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ADAPTABILITY OF RABBITS TO HOT CLIMATE CONDITIONS

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Abstract. *The article describes the results of research on clinical and haematological parameters of acceleration rabbits by seasons of the year when growing in the hot climate of Uzbekistan. The degree of heat tolerance and coefficient of endurance under different rearing systems have been determined.*

Keywords: *rabbits, males, young, body temperature, pulse, respiratory rate, heat tolerance, endurance, hematology.*

Introduction

Rabbit breeding is a promising branch of animal husbandry. Rabbits give tasty dietary meat, valuable raw fur and down, while using cheap and available feed: grass, hay, twig fodder, some grain, while in poultry farming only grain. For the production of 1 kg of weight is spent 3 k.u., this is more than in poultry 2 k.u., but much less than in pork, bacon 5-6 k.u., beef 6-7 k.u. Paying forage 2.3 times better than cattle. Among all types of meat, rabbit meat ranks among the first in protein nutrition, juiciness, tenderness, taste and digestibility, second only to turkey. There is less collagen and elastin in rabbit meat than in the meat of other animals, and this increases the level of complete proteins. Therefore, rabbit meat is more easily digested by the human body. Rabbit meat has all the essential amino acids. Rabbit meat is white, meaning it contains little myoglobin. Protein is 20-22%.

In different geographical and climatic zones, with different forage and other conditions, each zone has its own characteristics. Too high as well as very low temperatures affect the resistance of the organism. In this connection, the following tasks were solved: to study the clinical and hematological blood parameters of acceleration rabbits in connection with their adaptation to year-round keeping at high ambient temperatures. Analysis of different technologies shows a number of advantages of the acceleration method of keeping and breeding rabbits. Growing rabbits in rabbit houses involves the construction of expensive capital premises, high energy costs, which significantly increases the cost of rabbit meat. Growing rabbits indoors leads to a violation of the interaction of the body with the environment, physiological processes are disrupted, including thermoregulation, which leads to a decrease in productivity.

Material and methodology of the study. Studies were conducted at the Center for the Selection and Genetics of Rabbits on two groups of adult rabbits of the Californian breed and young rabbits at the age of 60 days, 10 animals in each. Rabbits were kept in mini-farms on open areas developed in the CCHC with regard to climatic conditions of the country. Clinical parameters were studied in adult animals and young animals at the age of 60 days in July. Respiration rate, pulse rate and body temperature were determined in the morning, afternoon and evening. Hematological parameters were studied in adult animals and young animals at the age of 60 days.

The degree of heat tolerance was determined by the refined formula of R. Benezre (1954):

$CT=X_1 +3.69X_2$, where

ST-degree of heat resistance;

X_1 and X_2 are pulse and respiration rate at a given ambient temperature.

Stability (adaptation) coefficient was determined by the formula

$$KA=\frac{Td}{Tu}+\frac{Dd}{Du}$$, where

CA- coefficient of endurance (adaptation);

Td is the body temperature of the animal during the daytime hours;

Tu - body temperature in the morning hours; Breathing rate per minute during the daytime hours;

Du - respiratory rate per minute in the morning hours.

Smaller values of the coefficient of endurance (adaptation) indicate a more pronounced resistance of the animal to the effects of elevated air temperatures.

Research results. In different geographical and climatic zones, with different forage and other conditions, each zone has its own characteristics. Too high as well as very low temperatures affect the resistance of the organism.

Table 1 Clinical parameters of the studied rabbits

Indicators	Acceleration method			Indoors.		
	Morning	noon	Evening	Morning	noon	Evening
Rabbitmothers						
Body temperature,^{0}C	38,6±0,02	39,2±0,021	38,9±0,019	38,7±0,02	39,4±0,021	38,6±0,019
Heart rate, times/minute	137±3,4	184±5,9	177±6,1	142±3,4	194±5,9	181±6,1
Breathing, times/minute	89±5,2	121±4,8	114±6,7	92±5,2	129±4,8	124±6,7
Males						
Body temperature,^{0}C	38,5±0,014	39,0±0,02	39,1±0,016	39,0±0,014	39,3±0,02	39,1±0,016
Pulse, times/minute	132±5,1	185±6,5	180±7,2	139±5,1	196±6,5	183±7,2

