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Original Research Article

Risk Factors for Glaucoma: A Hospital-based Case-control study

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Abstract:

Background: Glaucoma is a diverse group of eye diseases with a multifactorial etiology characterized by an acquired loss of retinal ganglion cells, progressive optic neuropathy with morphological abnormalities in optic nerve head, and visual field defect, in which raised intraocular pressure is a major and one of the modifiable risk factor and other risk factors includes age, gender, race, family history, systemic diseases, sociodemographic profile, etc. Glaucoma is a major public health problem, causing visual impairment which hampers day-to-day work.

Aims & Objective: 1. To study various risk factors For Glaucoma among patients attending OPD/IPD of RIO, GMCH. 2. To assess various socio-demographic, modifiable lifestyle-associated factors and other ocular diseases related to Glaucoma.

Materials and Methods: In this hospital-based case-control study, considering p=10%, the sample size was calculated to be 570. Out of which 285 Cases and 285 Controls were selected from OPD/IPD of RIO, GMCH in a ratio of 1:1 after adjusting for age and sex. Verbal/written consent was taken followed by a detailed history was documented through a standardized predesigned and pretested proforma.

Results: All the data were analyzed and statistical significance was determined using SPSS software. A high prevalence of glaucoma was seen among males and most of the glaucoma cases belong to age 50-59 years. Statistically, a significant association was seen between age and Glaucoma but an insignificant association was seen with Gender. A high level of IOP (OR: 96.08, CI: 40.565-123.10 p-value: <0.0001), history of smoking (OR:1.515, CI:1.086- 2.113, p-Value-0.0181), history of alcohol use (OR:1.514, CI:1.072-2.139, p- Value:0.0230), history of use of steroid (OR:1.604, CI:1.123- 2.291, p-Value:0.0118), History of Myopia (OR:1.711, CI:1.228- 2.385, p-Value:0.0019), History of Diabetes Mellitus (OR:1.472, CI:1.048-2.066, p-Value:0.0315), history of Hypertension (OR:1.463, CI:1.051-2.034, p-Value:0.0294) showed statistically Significant association with Glaucoma. Whereas, other factors failed to show statistically significant association with Glaucoma.

Conclusion: In this study, various factors like smoking, alcohol use, and steroid use, high BP, high blood sugar, and some ocular factors (high IOP, Myopia) were found to be related to risk for Glaucoma. The mechanisms by which these factors lead to an increased risk of Glaucoma are still poorly understood, further study is needed to understand the significance of these as well as other factors as a risk for developing Glaucoma.

Keywords: Glaucoma, Risk factors, Hospital-based case-control study.

Introduction

Glaucoma is a diverse group of eye diseases with a multifactorial etiology characterized by an acquired loss of retinal ganglion cells, progressive optic neuropathy with morphological abnormalities in optic nerve head, and visual field defect, in which raised intraocular pressure is a major and one of the modifiable risk factors [1] Although our modern understanding of glaucoma dates back only to the mid-19th century, this group of disorders was recognized by the Greeks as early as 400 BC. In Hippocratic writings, it appears as "Glaucosis," about bluish-green hue of the affected eye. This term, however, was also applied to a larger group of blinding conditions that included cataracts. It was

not until 19th century that glaucoma was recognized as a distinct group of ocular disorders [2]. Glaucoma is a major public health problem, causing visual impairment which hampers day-to-day work [3] and Glaucoma is considered a lifelong disease and is a leading cause of irreversible but preventable blindness. The risk factors for Glaucoma are not only surrounded by the boundary of an eye but much more beyond the eye. The risk factors include age and frailty, gender, myopia, genetics, family history, smoking, race, systemic hypotension and hypertension, vasospasm, use of systemic or topical steroids, migraine, obstructive sleep apnea syndrome, and most significantly, increased IOP, etc. [2] The case detection rates must be increased by increasing awareness about glaucoma, thereby reducing blindness due to glaucoma. Early detection of glaucoma through "Opportunistic case detection" by performing a comprehensive eye examination at all levels and all available instances, and appropriate referral or initiating treatment as early as possible will help to improve the patient's quality of life [4].

