

Original Article

Binocular Anomaly, Color Vision Deficiency and Dry Eye in Patients with Cancer

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Abstract

Objective: To determine the prevalence of color vision disorders and dry eye in patients with cancer.

Patients and Methods: This cross-sectional study was conducted in 2019 at Imam Hossein Hospital, Tehran, Iran, and included 307 eyes from 165 patients with cancer before initiation of systemic chemotherapy. All participants underwent Schirmer I testing, binocular vision and ocular motility assessment, and color vision evaluation with Ishihara plates and the Farnsworth D15 panel. Posterior and anterior segment examinations were also performed.

Results: Data from 307 eyes of 165 patients were analyzed. The mean age was 54.26 ± 13.39 years (range, 18–86). Overall, 74.6 % of eyes showed some degree of dry eye. The mean Schirmer value was 8.65 ± 8.69 mm. Abnormal color vision was detected in 6.74 % of eyes by Ishihara and in 17.28 % by the D15 test. Exophoria was present in 58.8 % of patients and esophoria in 29.1 %, while 2.1 % demonstrated abnormal ocular motility.

Conclusion: Dry eye, color vision deficiency and heterophoria were more frequent among patients with cancer than in the general population, underscoring the need for routine ophthalmic screening and follow-up in oncologic care.

Keywords: Cancer; Color Vision; Schirmer Test; Heterophoria; Dry eye.

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Introduction

Cancer comprises a large group of diseases characterized by uncontrolled cell growth that may spread to other organs, and it can affect nearly any part of the body ¹. The incidence, prevalence, and mortality of cancer are increasing worldwide for multiple reasons ²⁻⁶. According to the Global Cancer Observatory, approximately 18 million new cancer cases were identified in 2018. The most common cancers in men were lung, prostate, and stomach, while in women they were breast, lung, and cervical cancers ^{5,7}. In Iran, the high prevalence of cancer risk factors suggests that the number of cases will continue to rise in the near future ⁸. The health of the tear film can be influenced by the lacrimal glands, the anterior segment of the eye, the nervous system, environmental conditions, visual workload, systemic diseases, nutrition, and medications ⁹⁻¹¹.

Dry eye disease is a multifactorial disorder of the tear film and ocular surface, characterized by discomfort, visual disturbance, tear film instability, increased osmolarity, and ocular surface inflammation. It may be secondary to ocular or systemic disease, with a prevalence of 5–35 % ^{12,13}. The condition impairs visual acuity and quality of life, and diagnosis relies on clinical findings, with the Schirmer test being one of the most common diagnostic tools ^{12,13}.

Individuals with normal color vision can distinguish about ten million different colors, compared with only about thirty shades of gray ¹⁴. Color vision deficiency, or color blindness, is defined as the inability to perceive certain color shades ¹⁵. These defects may be congenital, affecting males predominantly, or acquired as a result of ocular disease or medication ^{16,17}. More than 4 % of the population is affected, resulting in

altered color perception ¹⁸.

Eye movements serve to shift fixation to a new object or to maintain the stability of an object on the fovea. Because each type of movement has its own anatomical substrate, ocular motility disturbances can often be localized to specific brain regions or linked to systemic disease in the appropriate clinical context. Thus, assessment of eye movements can be diagnostically valuable in many patients ¹⁹. Ocular motility can also be affected by medications and systemic conditions.

This study was designed to determine the prevalence of color vision deficiency, tear film abnormalities, and binocular vision disturbances among patients with cancer in Iran.

Patients and Methods

This cross-sectional study was conducted in 2019 on 330 eyes from 165 patients with cancer (91 women, 74 men; age range, 18–86 years) whose diagnoses were confirmed by a radiation oncologist. Patients presenting for the first time to the chemotherapy ward of Imam Hossein Hospital, Tehran, Iran were invited to participate prior to initiation of systemic chemotherapy.

