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The Relationship between Serum Selenium Levels and the Occurrence of Eye Tumors

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ABSTRACT

Background: Eye tumors are serious ocular diseases. Selenium is a component of selenoproteins involved in antioxidant defense, and its association with eye tumors warrants investigation.

Objectives: This study evaluated the association between serum selenium levels and eye tumors.

Methods: A case–control study was conducted at RS Prof. CPL. Universitas Sumatera Utara from June to July 2024, involving 20 patients with eye tumors and 20 controls. Each group included 11 women and 9 men. Serum selenium levels were measured using an enzyme-linked immunosorbent assay. Data were analyzed using the independent t-test and chi-square test, with $p < 0.05$ considered statistically significant.

Results: Mean serum selenium levels were significantly lower in the eye tumor group than in controls (100.03 ± 27.93 µg/L versus 213.15 ± 33.09 µg/L; $p < 0.001$). Lower selenium levels were also reported in malignant tumors than in benign tumors. Serum selenium levels were significantly associated with body mass index among patients with eye tumors ($p = 0.036$).

Conclusion: Lower serum selenium levels were associated with eye tumors. Further studies are needed to confirm the association and clarify the potential role of selenium in ocular tumor pathogenesis.

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INTRODUCTION

Eye tumors are uncommon but potentially vision- and life- threatening ocular diseases.[2] Although relatively rare, the incidence of eye tumors in Asia has shown an increasing trend over the years.[1,3] Jung et al reported that the incidence of eyelid tumors in Korea increased from 0.[27] per 100,000 population in 1999 to 0.[61] in 2016, with an annual increase of 4.[94]%.[1] Basal cell carcinoma (BCC) remains the most common histopathological type, followed by sebaceous gland carcinoma (SGC) and squamous cell carcinoma (SCC).[8] In Indonesia, epidemiological data on eye tumors are still limited and mostly restricted to several regional reports.[1,8] Several risk factors for the occurrence of variety of eye tumors include ultraviolet B (UV-B) radiation, immune system disorders, smoking, human papillomavirus (HPV) infection, mutations in the tumor suppressor gene p53, exposure to free radicals, and tumor microenvironment alterations.[4]

Selenium (Se) was discovered by the Swedish chemist Jonns Jacob Berzelius in 1817. It is a chemical element with atomic number 34 and metalloid properties. Selenium is a trace element that is naturally contained in many foods and also available as a food supplement. It is an essential nutrient for humans and also a constituent of more than two dozen selenoproteins that play important roles in reproduction, thyroid hormone metabolism, deoxyribonucleic acid (DNA) synthesis, and protection from oxidative damage and infection.[13]

Many studies have proposed that selenium may have benefits in preventing various types of cancer due to its antioxidant and chemoprotective properties.[5,13,17] A number of epidemiological studies have shown that populations with low selenium intake and low blood selenium levels experience an increased incidence of cancer, including breast, lung, stomach, bladder, ovaries, pancreas, thyroid, esophagus cancer, and melanoma.[9] Oxidative stress and tumor microenvironment dysregulation have also been implicated in eye tumor progression and malignant transformation.[4] Adequate selenium levels are important for cellular homeostasis through the antioxidant activity of selenoproteins, which may provide chemoprotective effects against carcinogenesis.[13]

Therefore, understanding the association between selenium levels and eye tumors may contribute to future preventive and therapeutic strategies.[1] However, despite growing evidence regarding selenium and systemic cancers, studies evaluating the relationship between serum selenium levels and eye tumors remain very limited, particularly in the Indonesian population. This study aimed to evaluate the association between serum selenium levels and eye tumors, which may provide insight into the potential role of selenium in eye tumor pathogenesis and prevention.

METHOD

Study design

This analytical observational study used a case–control design and was conducted at RS Prof. CPL. Universitas Sumatera Utara from June to July 2024.

Population and sample

The study included 20 patients diagnosed with eye tumors as the case group and 20 healthy individuals as the control group. Subjects were selected using consecutive sampling based on inclusion and exclusion criteria.

[Author confirmation required: specify the inclusion and exclusion criteria, control recruitment, sample-size justification, any matching procedure, and the affiliation of Taufik Ashar, which is currently listed under affiliation 2.]

Data collection

Demographic characteristics, body mass index (BMI), histopathological type, and clinical data were collected from medical records and direct examination.

Venous blood samples were collected from all participants for serum selenium examination. Blood specimens were centrifuged to obtain serum and stored at −20°C prior to analysis. Serum selenium levels were measured using the Enzyme-Linked Immunosorbent Assay (ELISA) method with a commercially available Human Selenium ELISA Kit (Elabscience®, Houston, TX, USA) according to the manufacturer's instructions. Calibration procedures were performed using standard calibration solutions provided by the manufacturer before each examination series. The reference range for normal serum selenium levels was 70–150 µg/L based on the kit manual and previous population studies. All samples were analyzed in duplicate to ensure accuracy and reproducibility. The intra-assay and inter-assay coefficients of variation were <10% and <12%, respectively. Serum samples were stored for a maximum duration of 3 months before laboratory analysis to maintain specimen stability and validity.

