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Ophthalmic manifestations among adults on chemotherapy at a tertiary hospital in southwestern Uganda: a cross sectional study

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Ophthalmic manifestations among adults on chemotherapy at a tertiary hospital in southwestern Uganda: a cross sectional study.

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Abstract

Background: Cancer patients on chemotherapy may develop ocular manifestations—eye abnormalities, which may occur due to the cancer, or effects of cancer treatment. A majority of these patients may not have any symptoms and remain undiagnosed, only to present late with severe visual impairment or blindness. Such vision loss can interfere with cancer treatment adherence, quality of life, mental health, productivity, and safety of the patient. Ocular manifestations in a cancer patient are an important prognostic indicator, with a lower 5-year survival rate of 21.4% among those with ocular manifestations compared to 45.7% among those without. At Mbarara regional referral hospital, a tertiary teaching hospital in Uganda, routine eye screenings were not being offered to cancer patients. This study aimed to assess the ophthalmic manifestations among adult cancer patients on chemotherapy Mbarara regional referral hospital.

Methods: This was a hospital based descriptive cross-sectional study than included 155 randomly selected adult cancer patients on chemotherapy. The sociodemographic and medical data via structured questions. We did comprehensive eye examinations for all the study participants. We entered, cleaned and analyzed the data using STATA 17. The results were presented as descriptive statistics.

Results: Most participants were male (64.5%), and the median age was 57 years. The most prevalent ocular manifestations were dry eye (34.2%), cataract (31.2%), optic atrophy (9.0%), and retinopathy (8.9%).

Conclusions: Ocular manifestations were common among cancer patients, with dry eye, cataract, optic atrophy, and retinopathy being most frequent. We recommend routine eye screening for patients on chemotherapy.

Keywords: Adults, cancer, chemotherapy, manifestation, ophthalmic, Uganda.

INTRODUCTION

Cancer cells divide uncontrollably and have the ability to spread, infiltrate, and destroy normal body cells and tissues (1,2). The global prevalence of cancer and cancer-associated morbidity is on the rise (3,4).In Uganda, common adult cancers include breast, ovarian, cervical, Kaposi's sarcoma, prostate, liver, esophageal, gastric, and hematologic cancers such as leukemia and lymphomas (5,6). Non-ocular cancers arise outside the eyeball and orbit (7). Patients with non-ocular cancers are likely to have ocular manifestations which may present with abnormal signs and symptoms which can occur on any part of the eye including the eyelids, eyeball, or the eye socket/orbit (8–10). These findings may occur due to the direct effect of the cancer on the eye, cancer spread to the eye, body's immune responses to the cancer, and as a result of effects of cancer treatment like drugs and radiotherapy(10–16).

Cancer can directly cause blood clotting and blood vessel damage (10,17), and damage the retinal pigment epithelium, potentially causing retinal detachment and blindness (18–20). Cancer may exert pressure on the optic chiasm, leading to poor vision, abnormal pupil, or optic nerve atrophy (15,21,22), and these cancers may be first detected by an ophthalmologist (15).

Metastasis to the eye or orbit from a distant cancer, as commonly occurs with lung and breast cancers (13,23,24) can lead to ocular manifestations like eye inflammation, vitreous hemorrhage, retinal hemorrhage, vascular occlusions, restriction of eye movements, pain, double vision, poor vision, or even blindness (25–30). The body's immune system, in an attempt to fight a non-ocular cancer, may produce circulating antibodies that mistakenly attack healthy cells in the eye (paraneoplastic syndromes). This can lead to retinopathy and a reduction or loss of sight (31–34).

Ocular manifestations may also occur as a result of complications of cancer treatment for example Cyclophosphamide, a drug used in the treatment of multiple myeloma, lung cancer, breast cancer, and

sarcoma, can cause blurred vision, excessive tearing, swelling of lids and conjunctiva, and dry eyes (16). Tamoxifen, a drug used to treat breast cancer, causes loss of color vision, retinopathy, macula edema, dry eyes, and keratopathy (35–38). Radiotherapy can lead to the formation and progression of cataracts, retinopathy, stenosis of the punctum, and dry eyes (14,39)

The prevalence of different ophthalmic manifestations in patients with non-ocular cancers has been shown to vary 11% and 90% (40–44) according to several studies in different geographic locations..

Ocular manifestations in patients with systemic cancer occur more frequently in adults than in children (45–48). Although chemotherapy may also cause other ocular side effects, especially in higher doses, the ocular manifestations occurring as a result of cancer tend to decrease among the leukemia patients on anticancer medication. This is most likely due to the suppression of the primary cancer. A study in Ethiopia found that ocular manifestations were three times higher in the newly diagnosed cases of leukemia compared to the cases who were already on treatment (49).