Inclusion criteria

Eligibility criteria included: confirmed diagnosis of cancer (excluding ocular cancers), good general condition (ECOG performance status 0–1), and age ≥ 18 years.

Ophthalmic examinations

All participants underwent a complete ocular and visual evaluation before chemotherapy.

Schirmer I test: Tear secretion was measured

using Schirmer I test without topical anesthesia. A standardized strip (5 × 35 mm) was placed in the outer one-third of the lower eyelid fornix under dim light with eyes closed. After five minutes, the length of wetting was recorded in millimeters^{20–25}. Both eyes were tested simultaneously. Results were classified as severe (≤ 2 mm), moderate (≤ 5 mm), mild (≤ 10 mm), or normal (> 10 mm)²⁶.

Color vision: Testing was performed monocularly at a distance of 50 cm under standard illumination (200–250 lux). Red–green color vision was assessed using Ishihara pseudoisochromatic plates, while broader color discrimination was evaluated with the Farnsworth D15 panel, which requires arranging 16 colored caps according to hue similarity.

Posterior segment: Direct ophthalmoscopy was performed using a Heine Beta 200 ophthalmoscope, without pharmacologic dilation, to assess the optic nerve head and macula.

Ocular motility: Eye movements were examined binocularly in nine gaze positions, with attention to smoothness and ease of movement at near fixation. Measurement of ocular motility has been suggested as a useful tool for evaluating therapeutic effects on cognitive and sensorimotor processes in clinical populations and may facilitate drug development for agents targeting specific neural systems²⁷.

Phoria and tropia: The presence and type of heterophoria or tropia were assessed using the cover test at near fixation in the primary gaze position.

Precautions

To prevent drug interactions and comply with ethical standards, no pharmacologic agents

(cycloplegics, mydriatics, topical anesthetics) or diagnostic dyes (such as fluorescein) were used. All examinations were performed with patients in a sitting position.

Statistical analysis

The minimum required sample size was estimated at 150 patients, based on an anticipated dry eye prevalence of 25 % in the general population, a 95 % confidence level, and a 5 % margin of error. To improve power and allow subgroup analyses, all eligible patients during the study period were included, yielding 160 patients (320 eyes). Data were analyzed using SPSS software version 22 (IBM Corp., Armonk, NY, USA). The normality of quantitative variables was checked using the Kolmogorov–Smirnov test. Since most variables were not normally distributed, comparisons between two groups (e.g., gender, age < 40 vs. ≥ 40) were performed using the Mann–Whitney U test, and comparisons among three or more groups (e.g., refractive error categories) were performed using the Kruskal–Wallis test. Associations between categorical variables were examined with the Chi-square test or Fisher's exact test where appropriate. A two-sided P value < 0.05 was considered statistically significant.

Ethics

The study protocol was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences, Tehran, Iran (code: IR.SBMU.RETECH.REC.1397.1006). All participants provided written informed consent, and the study adhered to the principles of the Declaration of Helsinki.

Table 1: Mean Schirmer I test values according to refractive error, age group, and gender

Group	N	Mean ± SD (mm)	Range (mm)	*P value
SE Group				
Myopia	81	9.32 ± 8.87	0–35	0.658
Hyperopia	92	7.46 ± 7.64	0–35	
Emmetropia	134	9.07 ± 9.22	0–35	
Age (yr)				
< 40	44	11.07 ± 9.23	0–35	0.012
≥ 40	263	8.25 ± 8.55	0–35	
Gender				
Female	167	8.56 ± 8.67	0–35	0.600
Male	140	8.77 ± 8.74	0–35	

N = number of eyes.

* Chi-Square and Mann–Whitney U test Tests were used for comparisons.

