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STUDY OF PREDICATIVE FACTORS OF INSOMNIA AND DEPRESSION IN GLAUCOMA PATIENTS

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ABSTRACT:

Background: The role of emotional factors in glaucoma has received wide recognition by investigators and clinicians from the very beginning. Prevalence of depression in glaucoma has been estimated to be 10 to 12 percent in previous studies. Insomnia is another psychiatric co-morbidity reported with glaucoma. Both depression and insomnia in glaucoma patients may significantly affect overall quality of life in these patients adversely. The present study explores the predictive factors of insomnia and depression in patients with Glaucoma.

Materials & Methods: A case-series type of observational study was carried out on 100 glaucoma cases attended at ESIC Model Hospital, Jaipur (Raj). The PHQ -9 and ISI were used to assess depression and insomnia respectively. Data in details were collected as per pre-designed Performa. Data collected were analyzed and inferred with chi-square test.

Result: Insomnia and depression was found in 37%, and 36% of glaucoma cases respectively and depression both were significantly associated with Age Visual acuity in both the eyes and severity of glaucoma. No other socio-demographic and disease variables had significant association with either insomnia or depression.

Conclusion: Insomnia and depression are commonly associated with glaucoma. Both insomnia and depression are associated with Age, Visual acuity in both the eyes and severity of glaucoma.

Introduction

Glaucoma is a chronic, progressive, and irreversible disease which can result in severe visual disability^[1,2]. The role of emotional factors in glaucoma has received wide recognition by investigators and clinician from

the very beginning. Glaucoma probably more than any other eye disease has been considered to be a psychosomatic disorder. Physical illnesses also create psychological sequel that precipitate psychiatric disorders severe enough to require independent attention.

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it has been postulated that mental health may impact clinical factors such as glaucoma medication adherence and persistence^[3-5]. Prevalence of depression in glaucoma has been estimated to be 10 to 12 percent in previous studies.^[6,7]

However, in severe glaucomatous disease, the prevalence of depression has been reported to be as high as 32.1%.^[8]

Furthermore, depression has been correlated with patients' perception of vision.^[9] However, in contrast to subjective measures of visual perception, objective measures of function such as visual acuity or visual field results have not been linked to glaucoma diagnosis or depression severity^[8,9] Insomnia is another psychiatric co-morbidity reported with glaucoma.^[10] Both depression and insomnia in glaucoma patients may significantly affect overall quality of life in these patients adversely.

In order to prevent and treat these psychiatric co-morbidities that develop with glaucoma, it is also important to find out the risk factor of these psychiatric co-morbidity. Hence this present study was planned to identify determinants of these psychiatric co-morbidity in glaucoma.

Materials and Methods

This case series type of observational study was carried out as joint venture of Department of Psychiatry and Department of Ophthalmology in ESIC Model Hospital, Jaipur, India which is a multi- specialty referral center in capital of Rajasthan. This hospital caters larger population from each corner of the state.

Hundred patients with glaucoma i.e. 50 males and 50 females were recruited from both outpatient department and ward during 1stJan. 2013 to 30th June 2013. Hindi speaking adult patients (18 - 88 Years)

with glaucoma from more than 6 months prior to enrollment were included in the study. Glaucoma was diagnosed based on glaucomatous disc cupping and reproducible visual field damage in one or both eyes. Patients with primary open-angle glaucoma (POAG), normal tension glaucoma (NTG), primary angle closure glaucoma (PACG) and secondary glaucoma (SG) were included in the study. Out of these identified cases, cases with present or past history of major psychiatric illness, current use of any medication which may result in psychiatric manifestations (systemic use of beta blockers), incisional eye surgery within the previous three months or laser treatment within the previous one month, disability in visual field testing due to causes other than glaucoma (e.g., cognitive impairment) and other severe vision- impaired eye diseases (e.g. cataracts (Lens Opacities Classification System III grade 2 or more and age-related macular degeneration) were excluded. After seeking informed consent 100 eligible subjects were evaluated on specially designed Performa to incorporate socio-demographic details and disease characteristics. Insomnia Severity Index (ISI) and PHQ-9 were applied to detect Insomnia and depression respectively. Depression was assessed by administering the nine-item PHQ- 9^[11,12], a self-report version of PRIME-MD11 which assesses the presence of major depressive disorder using modified Diagnostic and Statistical Manual, Fourth edition (DSM-IV) criteria. There is good agreement reported between the PHQ diagnosis and those of independent psychiatry health professionals (for the diagnosis of any one or more PHQ disorder, kappa = 0.65; overall accuracy, 85%; sensitivity, 75%; specificity, 90%).

