PECULIARITIES OF IMMUNOLOGICAL DISORDERS AND THE DEVELOPMENT OF COMPLICATIONS IN PATIENTS WITH UVEITIS OF TUBERCULOUS ETIOLOGY

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ABSTRACT

Background. Tuberculosis is an infectious disease that can severely affect the visual system, presenting with a broad spectrum of clinical manifestations, including various forms of uveitis. The role of the immune response in tuberculous uveitis is currently receiving increased attention regarding its diagnostic, therapeutic implications, and contribution to the development of ocular complications.

Aim. To investigate the peculiarities of immunological disorders and the development of complications in patients with uveitis of tuberculous etiology.

Materials and Methods. We studied clinical features, disease progression, and immunological parameters in 39 patients (60 eyes; aged [28–87] years; 13 men, 26 women) with relapsing tuberculous uveitis and pulmonary tuberculosis (disease duration [3–32] years). Standard ophthalmological and immunological examinations (first- and second-level tests) were performed. The control groups included 61 patients (98 eyes) with non-tuberculous uveitis and 35 healthy individuals.

Research Ethics. The study was conducted in accordance with the principles of the World Medical Association Declaration of Helsinki (1964–2024) and was approved by the Ethics and Bioethics Committee of Kharkiv National Medical University (Protocol No.5 of May 07, 2025). All patients provided written informed consent prior to participation.

Results. Complicated forms of tuberculous uveitis were identified in 49 eyes (81.7%). These were most frequently observed in generalized (100.0%) and anterior (95.2%) uveitis, while posterior uveitis was complicated in 58.3% of cases. The most common complications were uveal cataract (61.7%) and corneal involvement (46.6%). Immunological assessment revealed an immunodeficiency syndrome with a significant decrease in the number of T-lymphocytes, T-helper cells, and the helper/suppressor ratio ($p<0.05$) compared to the non-tuberculous group. Suppression of humoral immunity was also observed, manifested by a significantly greater decrease in the number of B-lymphocytes and immunoglobulin G concentration ($p<0.05$).

Conclusions. Tuberculous uveitis, compared to non-tuberculous etiology, is significantly more often complicated by uveal cataract, keratitis, and uveal glaucoma. Patients with tuberculous uveitis exhibit a significantly more pronounced decline in both cellular and humoral immunity parameters, demonstrating that endogenous immunosuppression plays a major role in the progression of complicated forms of uveitis.

Keywords: *ophtalmology, complicated forms of uveitis, T-lymphocytes, humoral immunity, ocular complications.*

Introduction

Tuberculosis remains a major global health threat; according to the World Health Organization, approximately 10.6 million people worldwide were living with this infectious disease in 2021 [2]. Caused by Mycobacterium tuberculosis [1], the infection can also severely affect the visual system. The proportion of uveitis cases attributed to tuberculosis varies widely depending on the region, ranging from [0.7–2.0] % up to 10.1% [3; 4].

Ocular involvement presents with a broad spectrum of clinical manifestations, including, but not limited to, anterior uveitis, intermediate uveitis, retinal vasculitis, posterior uveitis, scleritis, and optic neuropathy [5–8]. Despite advances in diagnostics, identifying and managing tuberculous uveitis remains challenging due to the varia-

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bility of the host's immune response. Currently, increasing attention is being paid to the immune response in tuberculous uveitis [9], both in terms of its diagnostic and therapeutic implications, as well as its role in the development of disease complications [10]. It is hypothesized that systemic depletion of immune resources, caused by the underlying tuberculous process, creates a foundation for the development of secondary immunodeficiency, which may significantly aggravate the course of uveitis. However, the exact patterns of cellular and humoral immunosuppression in these patients and their direct impact on ocular outcomes remain insufficiently studied.

The **aim** of this study was to investigate the peculiarities of immunological disorders and the development of complications in patients with uveitis of tuberculous etiology.

Materials and Methods

A prospective study was conducted involving a total of 135 individuals, who were divided into three distinct groups. Main Group (tuberculous uveitis) consisted of 39 patients (60 eyes) with uveitis of tuberculous etiology and concurrent pulmonary tuberculosis. Comparison Group (non-tuberculous uveitis) consisted of 61 patients (98 eyes) with uveitis of non-tuberculous etiology. Control Group consisted of 35 healthy individuals who provided baseline immunological values.