Results

Data from 307 eyes of 165 patients with cancer were analyzed, including 91 women (55.2 %) and 74 men (44.8 %). The mean age was 54.26 ± 13.39 years (range, 18–86). Analyses were performed per eye (307 eyes), unless otherwise specified. The largest age group was 50–60 years (25.5 %), and the smallest was 80–90 years (1.2 %). A total of 142 patients (86.1 %) were ≥ 40 years, and 23 patients (13.9 %) were <40 years. The most common malignancies were gastrointestinal cancers (36.4 %), followed by breast cancer (15.2 %). In women, breast cancer was the most frequent (27.47 %), while in men colorectal cancer predominated (18.92 %). Among those younger than 40 years, breast cancer was most common (20.83 %), whereas among those ≥ 40 years, colorectal cancer was most frequent (22.97 %). More than half of the patients (58.2 %) reported no comorbidity. The frequencies of diabetes, hypertension,

and hyperlipidemia were 15 %, 16.8 %, and 15.7 %, respectively.

The mean Schirmer I test value was 8.65 ± 8.69 mm (range, 0–35). Descriptive statistics according to refractive error, age group, and gender are presented in table 1. Age-stratified Schirmer values and color vision outcomes (Ishihara and D15) are summarized in table 2. Among participants, 22.5 % had severe dry eye, 22.8 % moderate, 29.3 % mild, and 25.4 % normal Schirmer values. Severe dry eye was observed in 24.5 % of women and 20 % of men. Normal Schirmer results were found in 25.75 % of women and 25 % of men. By refractive status, 29.63 % of myopes, 21.74 % of hyperopes, and 25.37 % of emmetropes had normal Schirmer values, with the remainder showing varying degrees of dry eye. In those <40 years, 41.3 % had normal Schirmer results, compared with 22.61 % in those ≥ 40 years (Table 3). Age-specific distribution of dry eye severity is shown in figure 1.

Table 2: Schirmer I test and color vision results by age group

Age (yr)	N (SIT)	SIT Mean $\pm$ SD	Range	Ishihara (N/ Abn)	D15 (N/ Abn)	*P values (SIT / Ishihara / D15)
90–80	2	.00	.00	2/2	0/2	
80–70	32	7.40 $\pm$ 6.55	0–35	20 / 3	6 / 0	
70–60	72	7.28 $\pm$ 7.21	0–35	61 / 4	24 / 12	
60–50	77	9.68 $\pm$ 9.93	0–35	69 / 5	36 / 6	
50–40	76	7.91 $\pm$ 8.58	0–35	66 / 0	32 / 0	
40–30	36	9.39 $\pm$ 8.19	0–35	33 / 3	24 / 8	
18–30	16	16.21 $\pm$ 10.84	4–35	12 / 2	12 / 0	
Total	307	8.65 $\pm$ 8.69	0–35	278 / 17	130 / 26	0.002 / < 0.001 / < 0.001

N = number of eyes.

* Chi-Square and Kruskal–Wallis test Tests were used for comparisons.

Table 3: Distribution of dry eye severity and color vision results by gender, refractive error, and age group

Variable	Category	Dry eye Severe	Dry eye Moderate	Dry eye Mild	Dry eye Normal	D15 Normal	D15 Abnormal	Ishihara Normal	Ishihara Abnormal	*P (Dry eye / D15 / Ishihara)
Gender	Female (n = 167)	41	37	46	43	78	18	143	10	
	Male (n = 140)	28	33	44	35	56	10	120	9	0.608 / 0.202 / 0.536
SE Group	Myopia (n = 81)	14	19	24	24	39	5	69	8	
	Hyperopia (n = 92)	23	28	21	20	35	14	83	5	
	Emmetropia (n = 134)	32	23	45	34	60	9	111	6	0.185 / 0.177 / 0.466
Age group	< 40 (n = 44)	7	7	13	19	32	6	40	4	
	$\geq$ 40 (n = 263)	62	63	77	59	102	22	223	15	0.025 / < 0.001 / 0.083
	Total (n = 307)	69	70	90	78	134	28	263	19	

N = number of eyes.