In this study Hindi version of PHQ-9 was used. It has been validated in Indian population and is considered to be reliable tool for diagnosis of depression. The PHQ-9 is a dual instrument that is used to establish a provisional depressive disorder as well as it provides a symptoms severity score. For the diagnosis of depression, we define clinical significant depression as: a PHQ-9 score of 8–9 as minor depression, a PHQ-9 score of 10 or greater as moderate depression; a score of 15 or more and one of the two cardinal symptoms (either depressed mood or anhedonia) as definite major depression. We considered PHQ 9 score of 10 or more as depression in this study. Insomnia was assessed on Insomnia Severity Index (ISI) [13]. ISI is one of the most commonly used disease-specific measures for self-perceived insomnia severity. The ISI has 7 items describing insomnia-related health impairments.

Each item is rated on a 5-point Likert scale with scores ranging from 0 to 4, indicating “none”, “mild”, “moderate”, “severe” and “very severe” sleep problems, respectively. The total ISI score is calculated by summing the scores from the 7 items, and range from a minimum of 0 to a maximum of 28, with higher scores reflecting more severe sleep problems. In clinical assessments, the ISI total summary score falls into 1 of 4 ISI categories; with scores 0–7, 8–14, 15–21, and 22–28 indicating no clinically significant insomnia, sub-threshold insomnia, moderate insomnia and, clinically severe insomnia, respectively. The psychometric properties of the ISI have been evaluated in earlier studies and

have been reported to have sound measurement quality for measuring perceived insomnia severity and the impact of insomnia in different populations [14]

We used Hindi version of the Insomnia Severity Index [15] which has a reliability of 0.91 and a corrected item correlation range of 0.56–0.87. Hindi version of the Insomnia Severity Index is a valid and reliable tool for the measurement of severity of insomnia.

All participants underwent comprehensive ophthalmic examinations and evaluated for glaucoma symptoms like pain, congestion etc. Anterior chamber depth examined by slit lamp, and visual acuity by refraction unit. Detailed fundus examination was also done and cup disc ratio was calculated. Automated static perimetry (Humphrey visual field analyzer 30-2) was used to detect peripheral visual field defects and gonioscopy was done to find status of angle (open or closed). Patients were categorized as mild, moderate and severe depending on the results of status of cup and fields.

Variables		No.	%
Sex	Male	50	50
	Female	50	50
	Total	100	100
Age	<30	6	6
	30-50	29	29
	50-70	58	58
	>70	7	7
	Total	100	100
Marital Status	Married	95	95
	Unmarried	5	5
	Total	100	100
Income	<5000	59	59
	5000-10000	34	34
	10000-15000	3	3
	>15000	4	4
	Total	100	100

Table 1 : Sociodemographic characteristics of the study population

Statistical analysis

All data collected were entered into Microsoft excel 2007 worksheet in the form of master chart. These data were classified and analyzed as per the aims and objectives with the help of MS Excel 2007 and Primer (version 6) statistical software. The data obtained were planned to be analyzed by using both descriptive and inferential statistics the data on sample characteristics described in terms of percentage and proportions in the form of tables and graphs whenever it was applicable. To find out difference in proportion chi square test was used. For significance 'p' value 0.05 or less was considered significant.

Results

Out of total 100 eligible glaucoma cases studied with assigned scales to identify psychiatric co-morbidity, it was observed that insomnia and

Depression was found in 37%, and 36% of glaucoma cases respectively.

Various Socio-demographic variables were studied in this study age, sex, marital status and Income and their distribution among study participants is shown in **Table I**. Male and Female ratio was kept 1:1 in this study. Maximum participants were from the age group 50 to 70 years (58%) and 95 % were married. 34% participants were having their monthly income between 5000 to 10000 rupees while only 4% had more than 15000 rupees per month. It was found that none of the Socio-demographic variable was associated significantly with depression except age. Depression was found to be statistically significant with growing age (p =0.014). Similarly, Insomnia was also not found to have significant association with socio demographic variables.

