.2±16.7 mm Hg, and other etiologies 47.4±9.4 mm Hg (Figure 5). This stratification reflects distinct pathophysiological mechanisms and informed etiology-specific pressure-lowering targets.

**Surgical Intervention Distribution** In our cohort (82 eyes), 46.3% (38/82) required surgical management, while 53.7% (44/82) were managed non-surgically. Among surgical cases,



**Figure 5 Etiology-specific mean IOP values** Other etiologies: Steroid-induced glaucoma, Posner-Schlossman syndrome, iridocorneal endothelial syndrome, malignant glaucoma, pigmentary glaucoma, and post-surgical glaucoma. IOP: Intraocular pressure.

the three leading etiologies were: NVG (39.5%, 15/38), lensinduced glaucoma (26.3%, 10/38), traumatic glaucoma (15.8%, 6/38), collectively representing 81.6% of surgical interventions. In the non-surgical group, the three predominant etiologies were: uveitic glaucoma (38.6%, 17/44), traumatic glaucoma (22.7%, 10/44), NVG (20.5%, 9/44), comprising 81.8% of cases. The four major etiologies requiring surgical intervention were: malignant glaucoma (100%, 2/2), pigmentary glaucoma (100%, 2/2), lens-induced glaucoma (83.3%, 10/12) and NVG (62.5%, 15/24; Table 1). This distribution reflects individualized treatment stratification based on disease severity, progression rate, and IOP control status.

#### DISCUSSION

Despite advancements in medical and surgical treatments, glaucoma remains a significant public health concern and a leading cause of irreversible blindness. Early intervention is crucial in preserving vision, but the disease continues to impact quality of life and socioeconomic well-being. Timely detection and treatment are essential in preventing avoidable blindness. While substantial epidemiological data exists for primary glaucoma, comprehensive evidence on SG remains scarce in China, particularly in Northwestern regions. This study therefore establishes the epidemiological profile of SG in Northwestern China, aiming to address this critical knowledge gap.

The study examined 82 eyes from 67 patients, with a similar male-to-female ratio of 54% to 46%, consistent with previous studies. Liu *et al*<sup>[10]</sup> found a male-to-female ratio of 1.69 in

Table 1 Distribution of clinical management strategies for secondary glaucoma (n=82 eyes)

Glaucoma type	Surgical (46.3%, 38/82)	Non-surgical (53.7%, 44/82)	Surgical intervention rate
Uveitic glaucoma	2.6% (1/38)	38.6% (17/44)	5.6% (1/18)
Traumatic glaucoma	15.8% (6/38)	22.7% (10/44)	37.5% (6/16)
Neovascular glaucoma	39.5% (15/38)	20.5% (9/44)	62.5% (15/24)
Lens-induced glaucoma	26.3% (10/38)	4.5% (2/44)	83.3% (10/12)
Posner-Schlossman syndrome	0	6.8% (3/44)	0
Malignant glaucoma	5.3% (2/38)	0	100% (2/2)
Post-surgical glaucoma	2.6% (1/38)	2.3% (1/44)	50% (1/2)
ICE syndrome	2.6% (1/38)	2.3% (1/44)	50% (1/2)
Pigmentary glaucoma	5.3% (2/38)	0	100% (2/2)
Steroid-induced glaucoma	0	2.3% (1/44)	0

ICE syndrome: Iridocorneal endothelial syndrome.

a cohort of 1129 SG patients in Central China, while Gong et al<sup>[9]</sup> reported that 66.94% of 11 730 SG patients in South China were male. Studies from India also observed a higher prevalence of SG in men<sup>[6-7]</sup>, which aligns with our findings. This male predominance could be attributed to genetic predispositions, hormonal differences, lifestyle factors, and environmental influences, including occupational exposure and lower health consciousness in men. Therefore, implementing early screening protocols and targeted preventive education on ocular injury protection for male populations in Northwest China is critical to reduce glaucoma-related vision loss, particularly given their high susceptibility to traumatic glaucoma identified in our cohort.