Main Group (tuberculous uveitis) included 13 men and 26 women aged 28 to 87 years. The duration of the disease ranged from 3 to 32 years, and all patients exhibited a relapsing course of uveitis. The etiology was established based on a comprehensive diagnostic approach that included positive intradermal and focal tuberculin tests, radiological findings of pulmonary tuberculosis, specific clinical ophthalmological signs, and a positive response to trial anti-tuberculosis therapy. Anatomically, the inflammatory process was localized in the anterior uvea in 21 eyes, in the posterior uvea in 24 eyes, and was generalized (panuveitis) in 15 eyes.

Comparison Group (non-tuberculous uveitis) was used to compare immunological disturbances and the frequency of complications. It consisted of 61 patients (98 eyes), where anterior uveitis was diagnosed in 41 eyes, posterior uveitis in 35 eyes, and generalized uveitis in 22 eyes. No statistically significant differences in anatomical distribution were observed between the main and comparison groups ($p>0.05$).

Healthy Control Group consisted of 35 healthy individuals matched for age and sex to provide reference ranges for the immunological parameters evaluated in the study.

Exclusion criteria were applied to ensure the accuracy of immunological data. Patients with systemic autoimmune diseases, HIV infection, other primary or secondary immunodeficiency states unrelated to tuberculosis, or those receiving systemic immunosuppressive therapy at the time of sampling were excluded.

Materials and Methods

All patients underwent standard ophthalmological examinations. Immunological evaluation involved first- and second-level diagnostic tests. The absolute and relative numbers of T and B lymphocytes, as well as T-lymphocyte subpopulations, were determined using indirect immunofluorescence with monoclonal antibodies [11; 12]. Quantitative determination of serum immunoglobulins (IgA, IgM, IgG) was performed by the Mancini G. (1965) radial immunodiffusion method [13], as modified by Fahey J.L. (1965) [14] and McKelvey E.M. (1973) [15].

Statistical processing of the results was performed using parametric statistics. The normality of data distribution for quantitative variables was assessed using the Shapiro-Wilk test. Because the data were normally distributed, parametric methods were chosen for further analysis. Descriptive statistics for quantitative data are presented as the mean and standard deviation (M±SD). To compare the mean values of quantitative parameters among three or more independent groups, a one-way analysis of variance (One-Way ANOVA) was applied. Post-hoc group comparisons were conducted using Tukey's Honestly Significant Difference (HSD) test. Differences were considered statistically significant at a level of $p<0.05$. Statistical analysis was carried out using the SPSS Statistics 27 (IBM, USA).

Research Ethics

The study was conducted in accordance with the principles of the World Medical Association Declaration of Helsinki (1964–2024) and was approved by the Ethics and Bioethics Committee of Kharkiv National Medical University (Protocol No.5 of May 07, 2025). All patients provided written informed consent prior to participation.

Results

To investigate the role of endogenous immunosuppression in the development of complicated forms of uveitis, we analyzed immune system disturbances and the frequency of complications of tuberculous uveitis (*Fig. 1*), occurring against the background of pulmonary tuberculosis.