Patients with non-ocular cancers are likely to have ocular manifestations, which may be the first sign and may occur well before even the diagnosis of cancer is made (32,50,51). Ocular manifestations in a cancer patient are an important prognostic indicator, with a lower 5-year survival rate of 21.4% among those with ocular manifestations compared to 45.7% among those without (52).

A majority of patients with cancer may have asymptomatic eye lesions and remain undiagnosed, only to present to an ophthalmologist late with severe visual impairment or blindness. Up to 49% of patients have been documented to experience blindness as a result of ocular symptoms, with 30% of instances experiencing blindness in both eyes as a result of the cancer (8,43,53). Such vision loss can negatively impact treatment adherence, quality of life, mental health, productivity, and safety (54–56).

This study aimed to investigate the ophthalmic findings in adults with non-ocular cancers undergoing chemotherapy at a tertiary teaching hospital in southwestern Uganda.

METHODS AND MATERIALS

Design

We conducted a hospital based descriptive cross-sectional study between February 2025 and May 2025 among adults with non-ocular cancers on chemotherapy. We obtained the ethics approval for this study from the Mbarara University of Science and Technology (MUST) Research and Ethics Committee, approval number **MUST-2024-1914**.

The reporting of this study conforms to the STROBE guidelines for reporting observational studies (57).

Setting

We conducted the study at Mbarara Regional Referral Hospital (MRRH) cancer clinic located in Mbarara city, in south-western Uganda. The MRRH is located about 290 kilometers south-west from Kampala, the capital city of Uganda. MRRH is a tertiary government-owned hospital that offers general and specialised medical services, and serves as a teaching hospital for the Medical School of Mbarara University of Science and Technology. The hospital was founded in 1940, and it has a bed capacity of 350. MRRH serves a population of about 4 million people in its catchment area, which comprises the districts of 13 districts, as well as neighboring population from neighboring countries like Rwanda, Burundi, the Democratic Republic of the Congo, and Tanzania. The MRRH houses a cancer unit that offers both diagnosis and free treatment services to cancer patients, serving as a regional branch of the Uganda Cancer Institute (UCI).

Study participants and selection criteria

We included eligible adult males and females 18 years and older who had non-ocular cancers and were receiving chemotherapy. We excluded cancer patients who were critically ill that could not withstand the interview and eye examinations.

Sample size and sampling technique

The Sample size, n was calculated using a formula for finite population (58)

$n = N*X / (X + N - 1)$

Where, $X = [(Z\alpha/2)^2 *P*(1-P)]/MOE^2$, $Z\alpha/2$ is the critical value of the normal distribution at $\alpha/2$ for α of 0.05= 1.96; P = 0.5%; MOE=margin of error at 5% (0.05) and N=the number of patients with non-ocular cancers at cancer clinic=253; $X = (1.962 \times 0.50 \times 0.5)/ 0.052 = 384$

Hence, $n = 253*384 / (384 + 253-1) = 152$. A 10% nonresponse rate was accounted for in the final sample size; hence, n=167 participants

After a random start, a systematic sampling of every fifth patient as used to recruit the study participants from the cancer clinic.

Data collection procedure

Informed consent was obtained from each participant a by research assistant. We obtained additional consent for photo of the eye. Each study participant received a nonmonetary compensation that included eye glasses and eye medications for those that required it and monetary for those that did not require glasses or medication.

Two trained research assistants, one nurse and one imaging technician, good in both English and local dialects collected the data. Structured questionnaires administered through one-on-one face-to-face interviews by research assistants were used to collect the sociodemographic data of the participants. The

questions were explained verbally in the local language (Runyangkole) to those who did not understand the English language. One section of the questions captured demographic information such as age, education level, and marital status, occupation, smoking and drinking history. The research nurse measured the weight and height. The diagnosis and treatment record of the participants were retrieved with permission from their files.

Each participant underwent a full eye examination by the principal investigator. The visual acuity (VA) was measured using the Snellen distance visual acuity chart with either the English alphabet (for those who could read) or the Tumbling E distant chart (for those who could not read) at a distance of 6 meters from the patient to ascertain their vision before other examinations. For cases who were bed-ridden, VA was measured using the World Health Organization (WHO) smart phone-based VA testing tool at a distance of 2 meters. Both the presenting VA and pinhole VA were measured. The VA was categorized as normal (6/6-6/), mild visual impairment (6/12–6/18), moderate visual impairment (6/24–6/36), severe visual impairment (6/60-3/60), and blind (<3/60).