[Author confirmation required: specify BMI classification thresholds, tumor diagnostic criteria, and the ELISA kit catalog number, analytical range, and validation for measuring elemental serum selenium.]

Data analysis

Data analysis was performed using Statistical Package for the Social Sciences (SPSS) version 25.^{0}. Numerical variables were presented as mean ± standard deviation, while categorical variables were presented as frequency and percentage. Comparative analysis between groups was performed using the independent t-test and chi-square test. A p-value of <0.^{05} was considered statistically significant.

[Author confirmation required: define the tests labeled a, b, and c in Table 1; confirm test selection for categorical BMI data and provide the analysis supporting the BMI–selenium association.]

Ethical statement

Ethical approval was obtained from the Health Research Ethics Committee of Universitas Sumatera Utara (No. 622/KEPK/USU/2024). Written informed consent was obtained from all participants.

RESULTS

The demographic of the study samples are shown in table 1. Samples in the case and control groups were dominated by women, numbering 11 people each (55%). The mean age of samples in the eye tumor group was 43.^{55} years old and in the control group was 41.^{65} years old. There were no differences in characteristics based on gender and age between the two study groups (p = 1.000 and p=0.694, respectively). Meanwhile, the mean body weight of subjects in the eye tumor group was 68.^{05} kg and in the control group was 62.^{10} kg. There were also no differences in characteristics based on body weight between the two study groups (p=0.140). Most of the subjects in the eye tumor group had an overweight BMI, with 9 participants (45%). While in the control group, 11 participants (55%) had a normal weight BMI. There were no differences in characteristics based on BMI between the two study groups (p=0.256).

Table 1. Demographic characteristics of the study participants

Demographic characteristics	Eye tumor (n=20)	Control (n=20)	p-value
Gender, n (%)			
Male	9 (45)	9 (45)	1.000a
Female	11 (55)	11 (55)	
Age, years			
Mean ± SD	43.55 ± 18.21	41.65 ± 11.31	0.694b
Median (Min – Max)	41 (19 – 85)	44 (23 – 64)	
Height, cm			
Mean ± SD	165.75 ± 9.02	161.65 ± 6.67	0.110b

Demographic characteristics	Eye tumor (n=20)	Control (n=20)	p-value
Median (Min – Max)	164.5 (152 – 183)	160 (150 – 177)	
Weight, kg			
Mean ± SD	68.05 ± 12.48	62.10 ± 7.86	0.140c
Median (Min – Max)	66.5 (54 – 93)	59.5 (52 – 78)	
BMI, n (%)			
Normal weight	6 (30)	11 (55)	0.256b
Overweight	9 (45)	5 (25)	
Obesity	5 (25)	4 (20)	

BMI: Body mass index; SD: Standard deviation; Min: Minimum; Max: Maximum. Superscripts a, b, and c are retained from the source; their statistical-test definitions require author confirmation.

Table 2 displays the results of the histopathologic examination of tumor tissue and tumor type. Based on the results of the examination, the most common type of tumor was intradermal nevus which was found in 6 patients (30%) followed by Keratinizing Squamous Cell Carcinoma in 3 patients (15%). Of the 20 samples, there were 13 patients (65%) with benign tumors and 7 people (35%) with malignant tumors.

Table 2. Histopathological distribution and tumor type

Variables	n = 20
Histopathology	n (%)
Benign cyst.	1 (5)
Benign Lesion	1 (5)
Conjunctival Intraepithelial Neoplasia	1 (5)
Conjunctival Intraepithelial Neoplasia Grade I (Mild Dysplasia)	1 (5)
Conjunctival Intraepithelial Neoplasia Grade 2 (Moderate Dysplasia + Epidermal Cyst)	1 (5)
Epidermal cyst.	1 (5)
Keratinizing Squamous Cell Carcinoma	3 (15)
Keratinizing Squamous Cell Carcinoma NOS, well differentiated	1 (5)
Nevus Intradermal	6 (30)
Squamous Cell Carcinoma	1 (5)
Squamous Cell Carcinoma, Well Differentiated	2 (10)
Squamous Papilloma Eyelid	1 (5)
Tumor type	n (%)
Benign	13 (65)
Malignant	7 (35)

NOS: Not otherwise specified. Histopathological labels and benign/malignant classification are reproduced from the source and require author verification, including the classification of conjunctival intraepithelial neoplasia.

Mean serum selenium levels were significantly lower in the eye tumor group than in the control group ($100.^{03} \pm 27.^{93}$ µg/L versus $213.^{15} \pm 33.^{09}$ µg/L; $p < 0.001$), as reported in the source abstract (Table 3). The

source also reported lower selenium levels in malignant than in benign tumors and an association between serum selenium levels and BMI among eye tumor patients (p = 0.036).

Table 3. Serum selenium levels in the eye tumor and control groups

Variable	Eye tumor (n = 20)	Control (n = 20)	p-value
Serum selenium, µg/L Mean ± SD	100.03 ± 27.93	213.15 ± 33.09	<0.001

SD: Standard deviation. Values are reproduced from the source abstract.