Our study found that the average age of SG patients was 53±17.4y, consistent with findings by Liu et al<sup>[10]</sup> and Komaratih et al<sup>[7]</sup>, who also observed that most SG patients are in their 50s and 60s. However, our results differ from Gong et al's study[9], which reported an average age of 44.45±19.45y for SG patients. These variations may reflect differences in economic conditions, medical standards, and regional etiologies. Aging is a key risk factor for glaucoma<sup>[11]</sup>, contributing to its progression due to factors like mitochondrial dysfunction, oxidative stress, and vascular changes in the optic nerve head<sup>[12]</sup>. Additionally, certain gut microbiota, such as Butyricicoccus and Akkermansia, may influence glaucoma development, and their decline with age could increase risk<sup>[13]</sup>. These factors highlight the importance of early screening and intervention, particularly for middle-aged and older individuals, to prevent vision loss.

This study identifies four predominant etiologies of secondary glaucoma in northwestern China: NVG (25.4%), traumatic glaucoma (23.9%), uveitic glaucoma (20.9%), and lensinduced glaucoma (14.9%). The following sections provide mechanistic analyses of these principal causes and propose targeted preventive strategies, thereby establishing an evidence-based framework for SG control in this region.

NVG emerged as the most prevalent subtype, predominantly affecting patients aged 40-79y in this study. While NVG typically comprises only 3.9% of all glaucoma cases globally [14], it is more common in Asia, where it accounts for 0.7%-5.1% of glaucoma cases, and 5.8% in China<sup>[15]</sup>. The high prevalence of NVG in this study may be influenced by regional demographic factors, including the rising incidence of diabetic retinopathy (DR) in Asia, particularly in northwestern China<sup>[16-17]</sup>. Notably, the incidence of DR has risen more rapidly in Asia than in North America and Europe<sup>[18]</sup>. In China, the prevalence of diabetes has risen dramatically from less than 1% in the 1980s to nearly 11% by 2013<sup>[19]</sup>, with northern regions, such as those in Northwest China, showing notably higher rates of DR<sup>[20]</sup>. This trend may be associated with the high sugar and starch intake typical of Northwestern China's dietary habits. The elevated NVG prevalence in this study likely reflects age distribution, regional demographics, and dietary patterns. The observed male-to-female ratio of 1:2 is consistent with previous studies, which report similar incidence rates between genders<sup>[17]</sup>. The prevalence of NVG in Northwestern China was 25.4%—higher than southern China (17.9%)[9] yet lower than Central China (43.3%)<sup>[10]</sup>. This gradient reflects distinct regional etiopathogenic patterns driven by differential risk factor exposures: diabetic retinopathy progression predominates in the Northwest, retinal vein occlusion dominates in the South, while uncontrolled hypertension-induced retinopathy underlies most central China cases. To address the growing burden of SG driven by the high prevalence of diabetes in Northwest China, we propose: 1) An integrated screening strategy incorporating IOP monitoring into public health diabetic retinopathy screening packages, with artificial intelligence (AI) systems automatically flagging high-risk patients; 2) A tiered intervention strategy where primary care facilities conduct initial screenings and patient education, county-level hospitals administer anti-vascular endothelial growth factor (VEGF) injections, and prefectural centers manage complex surgeries.

This approach enables timely detection and intervention for NVG while reducing healthcare costs.