As per WHO, there are approximately 76 million peoples in the globe who has been suffering from any form of Glaucoma [5]. This number is estimated to reach 111.8 million by 2040 [5] POAG and PACG are the most prevalent ones, being POAG at the top. Out of those 76 million people, 7.7 million develop moderate or severe visual impairment & 4.5 million blindness due to unaddressed Glaucoma [6]. In India, glaucoma is leading cause of irreversible blindness after cataract with at least 12 million people affected and nearly 1.2 million people blind from the disease. More than 90 percent of cases of glaucoma remain undiagnosed in the community [8]. It has been reported that glaucoma affects the quality of life to a greater degree in India than in the west [7]. Population-based studies suggest that more than 90% of glaucoma cases in the country remain undiagnosed. This contrasts with 40-60% rates of undiagnosed disease in more developed countries [9-13]. Glaucoma, although more commonly affects older adults above 40 years, it can occur in all age groups and all strata of society making it a major public health problem with significant health and economic consequences. Nearly 1/5 of the population affected by glaucoma become blind in one or both eyes [14].

In most of the condition glaucoma remain undiagnosed because of Unawareness & missed diagnosis at health-care centers. So, by changing our lifestyle as well as by improving the standard of ophthalmic examination through gonioscopy and optic disc evaluation we can reduce the incidence of glaucoma to a huge extent.

The classical characteristics of glaucoma's are [15]

1. Abnormality of anterior portion of the eye that results in increased IOP
2. Loss of retinal ganglion cells in a distribution that suggests injury occurred at optic nerve head (ONH)
3. Nerve fiber layer loss which corresponds to pattern of visual field loss.

According to the literature, about 60 types of glaucoma are known, however, most common are POAG and PACG.

The prevalence of various types of glaucoma including the major ones (POAG & PACG) is showing an upward trend in our country and for several reasons, this trend is likely to be increased in this part (Assam) of India also. Due to limited previous reports on this subject and the raising trend of various types of glaucoma incidence in Assam along with other North-East states, remain undiagnosed. So, an analysis of the magnitude of this problem in patients attending tertiary care Centre like the Regional Institute of Ophthalmology (RIO), GMCH, Gauhati, would provide us with important information regarding the risk factors for glaucoma and its disease process and investigate various risk factors for glaucoma in this part of Northeastern India.

Material and Methods

This was a hospital-based, case–control (1:1 ratio) study conducted in RIO, GMCH, and Guwahati from August, 2021 to July, 2022. Both cases and controls were selected from OPD/IPD of RIO during study period after they gave their consent.

Cases

Only Diagnosed Glaucoma patients (as per diagnostic protocol), who came to OPD/IPD of RIO, GMCH during study period except the following-

1. Patients refusing to participate in the study
2. Patients diagnosed/morbid with different terminal ophthalmological problems other than Glaucoma
3. Other Terminally ill (cancer, bedridden, etc.) patients & those who unable to respond

Psychologically deteriorated patient with Glaucoma (due to lack of appropriate cooperation)

Controls

Patients attending OPD/IPD of RIO, GMCH who after proper examination and investigations (by an ophthalmologist) were diagnosed with other ocular diseases except Glaucoma excluding -

1. Patients refusing to participate in the study
2. Both unilateral as well as bilateral blind patients
3. Terminally ill patients

Consent was (verbal/written) taken from both Cases and Controls.

Sample Size

In view of multiple risk factors being studied, to give an 80% power in a two- sided test with 5% alpha error for any factor whose exposure is assumed to be 40% among controls and assuming the associated odd ratios (OR) to be 2.0, total sample size was calculated to be 570. Thus, sample size of cases and control was 285 each, in a ratio of 1:1.

Data Collection

During the study period from August 2021 to July 2022, a total number of 2100 patients with Glaucoma were enrolled, out of which 1200 cases were diagnosed with POAG, and rest were with other types of Glaucoma.

All patients were identified as cases who met inclusion criteria for the study till the required sample size was achieved.

After taking informed consent, data regarding the various risk factors were collected from both cases and controls separately and were filled up in a predesigned, pretested interview schedule. Each of the cases and controls was interviewed face-to-face in the OPD/ IPD or other room of the OPD/IPD area (according to the convenience of the patient) in absence of any other family members or attendants. The interview was taken either in English, Hindi, or in the local language (Assamese) according to the level of their understanding. This face-to-face interview was done only after completion of general & Ophthalmological examination by an Ophthalmologist.