S. No.	Variables		Total Glaucoma Cases	*Glaucoma Cases with							
				Insomnia				Depression			
				Yes	%	No	%	Yes	%	No	%
1	Sex	Males	50	17	34	33	66	15	30	35	70
		Females	50	20	40	30	60	21	42	29	58
		Total	100	37	37	63	63	36	36	64	64
	Chi-square Test		0.172 at 1DF; P = 0.679 NS				1.085 at 1 DF; P = 0.298 NS				
2	Age (Year)	<30	6	0	0	6	100	1	16.67	5	83.33
		30-50	29	8	20.69	23	79.31	4	13.79	25	86.21
		50-70	58	29	50	29	50	28	48.28	30	51.72
		>70	7	2	28.57	5	71.43	3	42.86	4	57.14
		Total	100	37	37	63	63	36	36	64	64
Chi-square Test		11.252 at 3 DF; P = 0.013 S				11.117 at 3 DF; P = 0.014 S					
3	Marital Status	Married	95	36	37.89	59	62.11	34	35.79	61	64.21
		Unmarried	5	1	20	4	80	2	40	3	60
		Total	100	37	37	63	63	36	36	64	64
	Chi-square Test		0.111 at 1 DF; P = 0.739 NS				0.082 at 1 DF; P = 0.774 NS				
4	Income (Rs)	<5000	59	27	45.76	32	54.24	23	38.98	37	62.71
		5000-10000	34	10	29.41	24	70.59	12	35.29	24	70.59
		10000-15000	3	0	0	3	100	1	33.33	2	66.67
		>15000	4	0	0	4	100	0	0	4	100
	Total	100	37	37	63	63	36	36	64	64	
Chi-square Test		6.895 at 3 DF; P = 0.099 NS				2.496 at 3 DF; P = 0.649 NS					

Table II :Association of Socio-demographic Factors with Insomnia and Depression in Glaucoma Cases

However association of insomnia with increasing age was significant ($p < 0.013$.) (Table II) Regarding symptomatology of glaucoma cases, pain was found in 66% of cases, congestion in 23%, pupillary reaction in 53%, anterior chamber depth shallow in 28%, visual acuity 6/60 or less in right eye in 37% and in left eye 28%. When association of psychiatric co-morbidity

with symptomatology of glaucoma cases was observed using chi square test it was found that depression was found to be significantly associated with visual acuity 6/60 or less in RE and LE ($P=0.036, p=0.040$ respectively). Likewise insomnia was found significantly more in participants having visual acuity 6/60 or less in right eye (54.1% v/s 26.9%, $P = 0.018$) as well as in left eye