Breathing Frequency, times/minute	79±3,1	117±2,9	98±4,3	89±3,1	131±2,9	118±4,3
60-days old youngsters						
Body temperature, ^{0} C	38,4±0,011	38,9±0,23	38,7±0,02	38,5±0,011	39,3±0,23	38,9±0,02
Pulse, times/minute	141±6,8	193±8,6	181±7,5	152±6,8	219±8,6	192±7,5
Breathing Frequency, times/minute	94±5,3	129±4,9	121±5,6	98±5,3	141±4,9	136±5,6

When setting standards, it is necessary to consider not only species, but also breed, age, sex, physiological condition, fatness, suitability, conditions of keeping, feeding and care. It should be considered that high air humidity, both at high and low temperatures have a negative effect on the body's resistance due to violation of heat exchange. High velocity of cold air also disrupts heat exchange and suppresses protective adaptations of the animal's organism. Insufficient supply of fresh air disturbs normal respiratory functions. Indicators of the level of natural resistance of animals were lower in reinforced concrete premises. Physiological indicators related to resistance can also be used to identify resistant animals; it is possible to use the thermoregulatory capacity of the organism for this purpose.

The desire to maintain the internal environment is the most important physiological property of the organism of higher animals. An evolutionary constant is the maintenance of body temperature. In clinical practice, body temperature is the most characteristic indicator reflecting the course of life processes. Thus, body temperature is used as a parameter of animal susceptibility to infections. What is of particular importance is not the absolute body temperature, but how it is maintained when the environmental temperature changes.

Clinical parameters of experimental rabbits are presented in Table 1.

Analyzing Table 1, we found that rabbits reared according to the acceleration method, at air temperature $+38^0$ C felt more comfortable in the mineral farms than rabbits indoors. The presence of clean air, free access to feed and water, and the absence of stress affected the clinical parameters. The body temperature of female accelerated rabbits was 0.1 lower in the morning; 0.2 lower in the afternoon; and 0.3^0 C higher in the evening than that of rabbits raised indoors. In males, 0.5; 0.3 and 0^0 C, respectively; in 60-day-old rabbits, 0.1; -0.4; 0.2^0 C.

Accelerated rabbits were calmer, with female rabbits having a lower heart rate of 8, 10, 4 beats per minute; males by 7, 11, 3; young males by 11, 23, 11, respectively.

The study of rabbits' body reaction to hot weather by counting respiration rate showed that the rabbits in the mineral farms had better indicators. So the variation of breathing rate per minute in female rabbits during the day was 89-121, which is 3.4-6.6% lower than in rabbits kept indoors. In males this index was 11.9-12.6%, in young animals it was 4.2-9.3%.

Table 2

Heat tolerance indexes of experimental rabbits

Indicators	Growing in		difference +,-
	mini-farms	room	
Bunnycats	465,41±86,2	670,01±102,5	204,6
Males	423,51±77,9	679,39±99,6	255,88
60-day-old youngsters	661,3±91,7	739,29±113,1	77,99

Rabbits are vulnerable to changes in ambient temperature. The critical environmental temperature, according to many authors, for rabbits is $+35^0$ C. According to groups of international researchers, animal resistance to heat develops more slowly than to cold. The clinical parameters of the experimental rabbits were within the physiological norm, but there were differences between the groups. In our studies, the dependence of pulse rate and respiration rate in the morning and afternoon at ambient temperature $+38^0$ C was established, according to which the degree of heat tolerance of rabbits was calculated (Table 2).

The data in Table 2 show that the degree of heat tolerance of the rabbits of accelerator rabbits bred in the mineral farms outdoors was high compared to the rabbits bred indoors. Thus, accelerator rabbits exceeded their female counterparts by 43.7%, males by 60.4% and juveniles by 11.7% according to this indicator. Hematological parameters of experimental groups of rabbits were within normal limits, and there were differences in the groups due to rearing conditions (Table 4).