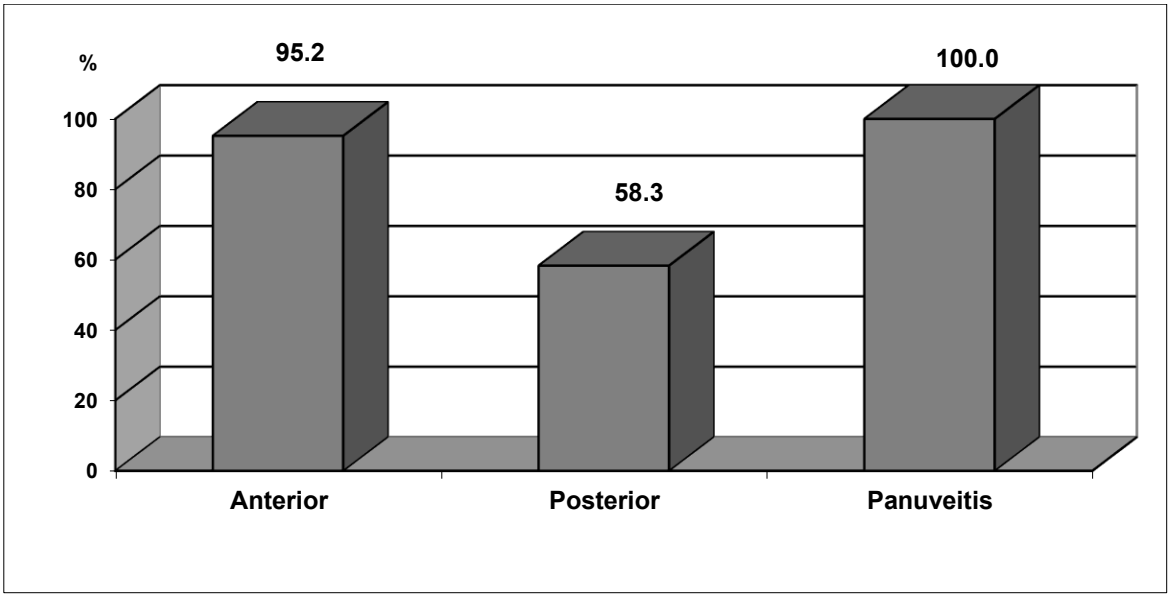


Fig. 1. Frequency of complicated forms of tuberculous uveitis depending on the anatomical localization of the inflammatory process.

Complicated forms of uveitis were identified in 49 eyes (81.7%). These were most frequently observed in generalized (100.0%) and anterior (95.2%) uveitis. In patients with posterior uveitis of tuberculous etiology, complications were noted in 58.3% of cases.

The most common complication of tuberculous uveitis was uveal cataract (61.7%). The disease presented as keratouveitis in 38.3% of cases, in 5 eyes (8.3%) the disease was complicated by corneal degeneration. Post-uveitic chorioretinal dystrophies were present in 17 eyes (28.3%), secondary uveal glaucoma in 13.3%, and iris atrophy in 13 eyes (21.7%). Uveitis was complicated by optic neuritis in 6 eyes (10%), by partial optic atrophy in 5 eyes (8.3%). Marked vitreous destruction and opacification were observed in 23 eyes (38.3%), while vitreous strands were noted in 4 eyes (6.7%).

Tuberculous uveitis was complicated by macular edema in 3 eyes (5%) and by subatrophy of the eyeball in 2 eyes (3.3%). Retinal detachment, ocular hypotony, central retinal vein thrombosis, and secondary strabismus were identified as rare complications, with one case (1.7%) reported for each.

In comparison with non-tuberculous uveitis (*Fig. 2*), tuberculous uveitis was significantly more often associated with uveal cataract (61.7% vs. 19.3%; $p<0.05$), keratitis (38.3% vs. 8.0%; $p<0.05$), and uveal glaucoma (13.3% vs. 2.4%; $p<0.05$).

The indicators of cellular and humoral immunity are presented in *Table 1* and *Table 2*.

It was established that patients with uveitis of tuberculous etiology exhibited a significantly more pronounced reduction in the number of T lymphocytes ($p<0.05$), T helper cells ($p<0.05$), and the helper/suppressor ratio ($p<0.05$).

In addition to cellular immunodeficiency, suppression of the humoral component of the immune system was also observed in these patients (Table 2), which manifested as a significantly greater decrease in the number of B lymphocytes ($p<0.05$) and in the concentration of immunoglobulin G ($p<0.05$).

Thus, the conducted research demonstrated that endogenous immunosuppression plays a significant role in the onset and progression of complicated forms of uveitis.

Discussion

The findings of our study highlight the complex clinical profile of tuberculous uveitis, particularly regarding its anatomical distribution and the high rate of associated complications. In our cohort, the posterior segment was the predominant site of inflammation (40%). This observation is consistent with the findings of numerous other researchers, who reported the proportion of posterior uveitis ranging from 38.89% to 83.3% [16–19].