Intraocular pressure (IOP) was measured from both eyes with participants in a seated position, using an i-care rebound tonometer model IC100 (manufactured by ICARE FINLAND OY)). Six measurements were taken and the average reading taken according to the manufacturer's recommendation. All participants were examined between 9 am to 1 pm to avoid significant diurnal variation in IOP. The tonometer was disinfected with between each participant. An IOP of ≤21mmHg in any eye was considered normal, while an IOP of >21 mmHg in any eye was considered high. The IOP of participants who had corneal scars were excluded from the analysis.

The pupillary light reaction was be examined with a penlight. The regularity, and quality, presence or absence of reaction and absence or presence of afferent pupillary defect (APD) or a relative afferent pupillary defect (RAPD) was recorded.

The basal tear production was evaluated using a Schirmer test (Schirmer-2), which was done using a Schirmer filter paper inserted in to the inferior fornix after instilling proparacaine 0.5% eye drops and waiting for 1 minute. The amount wetting of the filter paper recorded after 5 minutes. Less than 5 mm of wetting of Schirmer filter paper after 5 minutes was considered diagnostic of dry eye. Fluorescein sodium ocular strips (1 mg), was used for staining the cornea to test how quickly the stain in the tears would break up, the break-up time (TBUT). A TBUT of less than 10 seconds was be considered abnormal and indicative of dry eye.

The posterior segments of the eyes were examined using a slit lamp biomicroscope and a Volk 90D lens or an indirect ophthalmoscope (Keeler), after dilating the pupils using tropicamide 1% and phenylephrine 2.5% or eye drops. A Phelcom Eyer 2 fundus camera was used to take the retinal images.

Statistical analysis

Data were entered into Microsoft Excel, exported, cleaned, and analysed using Stata version 17. Continuous variables were summarised using means and standard deviations or medians and interquartile ranges, while categorical variables were summarised using frequencies and proportions.

RESULTS

A total of 155 participants were interviewed and examined, giving a response rate of 93%. Eight participants could not complete the eye examinations due to the discomfort/side effects of the chemotherapy that they received. Five participants had incomplete treatment records and were not included in the final analysis.

Table 1: Sociodemographic characteristics of the study participants (n=155).

Characteristic	Frequency	Percentage
Sex		
Male	100	64.5
Female	55	35.5
Age (Median age=61yrs, IQR=27-82 years)		
18-50 years	41	26.4
>50years	114	73.6
Marital status		
Married	131	84.5
Single	06	3.9
Separated	13	8.4
Widow/widower	05	3.2
Education level		
None	31	20.0
Primary	73	47.1
Secondary	32	20.6
Tertiary	19	12.3
Occupation		
Peasant	111	71.6
Formal employment	21	13.5
Business	19	12.3
Unemployed	04	2.6
Current alcohol intake		
No	130	83.9
Yes	25	16.1
Current smoker		
No	155	100.0
Yes	00	0.00
Body mass index (BMI)		
Underweight	24	17.8
Normal	84	62.2
Overweight	21	15.6
Obese	06	4.4

Table 1, above, shows the sociodemographic characteristics of the study participants**.** The median age was 61 years, with an interquartile range of 27-82 years. Larger proportions of the participants were male (64.5%), aged above 50 years (70.3%), and married (84.5%). A majority had attained at least a primary level of education. Most participants had normal BMI.

The most prevalent cancer diagnoses among the study participants (n=155).

Figure 1 shows the most prevalent cancer diagnosis among the study participants. Prostate, breast, esophagus, stomach, and colorectal cancers were the most common cancers, with hepatocellular, pancreas, skin, and thyroid being among the least common cancers.

Table 2: The classes of chemotherapeutic agents the participants were receiving (n=155).

Chemotherapeutic Category	Frequency (Percent)
Alkylating agents	71 (31.4)
Taxanes	64 (28.3)
Antimetabolites	35 (15.5)
Anthracyclines	15 (6.6)
Bisphosphonates	15 (6.6)
Topoisomerase inhibitors	09 (4.0)
Kinase inhibitors	08 (3.5)
Tamoxifen	03 (1.3)
Number/combination of chemotherapy drugs	
1 drug	47 (30)
≥2 drugs	108 (70)
Duration of chemotherapy	
<12 months	86 (55.5)
≥ 12 months	69 (44.5)

Table 2 above shows that the most commonly used groups of anticancer medicines were the alkylating agents, 31.4%, taxanes, 28.3%, and antimetabolites, 15.5%. The majority of the cancer patients, 70%, were on a combination of two or more anticancer medicines, while 30% were on a single anticancer medicine.