Results

Table 1: Distribution of cases as per Gender

Gender	Frequency	Percentage
Male	210	73.7
Female	75	26.3
Total	285	100

Table 2: Distribution of cases as per Age

Age Group	Frequency	Percentage
40-49	38	13.4
50-59	76	26.6
60-69	65	22.8
70-79	59	20.7
80-89	46	16.2
>90	1	0.3
Total	285	100

Table 3: Distribution of Cases according to Family History

Family History	Frequency	Percentage
Yes	55	19.3
No/Don ‘t Know	230	80.7
Total	285	100

Table 4: Relationship between Cases and Controls according to their Age

Age Group	Cases	Controls	Total	Chi-Square	p-value
40-49	38 (13.4%)	74 (26%)	112 (19.7%)	22.363	0.0336
50-59	76 (26.6%)	49 (17.1%)	125 (22%)		
60-69	65 (22.8%)	71 (25%)	136 (23.8%)		
70-79	59 (20.7%)	46 (16.1%)	105 (18.5%)		
80-89	46 (16.2%)	40 (14.0%)	86 (15%)		
>90	1 (0.3%)	5 (1.8%)	6 (1%)		
Total	285 (100%)	285 (100%)	570 (100%)		

Rural	111 (38.9%)	145 (50.9%)	256 (44.9%)			
Urban	174 (61.1%)	140 (49.1%)	314 (55.1%)			
Total	285 (100%)	285 (100%)	570 (100%)			

Table 5: Relationship of cases and controls according to their Gender

Gender	Cases	Controls	Total	Chi-Square	p-value
Male	210 (73.7%)	195 (68.4%)	405 (71%)	1.672	0.1960
Female	75 (26.3%)	90 (31.6%)	165 (29%)		
Total	285 (100%)	285 (100%)	570 (100%)		

Table 6: Relationship of cases and controls according to IOP Value

IOP Value	Cases	Controls	Total	Chi- Square	p-value	Odds Ratio CI
				339.18	<0.0001	
>21mmHg	240	20 (8%)	260			96.08
	(84%)		(46%)			(40.565-
						123.10)
≤21mmHg	45 (16%)	265	310			
		(92%)	(54%)			
Total	285	285	570			
	(100%)	(100%)	(100%)			

Table 7: Relationship of cases and controls according to family history

Family H/O Glaucoma	Cases	controls	Total	Chi-Square	p- value
Yes	55 (19.3%)	44 (15.4%)	99 (17.4%)	1.222	0.2689
No/Don ‘t knows	230 (80.7%)	241 (84.6%)	471 (82.6%)		
Total	285 (100%)	285 (100%)	570 (100%)		

Table 8: Relationship of cases and controls according to history of smoking

H/O smoking	cases	controls	Total	Chi- Square	p-value	Odds Ratio (CI)
				5.591	0.0181	1.515
						(1.086-2.113)
Yes	139(48.8%)	110(38.6%)	249(43.7%)			
No	146 (51.2%)	175 (61.4%)	321 (56.3%)			
Total	285 (100%)	285 (100%)	570 (100%)			

Table 9: Relationship of cases and controls according to history of alcohol use

H/O Alcohol	cases	controls	Total	Chi- Square	p-value	Odds Ratio (CI)
use				5.172	0.0230	1.514
Yes	115 (40%)	88 (30%)	203			(1.072-2.139)
No	170 (60%)	197 (70%)	367			
Total	285 (100%)	285 (100%)	570 (100%)			

Table 10: Relationship of cases and controls according to history of use of steroid

H/O Steroid use	Cases	controls	Total	Chi- Square	P-value	Odds ratio (CI)
				6.347	0.0118	1.604
Yes	105 (36%)	76 (26%)	181 (32%)			(1.123-
No	180 (64%)	209 (74%)	389 (68%)			2.291)
Total	285 (100%)	285 (100%)	570 (100%)			

Table 11: Relationship of cases and controls according to history of tobacco use

H/O of tobacco use	cases	controls	Total	Chi- Square	p-value
Yes	168 (58.9%)	156 (54.7%)	324 (56.9%)	0.8653	0.3523
No	117 (41.1%)	129 (45.3%)	246 (43.1%)		
Total	285 (100%)	285 (100%)	570 (100%)		

Table 12: Relationship of cases and controls according to History of Myopia

History of Myopia	Cases	Controls	Total	Chi-Square	p-value	Odds Ratio (CI)
Present	156 (54.7%)	118 (45.2%)	274 (48%)	9.621	0.0019	1.711 (1.228-2.385)
Absent	129 (45.3%)	167 (54.8%)	296 (52%)			
Total	285 (100%)	285 (100%)	570 (100%)			