Traumatic glaucoma was the second most common type after NVG in this study. Ocular trauma, classified as closed-globe or open-globe injury, can raise IOP through different mechanisms, contributing to traumatic glaucoma development<sup>[21]</sup>. These mechanisms include angle recession, hyphema-induced outflow obstruction, and lens displacement-mediated pupillary block. In developed countries, traumatic glaucoma incidence ranges from 0.5% to 9%[22], with orbital fractures being the leading cause<sup>[21]</sup>. Open-globe injuries have a 6.2% risk of developing glaucoma in the postoperative period<sup>[23]</sup>. A study found that glaucoma developed in 3.4% of patients within six months of blunt ocular trauma, rising to 10% after ten years<sup>[24]</sup>. The onset of glaucoma following eye trauma can vary significantly, with a latency period of up to 20y, emphasizing the importance of long-term follow-up<sup>[22]</sup>. Epidemiological data from industrialized countries estimate an annual eye injury incidence of 3-3.5 per 100 000 people, with males accounting for approximately 80% of cases. Ocular trauma demonstrates peak incidence around age 30y<sup>[22]</sup>. Our study found a male-tofemale ratio of 11:5 among traumatic glaucoma patients, with males accounting for 68.8% of cases, consistent with previous research. However, the average patient age was 50y (51 for males, 47 for females), which is older than previously reported. This age difference may be influenced by regional factors such as socioeconomic development, industrialization, and transportation infrastructure, which affect the age distribution of eye trauma. The prevalence of traumatic glaucoma in northwestern China was 23.9%, comparable to southern China (27.6%)<sup>[9]</sup> but higher than central China (17.3%)<sup>[10]</sup>. This elevated burden primarily stems from inadequate protective measures during agricultural machinery operations. This etiological predominance-particularly concentrated in 50-59y-necessitates targeted occupational safety interventions, including mandatory protective eyewear protocols for highrisk sectors such as agriculture and manufacturing.

In this Northwestern China cohort study, uveitic glaucoma accounted for 20.9% of secondary glaucoma cases—representing a significantly elevated prevalence that was 1.95-fold higher than southern China (10.7%)<sup>[9]</sup> and 4.35-fold greater than central China (4.8%)<sup>[10]</sup>. This pronounced geographic disparity likely reflects the region's triple burden: elevated autoimmune disorders (particularly HLA-B27-associated uveitis), genetic susceptibility polymorphisms, and distinct environmental exposures including intense ultraviolet radiation (UVR), frequent sandstorms, and extreme aridity-induced ocular surface inflammation.

Lens-induced glaucoma accounted for 14.9% of secondary glaucoma cases in northwestern China-representing a 1.55-

fold higher prevalence than southern China  $(9.6\%)^{[9]}$  and a 1.96-fold increase over central China  $(7.6\%)^{[10]}$ . This region faces dual challenges in disease control: medical resource disparities and environmental exposure risks. Rural northwest China experiences critical shortages in ophthalmic resources, significantly delaying cataract surgery timelines and increasing the risk of lens-induced glaucoma. Concurrently, intense UVR, arid climate, and frequent sandstorms accelerate lens protein denaturation, driving cataract progression rates faster than in Southern provinces.

In this study, IOP levels varied by etiology, with NVG patients exhibiting the highest mean IOP at  $50.8\pm17.0$  mm Hg. Previous studies show that NVG often causes a sharp increase in IOP, typically ranging from 40 to 60 mm Hg, causing severe pain<sup>[25]</sup>. This is due to the pathophysiology of NVG, where neovascularization triggers myofibroblast contraction in proliferating fibrovascular tissue, leading to synechial angle closure and irreversible angle-closure glaucoma<sup>[26]</sup>. NVG is also associated with elevated levels of VEGF and other molecules, including basic fibroblast growth factor, platelet-derived growth factor, insulin-like growth factor-1, and interferon- $\alpha$ , all of which contribute to its pathogenesis<sup>[25,27]</sup>.