Presenting visual acuity of the study participants (n=155)

Figure 2, shows, the presenting visual acuity. The majority of participants (46%) had normal visual acuity while 1.3% had severe visual impairment and 0.7% of the participants were blind in at least one eye.

Ophthalmic findings among the cancer patients on chemotherapy (n=155).

Figure 3, shows, the different ophthalmic manifestations among the study participants. Figures 4-6 are retinal images showing retinopathy, optic atrophy and retinal hemorrhages respectively. The median IOP for both eyes was 14 mmHg with an interquartile range of 8-25. The majority of participants (94.2%) had IOP <21mmHg while 5.8% had IOP of >21mmHg. The top five most common ocular findings were dry eye, 34.2%, cataract, 31.2%, madarosis, 11.6%, optic atrophy, 9.0%, and retinopathy, 8.9%. Other less common ocular manifestations were dilated conjunctival vessels 6.4%, tortuous retinal vessels, 4.1%, cotton wool spots 2.7%, conjunctival hemorrhage, and retinal hemorrhage, 2.1%.

DISCUSSION

This study examined the ocular findings adult patients on chemotherapy at a tertiary hospital in Uganda. The main ophthalmic findings were dry eye, cataract, optic atrophy, retinopathy, among others.

Dry eye

This study found the prevalence of dry eyes at 34.2% among cancer patients, which was similar to the 35% reported in another case-control study that had a similar sample size (59). Contrary to this study, another cross-sectional case-control study that used the validated Ocular Surface Disease Index (OSDI) and studied 200 cases of breast cancer patients found a 59.0% prevalence of dry eye (60). Another cross-sectional study that assessed 102 participants with breast cancer for dry eye using Tear Breakup Time (TBUT), the Schirmer test, and the Ocular Surface Disease Index found a prevalence of dry eye at 69.6% (61). These differences

could be attributed to the difference in the methods used for evaluating the dry eye and the fact they included only the female sex, since dry eye has been found to be significantly higher among the female sex (62).

Sub-conjunctival hemorrhage

In this study, sub-conjunctival hemorrhage was found in 3 (1.9%) of the cases. This is quite close to the 5 (5%) earlier documented in a multicenter case control study in Nigeria that studied adults with leukemia (63). In contrary to the findings of this study, another study revealed higher prevalence of sub-conjunctival hemorrhage at 19.4% although it had a smaller sample size (72 participants) and studied only patients with leukemia (42).

Cataract

In this study, cataract was found in 31.2% of the cancer patients on chemotherapy. This finding is significantly higher than the 10% previously documented among patients with systemic and neurological cancers (51). This difference could be attributed to the difference in the sample size, as Zheng et al had a lower sample size of 23 participants. Additionally since most of our participants were above 60 years, our finding could be due to age related cataract. Another cross-sectional study in Australia found a 23.5% prevalence of cataract among participants with skin cancer (64). This difference is possibly due to the population and environmental differences.

Optic atrophy

This study found optic atrophy in 9.0% of the cancer patients. This is lower than the previously documented 34.78 % (8 out of 23) among patients with systemic and neurological cancers (51). Their higher finding is possibly because a majority of their participants had pituitary adenoma, and optic atrophy is one of the most common findings in patients with pituitary tumors (21).

The causes of optic atrophy among cancer patients can be due to the effect of the cancers or the drugs used in the treatment of cancers. Taxanes, a common group of anticancer drugs, have been documented to have toxic effects on both the peripheral and the central nervous systems (65) and can cause optic neuropathy (66–68). However, because the taxanes were used in combination with other drugs to treat cancer among our participants, it is possible that other drugs also contributed to optic neuropathy. A study in Saudi Arabia identified tumors as one of the commonest causes of optic atrophy among adult patients (69).

Retinal hemorrhage

This study found retinal hemorrhage in 2.1% of the cases. Several studies have found higher prevalence, including a prevalence of 16.7% (42), 31.3% (63), and 41.2% (70). These studies included only patients with leukemias, which are associated with higher tendencies of bleeding, unlike our study that had fewer cases of leukemia, hence difference in prevalence.

Retinal vascular abnormalities

The prevalence of tortuous retinal vessels in this study was 4.1% a finding significantly lower than the 26.3% (63) and 50.0% (42) previously reported. These higher prevalence were found in almost exclusively in patients with leukemia, possibly indicating that hematological cancers have an effect on retinal blood vessels (71).