* Chi-Square Tests were used for group comparisons.

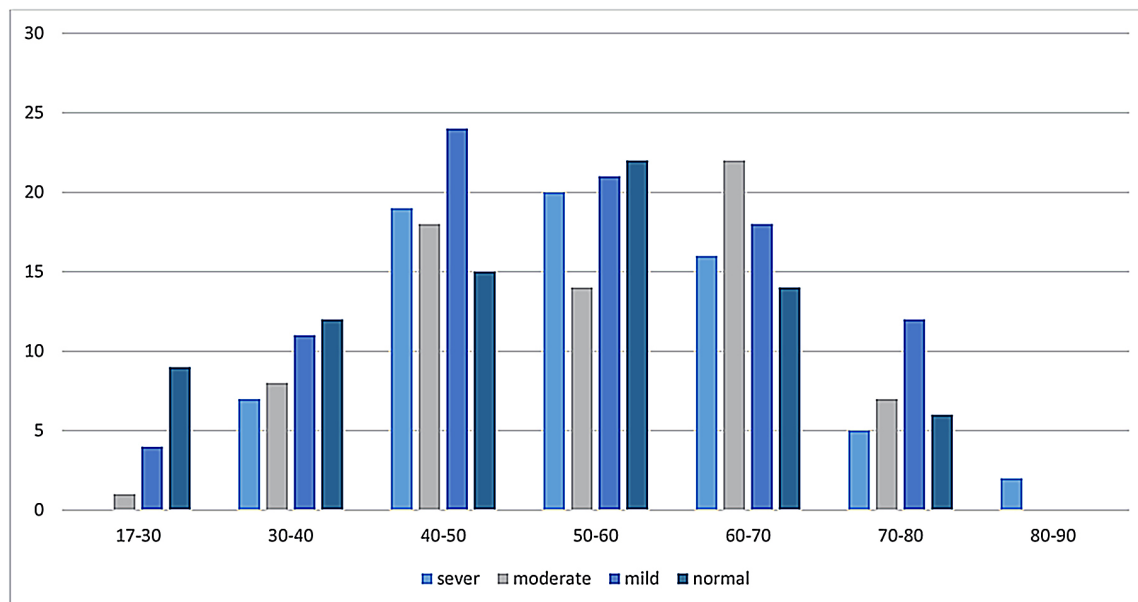


Figure 1: Frequency of dry eye severity by age group

Anterior segment findings

Nearly half of eyes (49.4 %) had no abnormalities. Cataract was observed in 11.5 % and anterior chamber flare in 12.4 %. Other findings included pinguecula (6.7 %), pseudophakia (10.3 %), pterygium (1.5 %), mild conjunctival hyperemia (3.0 %), miosis (2.4 %), pupillary abnormalities (3.3 %), eyelid edema (0.9 %), and minor corneal changes (1.2 %). Abnormalities were more common in patients ≥ 40 years, whereas most patients < 40 years had normal anterior segments.

Posterior segment findings

More than half of eyes (55.2 %) showed no abnormalities. Optic disc cupping ≥ 0.3 was present in 10 %. Other findings included mild disc pallor (9.7 %), blurred disc margins (7.9 %), pigmentary retinal changes (4.8 %), macular changes (1.8 %), posterior vitreous detachment (0.9 %), vascular ratio changes (0.9 %), diabetic retinopathy (0.6 %), and drusen (0.6 %). Younger patients more frequently had normal fundi, whereas

abnormalities increased with age. Disc changes were the most common finding overall.