Rabbits bred outdoors in mineral farms have the best blood morphological indices. Thus, they surpassed their analogues by 4.0% in hemocrit (proportion of erythrocytes from the total blood volume), by 9.9% in hemoglobin concentration. In terms of erythrocyte count, leukocyte count they had a lower value, which indicates a stable course of life processes. Blood performs a complex and important function in the body - it provides thermoregulation, supplies cells with nutrients and oxygen.

Table 3

4 Morphological indices of the blood of female rabbits

Indicators	**Unit of measure**	**Symbols**	**Norma**	**Content system**			
				In mine farms.		**Indoors**	
				M±m	**Cv , %**	**M±m**	**Cv , %**
Number of leukocytes	$*10\ /l^9$	WBC	5-12,5	9,14±0,29	12,54	9,04±0,29	12,54
Number of lymphocytes	$*10\ /l^9$	Lymph#.	30-85	53,13±1,39	9,64	53,05±1,32	9,64
Number of red blood cells	$10\ /l^{12}$	RBC	5-8	5,49±0,41	22,49	5,64±0,33	22,49

Hemaglobin concentration	g/l	HGB	17-24	22,2±0,32	11,26	20,2±0,59	11,26
Hemocrit	%	HCT	33-50	42,70±0,8	9,71	38,70±0,9	9,71
Volume of red blood cells	fm	MCV	29-37	35,62±0,7	10,26	33,74±0,8	10,26
Erythrocyte hemoglobin	pg	MCH	17-24	22,6±0,61	10,07	19,3±0,50	10,07
Platelet count	*10 /l^9	PLT	2,5-6,5	4,74±0,33	21,59	4,24±0,24	21,59
Calcium content	mg/%	Sa	7-12	10,1±0,21	8,1	9,6±0,34	10,4
Phosphorus content	mg/%	P	4,8-6,5	6,9±0,62	9,2	5,3±0,12	9,9

Conclusion

Creation of optimal conditions of keeping and breeding of rabbits on acceleration method in mineral farms in the open air, where there is free access to feed and water, the absence of stress contributes to better tolerance of high air temperature, better adaptation to hot conditions and stable resistance of the organism.

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BOTANICAL DESCRIPTION, CHEMICAL COMPOSITION AND MEDICINAL PROPERTIES OF *FERULA ASSA-FOETIDA*

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Abstract. *This article presents an analysis of literature data on plant species belonging to the genus Ferula L. that grow in the desert, semi-desert, foothill, and mountainous regions of Uzbekistan, including their distribution, botanical description, chemical composition, and medicinal properties.*

Keywords: *ferula assa-foetida, panaferol, kufestrol, zafarol, tefestrol, alkaloid, glycoside.*

Introduction

It is important to note that since ancient times, people have used plants not only as a source of food but also as medicinal organic substances. For example, the peoples of East Asia have traditionally used tea, African peoples have used coffee and kola nuts, the peoples of Central America have used cocoa, and the peoples of South America have used mate leaves. In addition, to expel intestinal parasites from the body, African peoples have used the flowers of the kusso plant, while South American and European peoples have used fern roots.

Moreover, from ancient times in Southeast Asia-particularly in India, China, Tibet, Korea, and Arab countries-patients have been treated with medicinal plants. Abu Ali ibn Sina, in his book *The Canon of Medicine*, provided information on more than 400 plant species. In nature, there are about 500,000 species of higher plants, of which approximately 12,000 are considered medicinal. In Uzbekistan, more than 4,200 plant species are found, and over 160 of them are used as medicinal and healing plants in human medicine and partly in veterinary practice.

Kovrak belongs to the Apiaceae (umbellifer) family and is a perennial monocarpic plant that grows to a height of 100–120 cm and flowers and bears fruit only once in its lifetime. In spring, kovrak sprouts and produces only basal leaves. Over the years, its leaves gradually increase in size, while the root thickens and accumulates a large amount of nutrients. After 7–13 years of growth, the plant forms a stem and begins to flower. In the year it enters the seed-producing stage, the length of its leaves reaches 50–60 cm, and their diameter can reach up to 1 meter. It blooms in March–April, forming a yellow, compound umbel-shaped inflorescence at the tip of its generative organ. The seeds ripen in May–June. The young green leaves of kovrak, its dried hay, and its mature seeds are consumed by animals. Kovrak seeds contain 14–19% protein, 8% fat, 37–47% nitrogen-free extractive substances, and 23–27% fiber [2; pp. 21–22, 18; p. 30].