Retinopathy

This study found retinopathy in 13 (8.9%) of the cases and none in the controls. The retinopathy findings included dull macula with peripheral retinal lesions and pigment changes. Several case reports have reported similar findings in the past (68,72,73). Some of the lesions have been reported to resolve spontaneously after discontinuation of medication, while others may lead to permanent damage (74,75), indicating the need for regular eye checkups for patients on chemotherapy.

Strengths and limitations of the study

This study revealed multiple ophthalmic findings among cancer patients on chemotherapy, a sub-population that often requires comprehensive medical care. However, the study had some limitations. Firstly, the study may have underestimated the prevalence of ocular manifestations since the severely ill participants were not be examined. Additionally the subtle retinal ophthalmic findings which were at early stages and not yet visible through fundus exam could have been missed since optical coherence tomography (OCT) was not done for all the participants.

CONCLUSIONS

Ophthalmic findings were common among cancer patients on chemotherapy. Dry eye, cataract, optic atrophy, and retinopathy were the most common ophthalmic findings. We recommend regular eye screening of all cancer patients on chemotherapy by eye care professionals.

DECLARATIONS

Ethics approval and consent to participate

We conducted the study in accordance with the World Medical Association Declaration of Helsinki. We obtained ethics approval from the Mbarara University of Science and Technology Research and Ethics Committee, approval number **MUST-2024-1914.**

Consent to participate

Voluntary written informed consent was obtained from all the participants. Consent to take photos of the eyes was also separately obtained.

Consent for publication

We obtained consent to publish ocular/retinal images from all participants.

Author contributions

Moses Owiny generated the idea. Moses Owiny, Teddy Kaga, and Amos Twinamasiko contributed to protocol development, prepared the manuscript, read and approved the final version and agreed upon the journal. We did not use any Generative Artificial Intelligence (AI) in creating text, references, images or other content. All authors are fully responsible for the accuracy and originality of this work.

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Competing interests

The authors declare that there are no conflicts of interest

Availability of data and materials

The datasets used and/or analysed during the study are available from the corresponding author upon reasonable request.

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Figure 1: Cancer diagnosis of participants (n=155)