S. No.	Variables		Total Glaucoma Cases	*Glaucoma Cases with							
				Insomnia				Depression			
				Yes	%	No	%	Yes	%	No	%
1	Pain	Yes	34	15	44.12	19	55.88	16	47.06	18	52.94
		No	66	22	33.33	44	66.67	20	30.3	46	69.7
	Total	100	37	37	63	63	36	36	64	64	
	Chi-square Test	0.705 at 1 DF; $P = 0.401$ NS				2.05 at 1 DF; $P = 0.152$ NS					
2	Congestion	Yes	23	9	39.13	14	60.87	8	34.78	15	65.22
		No	77	28	36.36	49	63.64	28	36.36	49	63.64
	Total	100	37	37	63	63	36	36	64	64	
	Chi-square Test	0.000 at 1 DF; $P = 0.996$ NS				0.012 at 1 DF; $P = 0.913$ NS					
3	Pupillary Reaction	Yes	53	24	45.28	29	54.72	22	41.51	31	58.49
		No	47	13	27.66	34	72.34	14	29.79	33	70.21
	Total	100	37	37	63	63	36	36	64	64	
	Chi-square Test	2.606 at 1 DF; $P = 0.106$ NS				1.020 at 1 DF; $P = 0.312$ NS					
4	Anterior Chamber depth	Normal	72	27	37.5	45	62.5	25	34.72	47	65.28
		Shallow	28	10	35.71	18	64.29	11	39.29	17	60.71
	Total	100	37	37	63	63	36	36	64	64	
	Chi-square Test	0.004 at 1 DF; $P = 0.949$ NS				0.038 at 1 DF; $P = 0.845$ NS					
5	Visual Acuity (Rt. Eye)	6/60 or less	37	20	54.05	17	45.95	21	56.76	26	70.27
		6/30 or	63	17	26.98	46	73.02	15	23.81	48	76.19
	Total	100	37	37	63	63	36	36	64	64	
	Chi-square Test	5.622 at 1 DF; $P = 0.018$ S				4.420 at 1 DF; $P = 0.036$ S					
6	Visual Acuity (Lt. Eye)	6/60 or less	28	16	57.14	12	42.86	15	53.57	13	46.43
		6/30 or	72	21	29.17	51	70.83	21	29.17	51	70.83
	Total	100	37	37	63	63	36	36	64	64	
	Chi-square Test	5.622 at 1 DF; $P = 0.018$ S				4.206 at 1 DF; $P = 0.040$ S					
7	Type of Glaucoma	Open Angle	75	26	34.67	49	65.33	25	33.33	50	66.67
		Closed	25	11	44	14	56	11	44	14	56
	Total	100	37	37	63	63	36	36	64	64	
	Chi-square Test	0.358 at 1 DF; $P = 0.550$ NS				0.521 at 1 DF; $P = 0.470$ NS					
8	Duration of Glaucoma	6-9 Month	19	3	15.79	16	84.21	4	21.05	15	78.95
		9-12 Month	7	3	42.86	4	57.14	3	42.86	4	57.14
		12-18	7	2	28.57	5	71.43	4	57.14	3	42.86
		18-24	13	5	38.46	8	61.54	4	30.77	9	69.23
		>24 Month	54	24	44.44	30	55.56	21	38.89	33	61.11
		Total	100	37	37	63	63	36	36	64	64
Chi-square Test	5.279 at 4 DF; $P = 0.260$ NS				3.693 at 4 DF; $P = 0.449$ NS						
9	Severity of Glaucoma	Mild	34	4	11.76	30	88.24	5	14.71	29	85.29
		Moderate	42	18	42.86	24	57.14	13	30.95	29	69.05
	Severe	24	15	62.5	9	37.5	18	75	6	25	
	Total	100	37	37	63	63	36	36	64	64	
Chi-square Test	16.602 at 2 DF; $P = 0.000$ HS				23.000 at 2 DF; $P = 0.000$ HS						

Table III: Association of Clinical Characteristics with Insomnia and Depression in Glaucoma Cases

(57.1% v/s 29.1%, $P= 0.018$). (**Table III**) Among all glaucoma cases of present study, 75% were open angle and 25% were closed angle glaucoma. Majority of cases (54%) had more than 24 months duration. Further, 34% cases were mild, 42% moderate and 24% severe cases of glaucoma.

On application of Chi Square test, depression and insomnia were significantly associated with severity of Glaucoma ($p < 0.05$), however association of insomnia and depression with type of glaucoma and duration of glaucoma were not found significant. (**Table III**)

Discussion

The prevalence of insomnia and depression in our sample was 37 percent and 36 percent respectively which is substantially higher than the normal level in general population. This finding correlates with earlier studies indicating that glaucoma is a significant predictor of depression.^[6,16] Another study conducted in Greece showed that the anxiety and depression levels were significantly higher in patients of primary open angle glaucoma (POAG) than those in healthy controls^[17]. Reduced participation in activities of daily living, **Seixas, Azizi, et al.**^[18] observed a significant association between visual impairment and insomnia symptoms in their study sample of 307 patients with almost 62 percent of patients reporting insomnia symptoms. Furthermore, a high prevalence of sleep disorders, such as insomnia, daytime sleep, sleep apnea can be found in patients with glaucoma.^[19] Individuals with visual impairment are at risk for sleep disturbances and sleep-disordered breathing^[20]

Patients with glaucoma are at risk for obstructive sleep Apnea (OSA).^[21,22] Glaucoma has also been reported to be associated with sleep-disordered breathing and circadian rhythm disruptions.^[23] Recent studies have shown that sleep problems, due to visual impairment can lead to more