On a global scale, there are nearly 200 species of *Ferula*. In our country, more than 50 species have been identified. Many species of *Ferula* are widely used in the pharmaceutical industry as remedies for treating diseases. Furthermore, resins and essential oils are obtained from some species, while the young flowering parts of *Ferula* are also used for food purposes.

The beneficial properties of *Ferula* have been known to people since ancient times. As a result, various nations around the world have long used extracts of this medicinal plant as an anti-

tumor, antitoxic, laxative, and immunomodulatory agent. In recent years, it has also been increasingly applied in veterinary practice as an anthelmintic agent against parasitic worms.

Purpose of the research.

The aim of this study is to analyze the available literature data on plants belonging to the genus *Ferula* L. that are distributed in different regions of our republic.

Degree of research development.

In recent years, the extraction of gum (resin) from kovrak roots and its export have intensified significantly [3; pp. 114–240]. Kovrak contains biologically active substances and exhibits high pharmacological and chemotherapeutic activity. Therefore, the prospects for the use of this plant are quite broad and promising [18; p. 30]. The resin of *Ferula assa-foetida* is used at the Tashkent Pharmaceutical Plant for the production of estrogenic preparations such as panaferol, kufestrol, and zafarol, which are applied to increase egg productivity in poultry [15; 23; p. 112; 20; pp. 131–132].

It should be particularly emphasized that the kovrak plant is widely distributed in mountainous and desert regions. In the Kyzylkum deserts, the distribution area of *F. assa-foetida* and *F. foetida* alone reaches about 2 million hectares [18; p. 30]. In addition, it has been established that chemical compounds isolated from species of the genus *Ferula* L. possess hormonal properties, which led to the development of the preparation panoferol. The panoferol preparation (a complex of extracts) is used in veterinary practice to improve egg quality in poultry, prolong their egg-laying period, and prevent infertility in cattle and ewes [3; pp. 114–240].

According to many authors, stinking ferula (assafoetida) is an excellent essential oil–bearing plant and, first of all, is considered a valuable medicinal plant as well as a feed source for farm animals. Moreover, it is an industrial plant of aromatic food importance, as it contains starch and sugar substances. Based on the biologically active compounds present in kovrak, in recent years the Institute of Chemistry of the Academy of Sciences of Uzbekistan and the Tashkent Pharmaceutical Plant have produced four widely used preparations for medicine, animal husbandry, and poultry farming—tefestrol, panaferol, kufestrol, and zafarol. Among these, tefestrol is used in medicine for the treatment of gynecological diseases, while panaferol, kufestrol, and zafarol are widely applied in veterinary practice, particularly in poultry farming, to enhance reproductive activity and to prevent infertility in sheep and cattle [15; 20; pp. 131–132].

Thus, plants belonging to the genus *Ferula* L., in addition to containing the above-mentioned natural biologically active substances, also attract great interest among specialists as reserve and medicinal plants rich in terpenoids and their analogues. For this reason, studying the distribution, ontogenesis, and biomorphological characteristics of terpenoid-containing plants of this genus is of great theoretical and practical importance. A comprehensive botanical and morphological study of *Ferula* L. species, along with the compilation of cartograms of their natural resources, helps to address theoretical and practical problems of the pharmaceutical industry related to drug production and preparation. Furthermore, such studies make it possible to assess their natural resources and create opportunities for their wide application in the national economy [19].

Taking into account the multifaceted use of stinking ferula in the national economy, scientifically substantiated criteria for its rational utilization have been developed in our country. An analysis of the literature shows that 96 species of the genus *Ferula* L. [18; p. 30] have been identified within the flora of our region. It should be particularly emphasized that 28 species of *Ferula* L. growing in Central Asia are endemic. Especially important from a practical standpoint

is the identification and propagation of the natural resources of stinking ferula, as well as the endangered Bukhara sumbul listed in the Red Book.