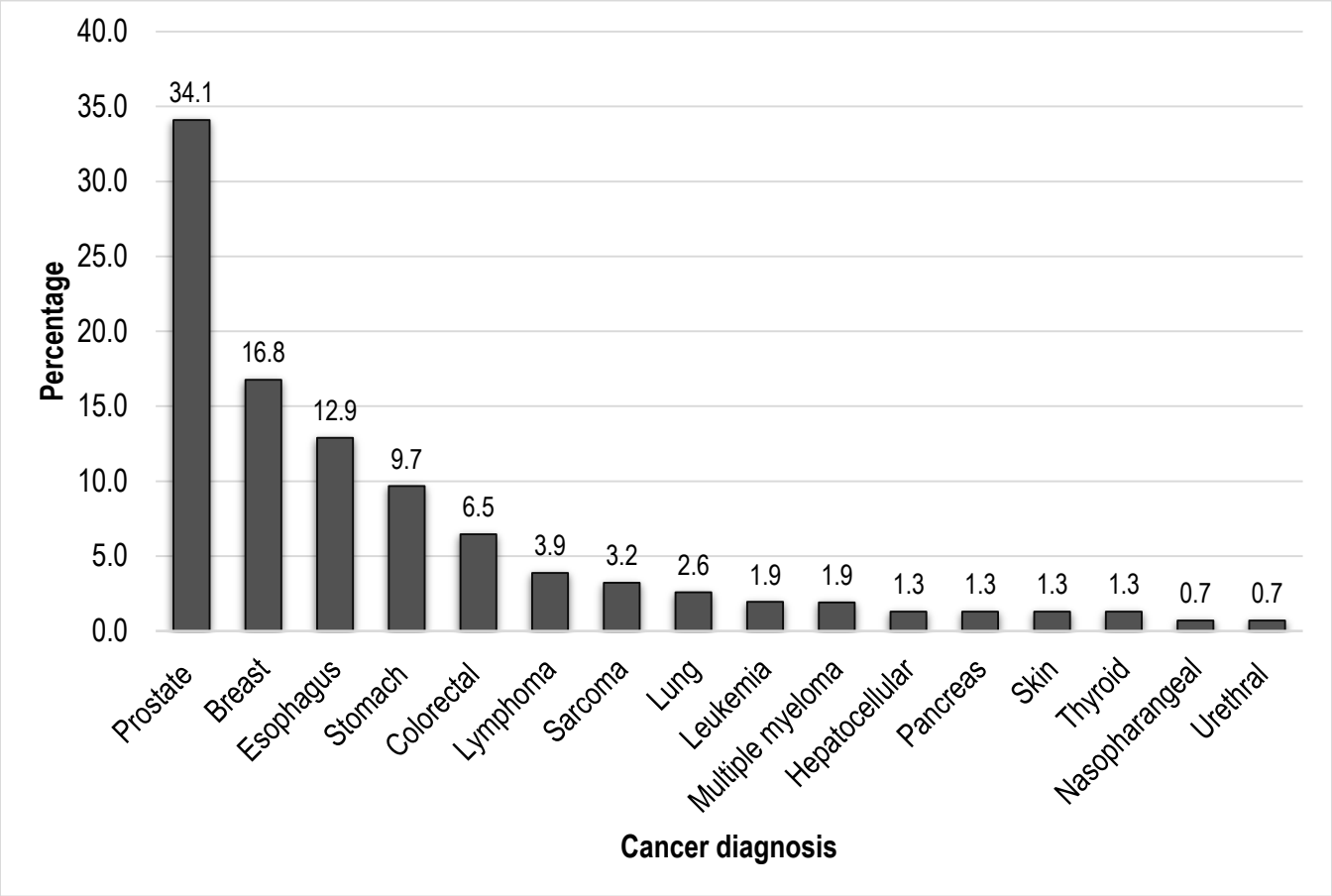


Figure 2: Presenting visual acuity of study participants (n=155).