In contrast, uveitic glaucoma patients in this study had a lower mean IOP of 36.8±10.6 mm Hg, reflecting the complex pathogenesis of uveitic glaucoma. During acute inflammation, cyclitis reduces aqueous humor production while increasing uveoscleral outflow, temporarily lowering IOP. However, as the disease progresses, elevated prostaglandin levels increase outflow resistance, causing IOP to rise<sup>[28-30]</sup>. Studies show that the 5-year cumulative risk of glaucoma is highest in viral uveitis (15.1%), compared to HLA-B27-associated uveitis (0.9%)<sup>[31]</sup>. Risk factors for glaucoma progression in uveitis include older age at onset, elevated IOP, chronic inflammation, and cystoid macular edema<sup>[31]</sup>. As most uveitic glaucoma cases in this study were of viral origin, their IOP levels were relatively lower compared to other subtypes.

The management of SG typically integrates medications, laser, and surgical interventions, tailored to the specific etiology<sup>[4]</sup>. In our Northwestern China cohort, surgical intervention was required in 46.3% of cases, while 53.7% were managed nonsurgically. Among surgical cases, the three leading etiologies were: NVG, lens-induced glaucoma and traumatic glaucoma, collectively representing 81.6% of surgical interventions. Procedures performed included cataract-related surgery, trabeculectomy, glaucoma drainage device implantation, and intravitreal anti-VEGF injections. The remaining 18.4% involved procedures such as anterior vitrectomy, anterior chamber paracentesis with reformation, and ultrasound cycloplasty (UCP). In the non-surgical group, the three predominant etiologies were: uveitic glaucoma, traumatic

glaucoma and NVG, comprising 81.8% of cases. This cohort was predominantly driven by uveitic glaucoma, where targeted anti-inflammatory therapy effectively controlled IOP in early disease stages, potentially obviating surgical need. The etiologies demonstrating the highest surgical intervention rates were: malignant glaucoma, pigmentary glaucoma, lens-induced glaucoma, and NVG-reflecting their pathophysiological for refractory IOP elevation unresponsive to medical therapy. These findings underscore the need for etiology-specific management protocols in Northwest China, particularly early anti-inflammatory therapy for uveitic cases and trauma prevention programs targeting high-risk populations. Surgical interventions (trabeculectomy/Ahmed valve) were primarily reserved for refractory cases where maximal medical therapy and laser trabeculoplasty failed to control IOP (>30 mm Hg on 3+ medications)<sup>[32]</sup>. In NVG, even if the IOP is within the normal range, the presence of iris neovascularization mandates immediate panretinal photocoagulation and anti-VEGF therapy. This is due to the central role of VEGF in the pathogenesis of NVG, where elevated VEGF levels drive the formation of abnormal blood vessels and subsequent angle closure. For patients with uveitic glaucoma and hyphema (UGH) syndrome, localized iris chafing in those with express shunts can be treated with laser iridoplasty. If an iris blood vessel is identified as the source of bleeding, argon or Nd:YAG laser can be used to control the hemorrhage<sup>[33-34]</sup>. Myopic, vitrectomized patients showing signs of UGH syndrome require special attention, with elevated IOP due to iris concavity or reverse pupillary block managed by peripheral laser iridotomy<sup>[35]</sup>. In cases where no other pathology is present, the definitive treatment for UGH syndrome is intraocular lens exchange<sup>[33]</sup>. In Northwestern China's resource-limited settings, the 46.3% surgical rate necessitates improved access to minimally invasive glaucoma surgery techniques.

This study establishes the comprehensive epidemiological profile of SG in Northwestern China, providing critical data to inform region-specific risk mitigation strategies and evidence-based clinical pathways. Future multicenter studies with expanded cohorts are warranted to validate these findings and elucidate region-specific etiological patterns across diverse Chinese populations.

## **ACKNOWLEDGEMENTS**

Clinical Research Center for Ophthalmic Diseases of Shaanxi Province; Education Department of Shaanxi Provincial Government for Pathogenesis and Prevention Transformation Medicine for Glaucoma Innovation Team; Clinical Key Specialty of Shaanxi Province; Xi'an International Science and Technology Cooperation Base for Ophthalmology and Visual Science; Xi'an Key Laboratory for the Prevention and Treatment of Eye and Brain Neurological Related Diseases;

Ophthalmology Science and Technology Innovation Team of Xi'an Medical University; Key Disciplines of Xi'an Medical University; Shaanxi San Qin Talent Special Support Plan Innovation and Entrepreneurship Team.