The interest of many researchers in the terpenoids contained in stinking ferula is explained by the fact that, like other natural compounds, they exert specific effects on humans, animals, and microorganisms. In addition to their various properties, these compounds also exhibit estrogenic activity, as a result of which estrogenic agents such as panoferol and tefestrol have been isolated [9; p. 120; 10]. Panaferol, kufestrol, and zafarol preparations are widely used in veterinary practice to increase egg production in poultry and to prevent infertility in sheep and cattle. The preparation tefestrol is used in the treatment of reproductive disorders, including dysmenorrhea, ovarian hypofunction, sexual weakness, infertility, and dysfunctional uterine bleeding [11; 12; pp. 18–22; 13].

According to the studies of the author [21; p. 350], the qualitative and quantitative indicators of alkaloids in various plants vary depending on their vegetative growth stages. In addition, these indicators are significantly influenced by the region and environmental conditions in which the plant grows. The content of chemical compounds in plants, particularly complex esters, varies within wide limits depending on plant age and seasonal changes. Therefore, when collecting raw materials, special attention must be paid to periods when the concentration of these substances is highest. In the process of isolating biologically active terpenoid compounds from stinking ferula, treatment with alkaline substances is applied [27; pp. 173–178].

As noted by the author [18; p. 30], the kovrak plant constitutes about 8–10% of the feed balance of Karakul sheep and other grazing animals. During the spring season, Karakul sheep consume up to 850–1000 g of fresh green kovrak leaves daily. In practice, the dried milky latex obtained from the assafoetida root is most commonly used. The latex extracted from the assafoetida root has a bitter taste and a smell resembling a mixture of onion and garlic, although its unpleasant odor is closer to that of garlic. The taste of assafoetida resin remains in the mouth for several hours and cannot be removed by rinsing with water, alcohol, or vinegar solutions. If assafoetida is brought into a room where the temperature exceeds 22°C, its strong odor permeates the air within minutes, and even prolonged ventilation for several days cannot eliminate it [17; p. 208].

According to another author, most varieties of kovrak grow together with large grasses found in mountainous and foothill regions. The history of the distribution of kovrak is highly complex, and many positive efforts have been made to spread it widely. Historical sources indicate that stinking ferula was widely distributed in North Africa as early as the 4th century BC. However, due to intensive extraction of resin from its roots, its population gradually declined in many regions and, by the 1st century AD, it had completely disappeared in some areas. At present, its numbers are also gradually decreasing in other regions. The main reason for the decline of this plant is the unregulated collection of resin in large quantities [7; p. 29; 8; p. 117]. According to available data, stinking ferula currently grows only in the territories of Iran, Afghanistan, and Uzbekistan.

In the livestock sector of our republic, Karakul sheep breeding is considered one of the main branches. The development of this sector requires efficient use of pastures, foothills, and desert areas, improvement of their reclamation status, and cultivation of forage crops adapted to desert climates. Desert forage plants include wormwood, camelthorn, wild grasses, kovrak, and other species. In the desert regions of our republic, stinking ferula is widely distributed, covering about 2 million hectares in the Kyzylkum deserts. Under desert conditions, Karakul sheep are mainly raised and bred. In early spring, when vegetation begins to sprout, kovrak also emerges,

and sheep start feeding on it. In May, the plant produces seeds, which are also readily consumed by sheep.

Central Asia, including Uzbekistan, is characterized by extremely rich flora, with about 30% of all plant species known in the CIS growing in this region. Many of these plant species are widely used in folk medicine and veterinary practice for the treatment of various diseases [12; pp. 18–22; 26; pp. 160–162]. According to researchers, stinking ferula grows abundantly in the desert regions of our republic, occupying approximately 2 million hectares of the Kyzylkum deserts. As mentioned above, Karakul sheep are primarily raised in desert conditions, and kovrak serves as an important forage plant during early spring and seed-setting periods.