However, literature data suggest that the anatomical localization of tuberculous uveitis varies significantly across different geographic regions and patient populations. For example, in a study

Table 1. Indicators of Cellular Immunity in Patients with Uveitis of Tuberculous and Non-Tuberculous Etiology

Study Groups		T-lymphocytes, cells/μL	T-helpers, cells/μL	T-suppressors, cells/μL	Immunoregulatory index
I. Tuberculous uveitis (n=39)		702±47	413±33	292±26	1.64±0.25
II. Non-tuberculous uveitis (n=61)		882±72	594±65	285±27	2.49±0.17
III. Healthy individuals (n=35)		1301±78	989±73	311±38	3.22±0.18
Significance of Differences, p	I–II	<0.05	<0.05	>0.05	<0.05
	II–III	<0.05	<0.05	>0.05	<0.05
	I–III	<0.05	<0.05	>0.05	<0.05

Table 2. Indicators of Humoral Immunity in Patients with Uveitis of Tuberculous and Non-Tuberculous Etiology

Study Groups		B-lymphocytes, cells/μL	Immunoglobulins, g/L		
			A	M	G
I. Tuberculous uveitis (n=39)		137.00±22.00	1.32±0.18	1.07±0.14	7.62±0.58
II. Non-tuberculous uveitis (n=61)		211.00±27.00	1.55±0.16	1.27±0.09	9.37±0.61
III. Healthy individuals (n=35)		218.00±32.00	1.58±0.13	1.21±0.10	9.31±0.53
Significance of Differences, p	I–II	>0.05	>0.05	>0.05	>0.05
	II–III	>0.05	>0.05	>0.05	>0.05
	I–III	<0.05	>0.05	>0.05	<0.05

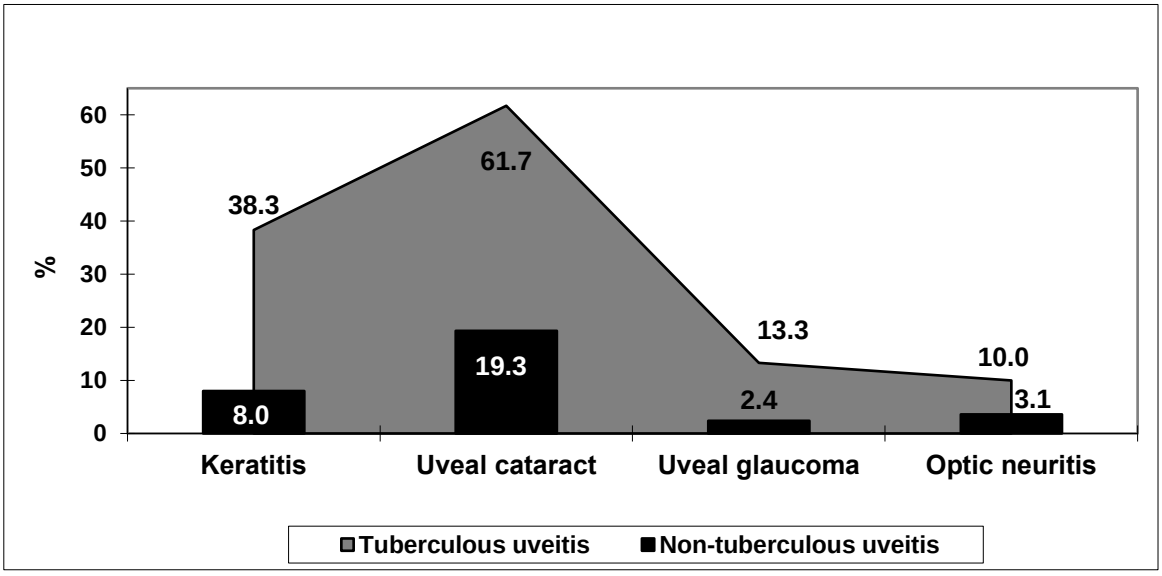


Fig. 2. Frequency of complications in tuberculous uveitis.

by Xie J. et al. (2023) [16], posterior segment involvement was the most common presentation among 84 eyes (83.3%), while anterior uveitis accounted for only 4.7% of cases, and panuveitis was observed in 11.9%. Similarly, Rahman H. et al. (2022) [21] reported that among patients with concurrent pulmonary tuberculosis, posterior uveitis was present in 69% of eyes, anterior uveitis in 23%, and panuveitis in 7%. Conversely, in a case series described by Tsui J.K. et al. (2023) [22], anterior uveitis was the predominant manifestation (50%). This variability underscores the heteroge-

neous nature of ocular tuberculosis, which may be influenced by systemic disease severity, host immune status, or regional strain differences.