Color vision

By Ishihara testing, 6.74 % of eyes were abnormal, compared with 17.28 % by the D15 test. Ishihara abnormalities were observed in 6.36 % of patients ≥ 40 years and 8.70 % of those < 40 years. Among Ishihara-deficient eyes, 43.75 % were myopic, 31.25 % hyperopic, and 25 % emmetropic. The highest rates were seen in patients with esophageal and colorectal cancers. With the D15 test, abnormalities were present in 18.75 % of women and 15.15 % of men, and in 15 % of patients < 40 years versus 18.03 % ≥ 40 years. Abnormalities were found across several cancer types, including breast, esophagus, brain, stomach, colon, lung, ovary, uterus, and oral cavity.

Binocular vision

Exophoria was present in 58.8 % of patients, esophoria in 29.1 %, exotropia in 4.5 %, and

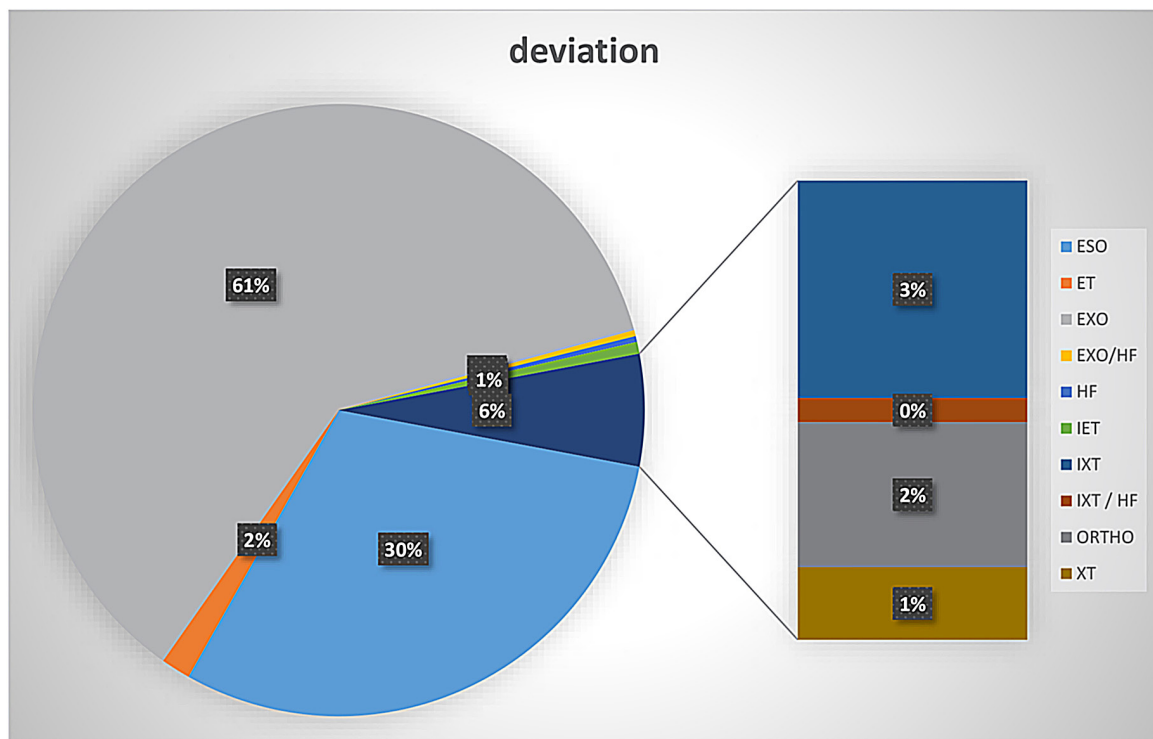


Figure 2: Frequency of phoria and tropia among participants

esotropia in 2.1 %, hyperphoria in 0.9 %, and orthophoria in only 1.8 %. Exophoria predominated across all refractive groups (Figure 2).

Ocular motility

Eye movements were normal in 97.9 % of patients. Abnormal ocular motility (2.1 %) was characterized by restricted or slow movements and was most frequently associated with cancers of the nose (28.57 %), uterus (28.57 %), spinal cord (14.29 %), throat (14.29 %), and lymphoma (14.29 %). Abnormal motility was slightly more common in men and was found predominantly in patients ≥ 40 years.