Foundations: Supported by the National Natural Science Foundation of China (No.82070964; No.82571210); Shaanxi Science Fund for Distinguished Young Scholars (No.2022JC-60); the International Scientific and Technological Cooperation Projects (No.2024GH-YBXM-20); the Open Research Funds of the State Key Laboratory of Ophthalmology (No.83000-32030002); Education Department of Shaanxi Provincial Government for Youth Innovation Team Research Program Project (No.23JP151; No.23JP150); General Projects of Hospital-level Research Topics in the Second Affiliated Hospital of Xi'an Medical University (No.22KY0111).

Conflicts of Interest: Liu Y, None; Yang J, None; Zhang RX, None; Lu Y, None; Sang W, None; Xi JW, None; Jia J, None; Guo DP, None; He Y, None.

#### REFERENCES

- 1 Kang JM, Tanna AP. Glaucoma. Med Clin N Am 2021;105(3):493-510.
- 2 Aldaas K, Challa P, Weber DJ, et al. Infections and glaucoma. Surv Ophthalmol 2022;67(3):637-658.
- 3 Chinese Ophthalmological Society Glaucoma Group, Chinese Medical Association Ophthalmology Branch Glaucoma Group. Chinese Glaucoma Guidelines (2020). *Chinese Journal of Ophthalmology* 2020;56(8):573-586.
- 4 Camp DA, Yadav P, Dalvin LA, *et al.* Glaucoma secondary to intraocular tumors: mechanisms and management. *Curr Opin Ophthalmol* 2019;30(2):71-81.
- 5 Greslechner R, Helbig H. Secondary glaucoma in the context of retinal disease. Klin Monbl Augenheilkd 2022;239(9):1111-1118.
- 6 Dubey S, Jain K, Mukherjee S, *et al*. Current profile of secondary glaucoma in a Northern India tertiary eye care hospital. *Ophthalmic Epidemiol* 2019;26(3):200-207.
- 7 Komaratih E, Rindiastuti Y, Primitasari Y. Profile of secondary glaucoma at a tertiary hospital in east Java. *Folia Medica Indonesiana* 2020;56(1):56-59.
- 8 Yamamoto T, Iwase A, Araie M, *et al*. The Tajimi Study report 2: prevalence of primary angle closure and secondary glaucoma in a Japanese population. *Ophthalmology* 2005;112(10):1661-1669.
- 9 Gong H, Ren J, Zheng B, *et al*. The profile of secondary glaucoma in China: a study of over 10, 000 patients. *J Glaucoma* 2021;30(10): 895-901.
- 10 Liu Q, Liu C, Cheng W, et al. Clinical analysis of secondary glaucoma in Central China. Sci Rep 2023;13(1):8439.
- 11 Huang L, Hong Y, Fu X, *et al*. The role of the microbiota in glaucoma. *Mol Aspects Med* 2023;94:101221.
- 12 Bhartiya S, Sharma N, Verma S, *et al.* Ocular and systemic factors associated with glaucoma. *J Curr Glaucoma Pract* 2022;16(3): 179-191.