Stinking ferula belongs to the Apiaceae (Umbelliferae) family and is a perennial herbaceous plant that can reach a height of up to 1.5 meters. According to the author, after 8–9 years the plant produces an upright stem that is thick and branched in its upper part. The basal leaves are petiolate, elongated or lanceolate, and divided into three lobes, whereas the stem leaves are smaller, repeatedly pinnately dissected, and arranged alternately with sheathing bases. The flowers are arranged in compound umbel inflorescences, are five-parted, and have a whitish-yellow color [18; p. 30].

According to another source, stinking ferula blooms in March–April and forms double achene fruits in April–May. The plant *Ferula assa-foetida* grows in steppes, foothills, sandy deserts, mountain soils, and occasionally in foothill plains of Central Asia. In particular, it is widely distributed in sandy and gravelly plains and foothills of the Tashkent, Samarkand, Kashkadarya, and Surkhandarya regions; in the sandy deserts of Bukhara, Navoi, and Karakalpakstan; in the Khujand region of Tajikistan and the Samarkand massif; in Turkmenistan on the Badakhshan plain; near Kelif; in the lower Amu Darya region; around the Kyzylkum desert; and in Kazakhstan, especially around the Aris station and the city of Turkistan in the Shymkent and Jambul regions, where extensive plantations occur, and in some areas the plant forms dense stands.

…forming dense thickets [16; pp. 276–313]. According to the researcher, 96 species of kovrak (*Ferula* L.) occur in the mountains and foothills of Central Asia, of which 55 species grow in the Western Tien Shan region. Among them, 30 species contain biologically active sesquiterpene lactones, terpenoid coumarins, and complex ester compounds. Some of these substances are of great importance for pharmacological research [2; pp. 21–22].

Another author notes that studies of terpenoid compounds found in kovrak plants have shown that coumarins are present in *Scorodesma*, which is considered one of the most ancient species of kovrak, whereas all other species contain terpenoid coumarins and sesquiterpene lactones. It has also been reported that the roots of *Peucedanoides* are rich in complex esters. Biologically active substances are present in different parts of these plants, and their quantity varies depending on the developmental stage of the plant and ecological conditions [1; p. 20].

The young green leaves of stinking ferula, its hay, and its mature seeds are consumed by animals. The seeds of kovrak contain 14–19% protein, 8% fat, 37–47% nitrogen-free extractive substances, and 23–27% crude fiber [4; pp. 7–70; 6; p. 384].

Chemical composition

Alkaloids are complex organic compounds containing nitrogen. They readily dissolve in water and form salts with acids. Most alkaloids occur as crystals in their pure form, while in plants they are usually found in the form of salts. The alkaloid content of a plant varies depending on the season and developmental phase. Newly sprouted seedlings contain small amounts of alkaloids, which then gradually increase and reach a maximum during the flowering stage, after which they

slowly decrease. The first alkaloid identified was morphine, isolated from the opium poppy. Later, widely used alkaloids such as atropine, echinopsine, quinine, pilocarpine, cocaine, berberine, and reserpine were isolated from various plants. Alkaloids have a broad range of effects, primarily influencing the central nervous system and causing vasoconstriction.

Glycosides are complex nitrogen-free compounds consisting of a sugar component (glucose, galactose, rhamnose) and a non-sugar component (aglycone or genin). In their pure form, they are crystalline substances that readily dissolve in water and alcohol and usually have a bitter taste.

Saponins decompose upon hydrolysis into a carbohydrate part and an aglycone. They dissolve easily in water and alcohol and produce foam when shaken. Plants such as thermopsis, polemonium (cyanosis), primrose, and istod root have expectorant properties; kidney tea acts as a diuretic; and St. John’s wort has choleretic and tonic effects. Saponins also show positive effects in cases of vascular atherosclerosis.

Flavonoids are widely distributed in the plant kingdom. They play an important role in complex oxidation–reduction processes and tissue respiration within plants. Isolated flavonoids occur as crystals and may be yellow, orange, red, or less commonly colorless. They mainly contain monosaccharides and, less frequently, disaccharides.