Table 13: Relationship of cases and controls according to History of Eye Surgery

H/O Eye Surgery	Cases	Controls	Total	Chi-Square	p-value
Yes	40 (14.0%)	35 (12.2%)	75 (13.1%)	0.2457	0.6202
No	245 (86.0%)	250 (87.8%)	495 (86.9%)		
Total	285 (100%)	285 (100%)	570 (100%)		

Table 14: Relationship of cases and controls according to Types of Diabetes Mellitus

Type of DM	Cases	Controls	Total	Chi- Square	p-value
				0.02803	0.8670
Type-1	16 (13%)	11 (11.3%)	27 (12.2%)		
Total	123 (100%)	97 (100%)	220 (100%)		

Table 15: Relationship of cases and controls according to history of Hypertension

H/O Hypertension	Cases	Controls	Total	Chi- Square	p-value	Odds Ratio(CI)
	n%	n%	n%	4.745	0.0294	1.463 (1.051-2.034)
Present	158 (55.4%)	131 (46%)	289 (51%)			
Absent	127 (44.6%)	154 (54.0%)	281 (49%)			
Total	285 (100%)	285 (100%)	570 (100%)			

Table 16: Relationship of cases and controls according to history of Thyroid disorder

H/O	Cases	Controls	Total	Ch-	p-value
Thyroid				Square	
Disorder				0.1175	0.7318
Yes	110	115	225		
	(38.6%)	(40.4%)	(39.5%)		
No	175	170	345		
	(61.4%)	(59.6%)	(60.5%)		
Total	285	285	570		
	(100%)	(100%)	(100%)		

Table 17: Relationship of cases and controls according to Types of Thyroid disorder

Types of Thyroid disorder	Cases	Controls	Total	Chi- Square	p-value
				0.006903	0.9338
Hyperthyroidism	52 (47.2%)	55 (47.9%)	107		
Hypothyroidism	58 (52.8%)	60 (52.1%)	118		
Total	110 (100%)	115 (100%)	225 (100%)		

Table 18: Relationship of cases and controls according to history of Migraine Headaches

H/O	Cases	Controls	Total	Chi-	p-value
Migraine				Square	
Headaches				0.2672	0.6052
Present	56	62	118		
	(19.6%)	(21.8%)	(20.7%)		
Absent	229	223	452		
	(80.4%)	(78.2%)	(79.3%)		
Total	285	285	570		
	(100%)	(100%)	(100%)		

Table 19: Relationship of cases and controls according to history of Vasospasm related disorders

H/O	Cases	Controls	Total	Chi-Square	p-value
Vasospasm-related disorders				0.7327	0.1167
Present	44	48	92		
	(15.4%)	(16.8%)	(16.1%)		
Absent	241 (84.6%)	237 (83.2%)	478 (83.9%)		
Total	285 (100%)	285 (100%)	570 (100%)		

Table 20: Relationship of cases and controls according to history Obstructive sleep apnoea

H/O Obstructive sleep apnoea	Cases	Controls	Total	Chi-Square	p-value
				0.2256	0.6348
Present	39 (13.6%)	44 (15.4%)	83 (14.5%)		
Absent	246 (86.4%)	241 (84.6%)	487 (85.5%)		
Total	285 (100%)	285 (100%)	570 (100%)		

Glaucoma is a heterogeneous group of diseases that primarily affects peripheral vision. In some others, it is regarded as a heterogeneous neuropathy that causes irreversible blindness. Worldwide, it is the second most common cause of blindness after cataracts. The Male to Female Ratio in India & World is 1.06:1 & 1.36:1 respectively. [16-19] in our study, prevalence of Glaucoma in Males is more than the females. Which is supported by R George et al. [16], VV KapetanakisIt et al. [17], YC Tham et al. [18], and K Allison et al. [19].

Our study, showed a statistically significant association between Glaucoma and Gender as a risk factor. This is supported by Framingham Eye Study [20], Rotterdam Study [21], Barbados Eye Study [22], etc.

In our study, a higher Prevalence of Glaucoma is seen in age group 50-59 years. This result is same with MW Tuck et al. [23] except for age group 80-89 years.

In our study, increasing age found to be a risk for Glaucoma. This is supported by AR Rudnicka et al. [24], Medical Advisory Secretariat, UK [25], PJ Foster et al. [26], Baltimore Eye Study [27], Barbados Eye Study [28], G Guedes et al. [29], Antonio Greco et al. [30], etc.