Discussion

In our study the prevalence of dry eye in patients with cancer was higher than in the general population. In healthy individuals, dry

eye prevalence is reported at 11 %–17 %, and globally it ranges between 5 % and 50 %²⁸⁻³⁰. In this study, however, 74.6 % of eyes showed evidence of dry eye. The proportion of normal Schirmer test results in patients ≥ 40 years was nearly half that in those < 40 years, consistent with previous findings that dry eye prevalence increases with age^{31,32}. As lacrimal gland function declines with age, tear secretion decreases, and dry eye occurs in 5 %–30 % of older adults^{11,33}.

We observed that dry eye was more common in hyperopes, likely reflecting their older age distribution. Even in participants without comorbidities, dry eye was more frequent than in the general population. Among those with comorbidities, hypertension, hyperlipidemia, and diabetes were most strongly associated with dry eye, consistent with earlier research suggesting that diabetes and antihypertensive drugs increase its risk³⁴⁻³⁷.

Color vision deficiency was more frequently

detected by the D15 test than by Ishihara plates, nearly 2.5 times higher, reflecting the broader diagnostic capacity of D15. Color vision deficiency affects up to 8 % of men and 0.5 % of women^{38,39}. In this study, Ishihara abnormalities were slightly more common in men and in patients <40 years, consistent with previous studies showing male predominance of red–green deficiencies^{40–42}. In contrast, D15 revealed more abnormalities in women and in patients ≥ 40 years. Earlier research has shown prevalence rates of 1 %–8 % in men and 0.4 %–3 % in women^{38,43–45}. While some studies found no age-related changes in red–green sensitivity, they did report small age-related declines in red–blue discrimination, attributed to lenticular changes⁴⁶. Other investigations suggest that nearly half of elderly individuals may develop color vision changes, which worsen with age⁴⁷.

In this study, no clear association was observed between cancer type and color vision deficiency, although abnormalities were more frequent in esophageal cancer. Red–green defects were most common overall. Among hyperopes, D15 detected nearly twice as many abnormalities as Ishihara, suggesting the presence of non–red–green defects. Prior studies have found no consistent association between refractive error and color vision deficiency^{48,49}. Because the patterns observed here did not conform to classic congenital defect types, we were unable to further subtype the deficiencies.

More than half of eyes had no posterior segment abnormalities. The most frequent finding was optic disc cupping (10 %), followed by disc pallor (9.7 %). Disc cupping is a key feature in glaucoma assessment, though not all cupping indicates glaucoma^{50–52}. The cup-to-disc ratio normally ranges between 0.1 and 0.4, but up

to 5 % of healthy individuals may have a ratio >0.6 ⁵³.

Regarding binocular vision, exophoria and exotropia were more than twice as frequent as esophoria and esotropia, while orthophoria was rare. Exophoria predominated across all refractive groups, whereas esophoria was more common in hyperopes and emmetropes. Exotropia and esotropia were more frequent in myopes, and hyperphoria occurred only among myopes. Previous studies have also reported associations between refractive error and heterophoria⁵⁴.

This study has certain limitations. It was performed at a single center with a cross-sectional design, which limits generalizability and prevents causal inferences. The sample size was modest, and a small number of eyes had incomplete test data. Analyses were conducted per eye rather than per patient, which may have introduced inter-eye correlation. Future studies with larger, multicenter cohorts and longitudinal follow-up are needed to clarify the impact of specific cancer treatments on dry eye, color vision, and binocular function.

Conclusion

Dry eye, color vision deficiency and heterophoria were more frequent among patients with cancer than in the general population, underscoring the need for routine ophthalmic screening and follow-up in oncologic care.

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Footnotes and Financial Disclosures

Conflict of interest:

The authors have no conflict of interest with the subject matter of the present manuscript.