Coumarins and furocoumarins are natural compounds that, in their pure form, are colorless and fragrant crystals. In plants, they occur either in free form or as glycosides combined with sugars. Hundreds of coumarin compounds are known, and their content in plants ranges from 0.2% to 5%, sometimes reaching up to 10%, with higher concentrations found in roots and fruits. They are particularly common in legumes and umbelliferous plants. Spasmolytic drugs are mainly derived from furocoumarins.

Lignans are found in plant roots, leaves, bark, and wood, for example in juniper, sesame, and other plants, either in free form or as glycosides. They are effective in the treatment of cancerous conditions and hemorrhagic diathesis.

Essential oils are volatile, strongly aromatic substances composed of terpene hydrocarbons and their derivatives. They are extracted from plants by steam distillation. Essential oils are found mainly in the flowers, leaves, and fruits—and less frequently in the roots—of plants such as wormwood, yarrow, and mountain basil. Their content ranges from 0.001% to 20%, most commonly around 2–3%. More than 2,500 types of essential oils have been identified. Due to their instability, special care must be taken during the collection, drying, and storage of essential oil–bearing raw materials. Essential oil preparations exhibit anti-inflammatory, antimicrobial, and antiviral effects, influence the central nervous system and cardiovascular system, and possess stimulating, analgesic, antitussive, and blood pressure–lowering properties.

Resins (oleoresins) are complex organic compounds with a semi-liquid or semi-solid consistency and a chemical structure similar to essential oils. They are found in coniferous trees, birch buds, rhubarb roots, and the roots of the kovrak plant. Resins have bactericidal and anthelmintic effects.

Organic acids (malic, citric, oxalic, salicylic, and acetic acids) occur in seeds, fruits, roots, leaves, and stems in free form or as salts. They participate in metabolism and stimulate the activity of salivary glands, bile secretion, and pancreatic function.

Mineral salts of inorganic acids occur in plants in dissolved form or as oxalate crystals. They play an important role in metabolism, enzyme and hormone synthesis, blood formation, and cardiac function.

…affects cardiac activity, increases nerve fiber conductivity, and is a constituent of skeletal bones.

Microelements are catalysts of metabolic processes in living organisms. A number of diseases arise as a result of deficiencies of certain microelements in the body. They are components of enzymes and active organometallic compounds and act as catalysts in many biochemical processes. Microelements include cobalt, copper, zinc, nickel, lead, iodine, manganese, and others. Their content in plants is extremely low. The balance of microelements in the human and animal body is maintained through microelements supplied with food and water.

Vitamins are biologically active substances that are extremely important for vital functions of the organism. They play a key role in metabolism, in the assimilation of major nutrients—proteins, fats, and carbohydrates—and in the protective functions of organs and organ systems. The body requires a continuous intake of about 20 different vitamins from external sources through food.

Starch is a polysaccharide and an important reserve carbohydrate that accumulates in the cells of all higher plants. After biologically active substances are extracted from plants, starch remains as a ballast substance; however, it also possesses certain physiological properties, such as a protective and coating effect on the gastrointestinal tract.

Conclusion

Based on the analysis of the literature data presented in this article, it can be concluded that, to date, the medicinal and phytotherapeutic properties of plants belonging to the genus *Ferula* L. have been relatively well studied in human medicine, whereas their use and effects in veterinary practice remain insufficiently explored. Taking the above into account, comprehensive and in-depth studies of this medicinal plant, including investigations of its phytotherapeutic and anthelmintic effectiveness, are of great importance.

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DIGITAL TOOLS FOR MANAGING FINANCIAL SUSTAINABILITY IN UZBEKISTAN'S AGRICULTURE: FINANCIAL MONITORING, EARLY RISK WARNING, AND ENHANCED TRANSPARENCY

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Abstract. *The financial sustainability of Uzbekistan's agricultural sector remains sensitive to the seasonality of cash flows, price volatility, climatic risks, and gaps in information connectivity among farms, banks, insurers, and public support institutions. Under these conditions, digital tools for managing financial sustainability are viewed as an applied infrastructure that enables a transition from reactive, ex post control to a proactive model of financial monitoring, early risk warning, and enhanced transparency.*

Keywords: *financial sustainability, agriculture, Uzbekistan, digitalization, financial monitoring, early warning, risk-oriented approach, indicators, scoring, transparency, government support, agricultural insurance, big data, remote sensing.*

Introduction

The financial sustainability of Uzbekistan's agricultural sector is shaped under conditions of high uncertainty, including the seasonality of revenues and expenditures, dependence on export price conditions for certain crops, climatic and water-related risks, and heterogeneity in farm management practices. As a result, even economically viable producers face cash flow gaps, deterioration of debt indicators, and a decline in investment activity.