A major clinical challenge in the management of tuberculous uveitis is the severe structural damage it inflicts on the eye. According to our findings, complications were observed in 81.7% of cases, which is in close agreement with the results of Tsui J.K. et al. (2023) [22], who reported uveitis-related complications in 70% of patients. Current literature indicates a wide variability in the frequency and types of tuberculous uveitis complications, including: macular edema – 8.2% to 44.1% [16; 18; 20; 23–26]; retinal ischemia – 36.9% [16]; cataract – 14.2% to 20.1% [20; 24–26]; subretinal neovascular membrane – 1.7% to 36.3% [16; 18; 20; 24; 26]; ocular hypertension and glaucoma – 3.3% to 30% [16; 20; 24–26]; vitreous hemorrhage – 16.3% to 21.3% [18; 25]; tractional retinal detachment – 3.3% to 15.5% [16; 25]; epiretinal membrane – 3.3% to 7.9% [24; 25]; retinal vein occlusion – 3.7% [24]; and optic nerve atrophy – 4.9% [25].

In our patient cohort, the most frequent complications were uveal cataract (61.7%) and corneal involvement (46.6%). Notably, the rate of uveal cataract in our study substantially exceeds the standard ranges reported in the literature [20; 24–26]. We hypothesize that this elevated frequency is intrinsically linked to the profound endogenous immunosuppression identified in our results. The inability of the compromised cellular and humoral immune systems to effectively clear the infection likely leads to a chronic, relapsing inflammatory state, resulting in severe collateral tissue damage. The destructive potential of this prolonged inflammation is further evidenced by the occurrence of severe, end-stage complications, such as subatrophy of the eyeball, which was noted in 3.3% of our cases.

Ultimately, the extensive anatomical damage and high complication rates associated with tuberculous uveitis indicate a critical need for improved early diagnosis and more targeted treatment strategies. Managing these patients requires addressing not only the infectious agent but also the underlying immune dysregulation.

A ***limitation*** of this study is the relatively small number of patients examined, highlighting the need for future large-scale studies to validate these mechanisms.

Conclusions

1. Uveal cataract (61.7%) and corneal involvement (46.6%) were identified as the most frequent and sight-threatening complications in patients with tuberculous uveitis.

2. Tuberculous etiology is a major risk factor for severe structural ocular damage; compared to non-tuberculous uveitis, it is significantly more likely to result in the development of uveal cataract, keratitis, and secondary uveal glaucoma.

3. Patients with tuberculous uveitis exhibit a profound secondary immunodeficiency, characterized by a significantly more pronounced depletion in both cellular (T-lymphocytes, T-helper cells) and humoral (B-lymphocytes, IgG) immunity parameters.

4. Endogenous immunosuppression plays a pivotal pathophysiological role in the onset and progression of complicated forms of tuberculous uveitis, indicating that effective management requires addressing not only the infectious agent but also the underlying systemic immune dysregulation.

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Declarations

Conflict of interest is absent.

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The authors of the manuscript state that in the process of conducting research, preparing, and editing this manuscript, they did not use any generative AI tools or services to perform any of the tasks listed in the Generative AI Delegation Taxonomy (GAIDeT, 2025). All stages of work (from the development of the research concept to the final editing) were carried out without the involvement of generative artificial intelligence, exclusively by the authors.

Authors' Contributions

Contribution / Authors	A	B	C	D	E	F
Panchenko M.V.	+	+			+	+
Honchar O.M.			+	+		+
Panchenko H.Y.				+		+
Kitchenko I.V.			+		+	+

Notes: A – concept; B – design; C – data collection;
D – statistical processing and interpretation of data; E – writing or critical editing of the article;
F – approval of the final version for publication and agreement to be responsible for all aspects of the work.

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