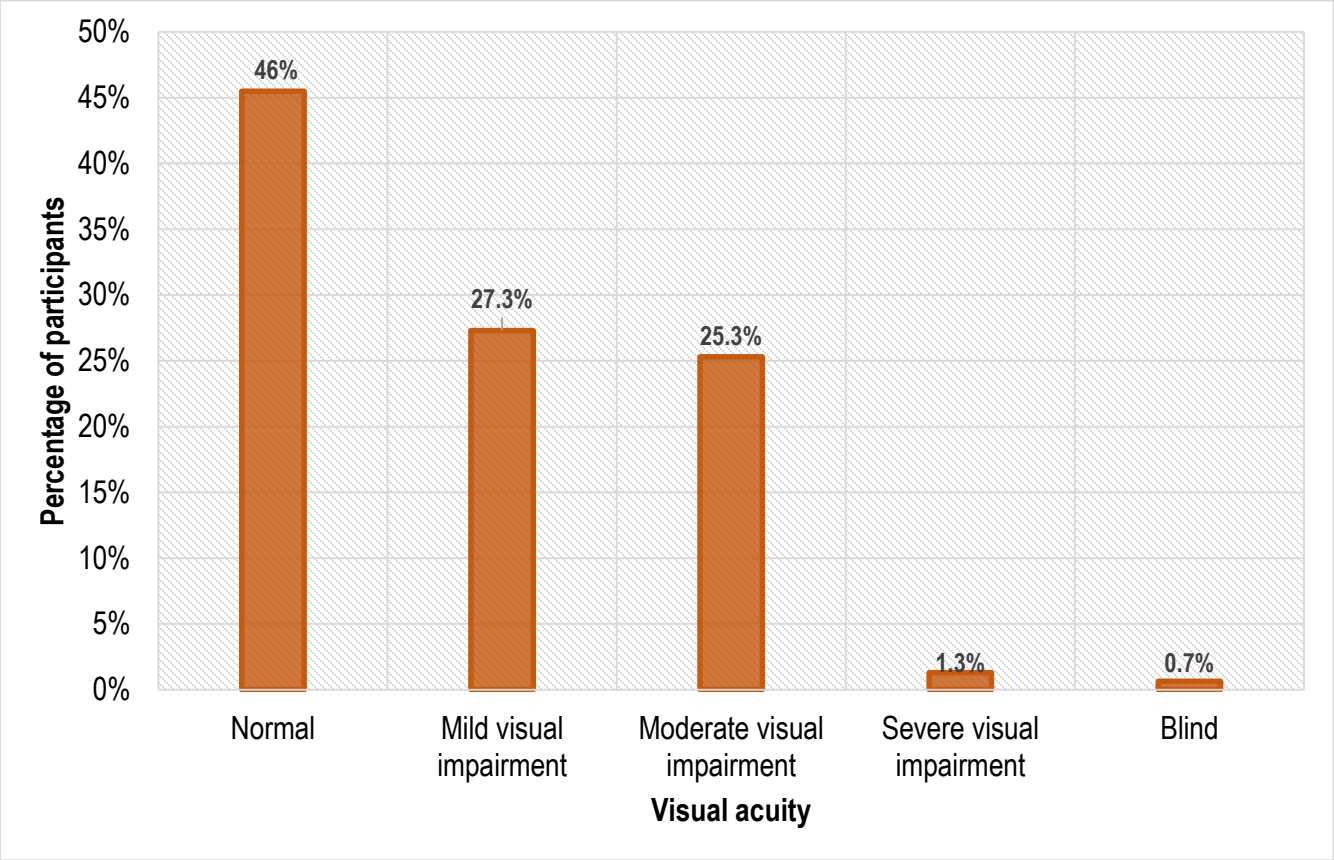


Figure 3: Ophthalmic manifestations among the cancer patients on chemotherapy (n=155).

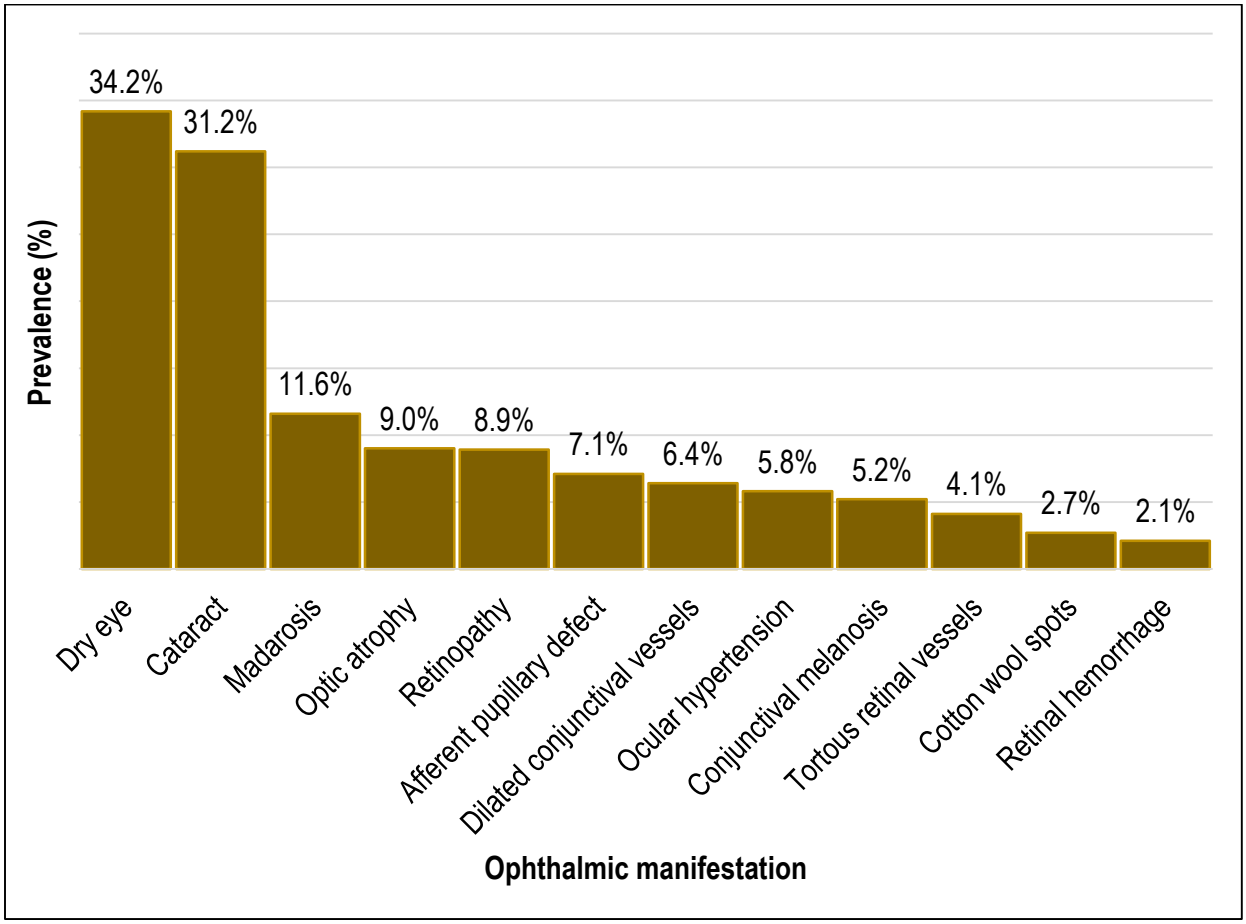


Figure 4: **A**: Right (OD) and left (OS) retinal images showing retinopathy (red rings) in a 48 years old female with cancer of the esophagus. **B**: Right (OD) and left (OS) retinal images showing retinopathy (red rings) in a 47 years old female with cancer of the lung.