Our study shows a statistically significant association between high IOP and Glaucoma (P-value: <0.0001). This is supported by almost all the studies like Anne L Coleman et al. [31], YC Tham et al. [18], Los Angeles Latino Eye Study [24], The Rotterdam Study [21], Blue Mountains Eye Study [22], etc. Infect, IOP is one of the well-established modifiable risk factors for Glaucoma. In our study there is a statistically insignificant association between family history & Glaucoma (P-value: 0.2689). This is in contrast with A Le et al. [26], Tielsch et al. [15] {family history of glaucoma was higher in siblings (odds ratio: 3.69) than in parents (OR: 2.17) or children (OR:1.12)}

In our study statistically insignificant association was seen between smoking and Glaucoma (P-value: 0.2689). This is supported by Wise et al. [32] (P-value-0.28)

In our study, no association was seen between history of obstructive sleep apnea and Glaucoma (P-value: 0.6348). This result is supported by CA Girkin et al.

[33] (p-value = 0.18, OR = 1.80, 95% CI 0.76-4.23). Timothy V Roberts et al. [34], Tejaswini Prashant Khandgave et al. [35] found no association. In contrast, Lin et al. [36] 2013, Chen et al. [37] 2014, found association.

In our study an insignificant association was seen between history of migraine/ vasospastic disorders and Glaucoma (p-value: 0.6052). This result is supported by A Pradalier et al. [38] where they stated that migraine was not associated with any form of Glaucoma (P-value: 0.07). Landers et al. [39], Lin et al. [36] also found same result. Whereas, C Cursiefen et al. [40], showed a significant association for, normal tension Glaucoma P-value was <0.05 & high-tension Glaucoma P-value was <0.01, Blue Mountains Eye study [41], also found positive association. In our study, an insignificant association was seen between history of thyroid disorders and Glaucoma (P-value: 0.7318). This is supported by P Karadimas et al. [42], (P-value: 0.3, R: -0.08), Stephen P Motsko et al. [43]. In contrast KD Smith et al. [44], Boles Carenini B et al. [45], etc. found an association (P- value: 0.02,0.001,0.011 respectively)

In our study, there is a significant association between Hypertension & Glaucoma (P-value: 0.0294) This is supported by various studies like JMS Langman et al. [46] Blue Mountains Eye Study etc. In contrast, Amit K Deb et al. [47], Lingam Vijaya et al. [48] found contra indicatory interpretation.

In our study, a statistically significant association was seen between diabetes mellitus and Glaucoma

(P-value: 0.0315). Which is supported by Los Angeles Latino Eye Study, Vikas Chopra, et al. [49], P Mitchell et al. [50], Louis R Pasquale et al. [51], Beaver Dam Eye Study [52] (P-value: 0.004). In contrast to our study, Ellis et al. 2000 [53] (RR=1.57, 95% CI 0.99-2.48), De Voogd et al. 2006 [54] (RR=0.65, 95% CI 0.25-1.64), Vijaya et al. 2014 [55] (OR=1.07, 95% CI 0.62-1.82) found insignificant association.

In our study, a statistically significant association was seen between history of myopia and Glaucoma (P-value: 0.0019). Which is supported by Casson et al. [56], Ramakrishnan et al. [57], Xu et al. [58]. In contrast Wong et al. [59], Garudadri et al. [60], Perera et al. [61] found insignificant association.

In our study a statistically significant association is seen between history of smoking and Glaucoma (P-value: 0.0181), which is supported by Mónica Pérez- de-Arcelus et al. [62], Fan et al. [63], Renard et al. [64] In contrast, Kang et al. [65], Kaimbo et al. [66], Wang et al. [67], found insignificant association.

In our study, statistically significant association is seen between history of steroid use and Glaucoma (P-value: 0.01), which is supported P Mitchell et al. [68], E Garbe et al. [69], Opatowsky et al. [70], Shroff et al. [71]. In contrast, Chang et al. [72], Alsaadi et al. [73] found insignificant association.

In our study a statistically significant association between alcohol use and Glaucoma. (p-value: 0.0230). which is supported by Wise et al. [74], A meta- analysis by V Kelsey et al. [75], Framingham Eye Study [20] (P-value:<0.01) in contrast Leske et al. [28], Kang et al. [65] found insignificant association.

Conclusion

In our study various risk factors are significantly associated with Glaucoma like High IOP, Myopia, Non-Modifiable factors like increasing age & marital status, Systemic diseases like Hypertension & Diabetes Mellitus and several modifiable risk factors like smoking, alcohol use, and steroid use etc. further study is needed in this domain to establish risk factors and to take proper steps to reduce it.

Ethical Clearance: Obtained from IEC, GMCH, Guwahati

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