Distribution of Insomnia among participants



debilitating conditions (e.g., delayed or advanced sleep-phase syndrome and irregular sleep-wake cycles), which can lead to insomnia and circadian rhythm disorders.^[24]

Involvement of intrinsically photosensitive retinal ganglion cells ipRGCs as well as regular RGCs in glaucoma has been postulated in recent years. Several animal models studies of glaucoma have demonstrated a degenerative loss of ipRGCs or melanopsin photopigment leading to impairment of circadian rhythms regulation, pupillary light responses and other non-image-forming functions.^[25]

Amongst the socio demographic variables younger older age was found significantly associated with insomnia and depression in this study population.

Mabuchi et al^[6] in his study have found significant correlation between depression and older age.

Skalicky and Goldberg ^[8] used Geriatric Depression Scale-15 questionnaire and reported that older age was a risk factor for depression in glaucoma patients. Chronicity of the illness, risk of blindness and various treatment challenges faced by elderly age group who are otherwise also compromised in terms of general debility and other physical problems may have been responsible for this association between old age and depression ^[26].

Wang H et al ^[27] in his study have found that global sleep quality decreased with age in both healthy controls and POAG patients. With increasing age, the density of the lens increases thereby reducing light transmission, particularly for the short wavelength (blue) light to which the circadian system has been shown to be most sensitive. ^[28]

On the other hand, the occurrence of circadian timing disturbances with age may also be due to neurodegenerative changes in the SCN which may cause decreased regulation function of the non- image-forming system ^[29]

While analyzing clinical, variables insomnia and depression were found associated with visual acuity less than 6/60 in either of the eyes and severity of glaucoma regardless of the type of glaucoma.

Association between severity of visual field defect with depression has been reported earlier by **Mabuchi** ^[30].

Staticky and Goldberg ^[8] also reported that depression was more prevalent with increasing glaucoma severity.

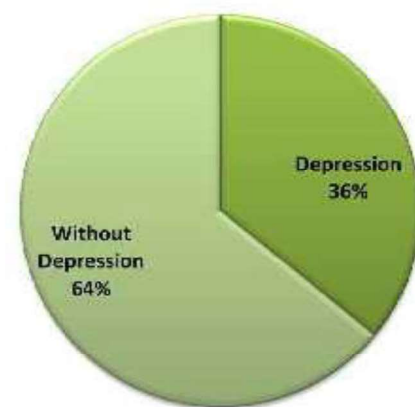
Erg et al ^[31] observed that POAG inpatients had higher score for depression with BDI than outpatients, citing the reason that the severity of glaucoma had been more in inpatients than the outpatients. With

progressive increase in vision loss consequent worsening of glaucoma, the impairment in ability to function optimally escalates and social restrictions get imposed which may perpetuate emotional and sleep problems in these patients.

Chuandi Zhou et al ^[32] have attributed self-reported visual functions being consistently

correlated with anxiety and depression in glaucoma patients and has emphasized self-reported visual function as predictor of anxiety in glaucoma patients. **Lund mark et al** ^[32] also reported a disproportionate relationship between depression and visual field loss. They suggested that patient related outcomes are more reflective of their psychological status than objective clinical measures, such as MD of visual field, visual acuity and IOP.

Distribution of Depression among Participants



Nevertheless, contrary to the above observations, our finding suggest that objective measures are equally important in predicting psychological status. In our study visual acuity and severity of glaucoma were strongly correlated with insomnia and depression. These objective clinical measures are the principal component in determining the severity of glaucoma which in turn has been correlated with psychological symptoms in many studies ^[8,30]. Hence it is imperative to understand and vindicate the correlation between objective clinical measures and psychological symptoms, instead of merely relying much on clinical symptoms as risk factor for anxiety and depression in glaucoma patients.

Conclusion

Findings of this study indicate the high prevalence of insomnia and depression in glaucoma patients. Old age is predictor of insomnia and depression.

Objective clinical parameters exhibit great potential in evaluating psychological factors. Consequently the psychological factors should equally be considered of paramount importance to deliver a comprehensive treatment. Hence clinician should be made acquainted to identify and address the concomitant sleep problems and depression and a proper psychiatric referral if needed to provide comprehensive care.

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