[Author confirmation required: provide numerical results and statistical tests for the benign–malignant comparison and BMI–selenium association. Confirm the high control-group selenium level relative to the stated reference range of 70–150 µg/L.]

DISCUSSION

This study demonstrated a significant association between low serum selenium levels and the incidence of eye tumors. The mean serum selenium level in patients with eye tumors was significantly lower compared to the control group, and lower selenium levels were also observed in malignant tumors compared to benign tumors. Previous studies in Asian populations reported normal serum selenium levels within a relatively higher range compared to cancer patients, supporting the findings of the present study.[6] These findings support previous studies suggesting that selenium deficiency may contribute to carcinogenesis through increased oxidative stress and impaired antioxidant defense mechanisms.[13,16,18]

Radomska et al reported that selenium acts as an important antioxidant through selenoproteins, which protect cells from oxidative damage, regulate inflammatory responses, and maintain cellular homeostasis.[12] Oxidative stress itself has been recognized as one of the important mechanisms involved in tumor initiation and progression, including eye tumors.

In this study, the majority of eye tumor patients were women with a mean age of 43.[55] years. Similar findings were reported by Ningron et al, who found that most orbital tumor patients were adults aged above 45 years.[20] Meanwhile, Wang et al reported that eyelid tumors are more commonly diagnosed in middle-aged and older populations due to cumulative exposure to environmental risk factors such as ultraviolet radiation.[8] Several studies also suggest that hormonal and immunological factors may influence tumor susceptibility among women, although the exact mechanism remains unclear.[9,10,11]

The most common histopathological type found in this study was intradermal nevus, followed by keratinizing squamous cell carcinoma. This finding differs from larger epidemiological studies in Asia, where basal cell carcinoma (BCC) was reported as the predominant eyelid malignancy.[13] Jung et al reported that BCC accounted for 67.[5]% of eyelid skin cancers in Korea, followed by sebaceous gland carcinoma and squamous cell carcinoma.[1] Similarly, Wang et al found that BCC was the most frequent eyelid tumor subtype in South China.[7] The difference in histopathological distribution in the present study may be related to the relatively small sample size and variations in demographic characteristics and geographic factors.[3]

The present study also showed that patients with malignant tumors had lower serum selenium levels than those with benign tumors. This result is consistent with studies in other malignancies demonstrating an inverse relationship between selenium levels and cancer severity. Kluza et al reported significantly reduced selenium concentrations in ovarian cancer patients, while Narod et al demonstrated that low serum selenium levels were associated with increased cancer risk.[5,11] Selenium deficiency may reduce antioxidant capacity and impair the activity of glutathione peroxidase and other selenoproteins, thereby increasing susceptibility to DNA damage and tumor progression.[19] Previous studies have shown that imbalance of trace elements, including selenium, is associated with carcinogenesis and cancer progression.[10]

In addition, selenium levels were significantly associated with body mass index (BMI) among eye tumor patients in this study. Previous research by Fontenelle et al demonstrated that overweight and obese individuals tend to have altered selenium metabolism and increased oxidative stress status.[15] Obesity itself has been associated with chronic low-grade inflammation and increased production of reactive oxygen species,

which may further contribute to carcinogenesis. Therefore, nutritional status and metabolic factors may influence selenium bioavailability and its protective role against tumor development.[14]

Despite these findings, this study has several limitations. The sample size was relatively small and conducted in a single center, which may limit generalizability. In addition, dietary selenium intake, environmental exposure, and genetic factors affecting selenium metabolism were not evaluated. Nevertheless, this study provides preliminary evidence regarding the relationship between serum selenium levels and eye tumors in the Indonesian population, where related epidemiological and biomolecular data remain limited. Further multicenter studies with larger sample sizes are needed to clarify the role of selenium in eye tumor pathogenesis and its potential use as a biomarker or preventive strategy.

CONCLUSION

Lower serum selenium levels were significantly associated with the occurrence of eye tumors. Patients with malignant tumors also demonstrated lower selenium levels compared with benign tumors. These findings suggest a potential role of selenium in ocular tumor pathogenesis and oxidative stress regulation. Further multicenter studies with larger sample sizes are needed to confirm these findings and evaluate the potential role of selenium as a biomarker in ocular tumors.

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LIST OF ABBREVIATIONS

BCC: Basal cell carcinoma; BMI: Body mass index; DNA: Deoxyribonucleic acid; ELISA: Enzyme-linked immunosorbent assay; HPV: Human papillomavirus; NOS: Not otherwise specified; SCC: Squamous cell carcinoma; SD: Standard deviation; Se: Selenium; SGC: Sebaceous gland carcinoma; SPSS: Statistical Package for the Social Sciences; UV-B: Ultraviolet B.

ETHICAL APPROVAL

The study was approved by the Health Research Ethics Committee of Universitas Sumatera Utara (No. 622/KEPK/USU/2024). Written informed consent was obtained from all participants.

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