- 13 Vergroesen JE, Jarrar ZA, Weiss S, *et al*. Glaucoma patients have a lower abundance of butyrate-producing taxa in the gut. *Invest Ophthalmol Vis Sci* 2024;65(2):7.
- 14 Urbonavičiūtė D, Buteikienė D, Janulevičienė I. A review of neovascular glaucoma: etiology, pathogenesis, diagnosis, and treatment. *Medicina (Kaunas)* 2022;58(12):1870.
- 15 Tang Y, Shi Y, Fan Z. The mechanism and therapeutic strategies for neovascular glaucoma secondary to diabetic retinopathy. *Front Endocrinol* 2023;14:1102361.
- 16 Senthil S, Dada T, Das T, et al. Neovascular glaucoma-a review. Indian J Ophthalmol 2021;69(3):525-534.
- 17 Kalogeropoulos D, Moussa G, Sung VC, *et al.* Neovascular glaucoma: an update. *Klin Monbl Augenheilkd* 2023;240(3):305-315.
- 18 Tan TE, Wong TY. Diabetic retinopathy: looking forward to 2030. Front Endocrinol 2022;13:1077669.
- 19 Wang L, Peng W, Zhao Z, et al. Prevalence and treatment of diabetes in China, 2013-2018. *JAMA* 2021;326(24):2498.
- 20 Hou X, Wang L, Zhu D, *et al.* Prevalence of diabetic retinopathy and vision-threatening diabetic retinopathy in adults with diabetes in China. *Nat Commun* 2023;14:4296.
- 21 Ng JK, Lau O. Traumatic Glaucoma. 2023 Aug 14. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; 2025 Jan.
- 22 Schlote T, Rohrbach M. Traumatic glaucoma-a survey. *Klin Monbl Augenheilkd* 2005;222(10):772-782.
- 23 Bojikian KD, Stein AL, Slabaugh MA, *et al.* Incidence and risk factors for traumatic intraocular pressure elevation and traumatic glaucoma after open-globe injury. *Eye* (*Lond*) 2015;29(12):1579-1584.
- 24 Muallem MS, Wilensky J. Glaucoma after ocular contusion. *J Glaucoma* 2006;15(3):274.

- 25 Dumbrăveanu L, Cușnir V, Bobescu D. A review of neovascular glaucoma. Etiopathogenesis and treatment. *Rom J Ophthalmol* 2021;65(4):315-329.
- 26 Greslechner R, Helbig H, Spiegel D. Secondary open-angle glaucoma: pseudoexfoliative glaucoma, pigmentary glaucoma and neovascular glaucoma. *Ophthalmologe* 2022;119(4):425-438.
- 27 Havens SJ, Gulati V. Neovascular glaucoma. *Retinal Pharmacotherapeutics* 2015:196-204.
- 28 Baneke AJ, Lim KS, Stanford M. The pathogenesis of raised intraocular pressure in uveitis. *Curr Eye Res* 2016;41(2):137-149.
- 29 Seow WH, Lim CHL, Lim BXH, et al. Uveitis and glaucoma: a look at present day surgical options. Curr Opin Ophthalmol 2023;34(2):152-161.
- 30 Siddique SS, Suelves AM, Baheti U, *et al*. Glaucoma and uveitis. *Surv Ophthalmol* 2013;58(1):1-10.
- 31 Niederer RL, Wong ABC, Ma T, *et al.* Predictors of glaucoma in patients with uveitis and scleritis. *Eye (Lond)* 2023;37(6):1254-1257.
- 32 Wagner IV, Stewart MW, Dorairaj SK. Updates on the diagnosis and management of glaucoma. *Mayo Clin Proc Innov Qual Outcomes* 2022;6(6):618-635.
- 33 Sen S, Zeppieri M, Tripathy K. Uveitis glaucoma hyphema syndrome. 2024 Feb 29. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; 2025.
- 34 Hermoso-Fernández FM, Gonzalez-Gallardo C, Cruz-Rojo M. Retinal detachment in UGH Syndrome after cataract surgery. *Rom J Ophthalmol* 2021;65(4):395-398.
- 35 Dhillon B, Duff-Lynes SM, Blake CR. A novel method of using transillumination, conjunctival markings and Pascal solid state laser to treat uveitis-glaucoma-hyphema syndrome. *Am J Ophthalmol Case Rep* 2022;25:101296.