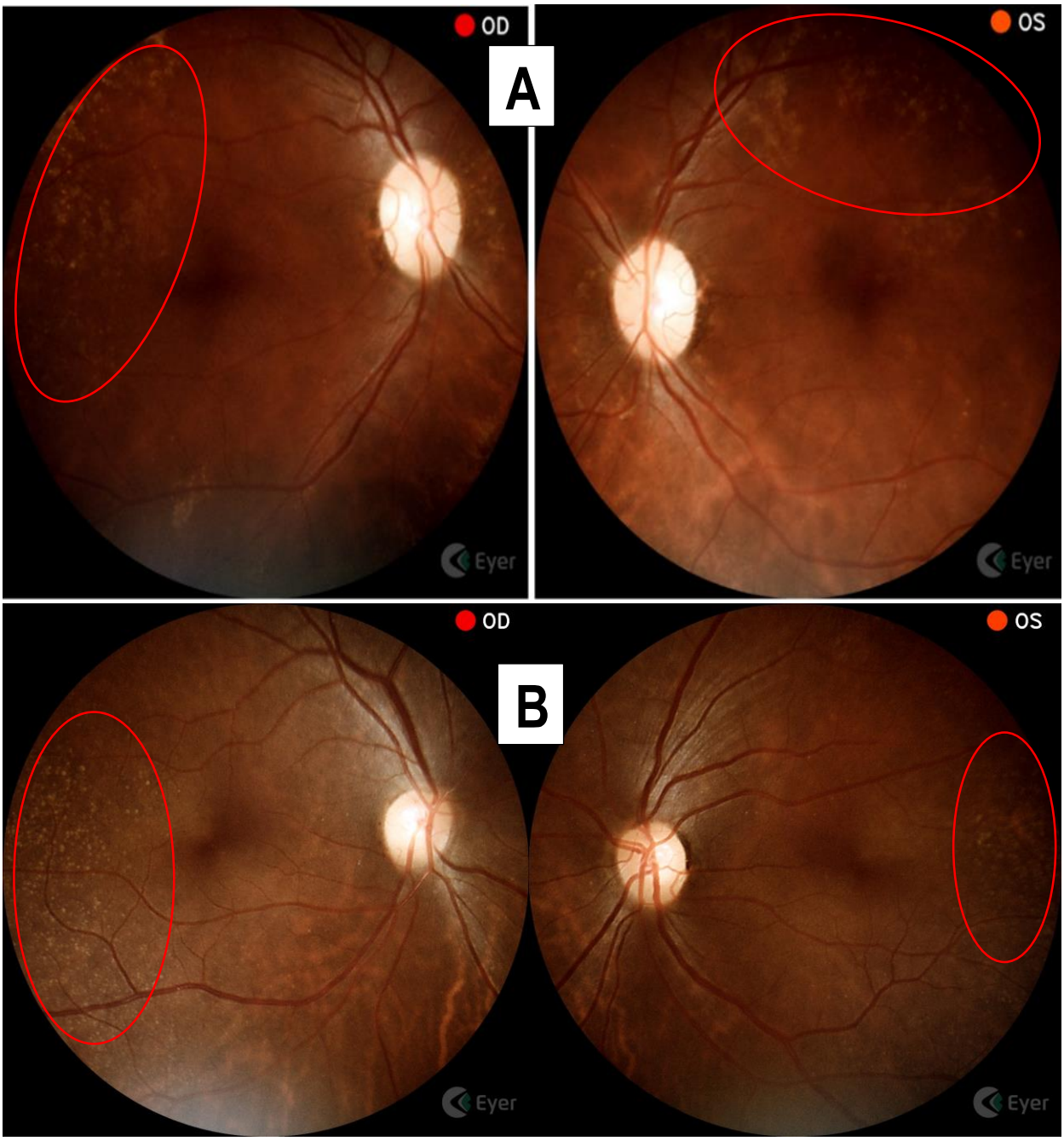


Figure 5: Right (OD) and left (OS) retinal images pale optic discs (optic atrophy) in a 73 years old male with prostate cancer.



Figure 6: left retinal hemorrhages (redarrows) in a 57 years old female with sarcoma