Research Methodology

The methodological foundation of the article is formed at the intersection of the risk-oriented approach, the concepts of managerial accounting and financial diagnostics, and digital transformation approaches (data-driven management). A systemic and process-based approach is applied, in which financial sustainability is interpreted as the result of consistency among the flows of **revenues–costs–financing–risks** across the production cycle (sowing–cultivation–harvesting–marketing) and the support frameworks (crediting, insurance, and subsidization). The risk-oriented approach is implemented through the construction of a **"sustainability risk map"** (liquidity, debt, interest rate risk, market risk, production and climatic risk, and the risk of unreliable reporting/information asymmetry), as well as by linking monitoring indicators to the probability of adverse events and the expected losses associated with them.

Main Part

The target logic of digital management of financial sustainability in the agricultural sector is built as a continuous cycle of **"data → indicators → early warning signals → managerial response → impact control."** Unlike traditional financial analysis, which is conducted periodically and based on a limited set of reporting forms, the digital framework is oriented toward regular updates of key indicators (daily/weekly/monthly), automated data quality checks, and the

generation of warnings before a crisis event occurs (debt default, liquidity gaps, or a sharp decline in margins).

Table 1. Data Map for Digital Financial Monitoring of an Agricultural Producer (Data Mart)

Data Block	**Examples of Indicators / Data Fields**	**Update Frequency**	**Responsible Unit**	**Quality Control (Validation)**	**Managerial Use**
Financial Statements and Managerial Accounting	Cash flow statement (inflows/outflows), accounts receivable/payable, cost structure, gross and operating margins	monthly (at a minimum), preferably weekly for cash flow (CF)	Accounting Department / Finance Department	reconciliation of line items, control of negative/anomalous values, bank reconciliation	calculation of liquidity indicators, cash flow gaps, and margin metrics
Banking Transactions and Debt Profile	account turnover, repayment schedule, interest, arrears, covenants	daily / weekly	bank + finance department	reconciliation of balances, verification of payment dates and amounts, control of duplicate transactions	early signals of debt burden, solvency forecasting
Government Support and Subsidies	applications, amount/status, earmarked purpose, disbursement timelines	event-based + weekly status updates	government support registries + finance department	control of duplicate applications, compliance with eligibility criteria, reconciliation with actual expenditures	enhanced transparency and liquidity forecasting
Insurance	coverage, insured amount, deductible, insured event/loss, claim settlement timelines	event-based + monthly updates	insurer + farm	verification of policy completeness, matching of crops and cultivated areas	reduction of the financial shock from yield-related risks

Production Proxy Factors	cultivated areas, crop type, production calendar, yield (actual/planned), stress indices and weather anomalies	weekly / monthly	agricultural service / agronomy	comparison with the plan, outlier control, cross-checking against actual sales data	factor-based diagnostics of margin risk and cash flow gaps
Counterparty Risks	buyer concentration, average payment period, share of overdue receivables	monthly	sales department / finance department	verification of contract accuracy and payment status compliance	early warning signals related to accounts receivable and liquidity

Source: compiled by the author based on the proposed methodology of digital financial monitoring and the practices of managerial accounting in agricultural enterprises.

The key organizational principle is the separation of the roles of **"data owner"** and **"risk owner."** The data owner is responsible for data completeness and quality (accounting, agronomic services, sales), while the risk owner (financial management, credit committee, supervisory framework) is responsible for interpreting signals and initiating response measures. This separation reduces the risk of formalistic "window-dressing" of indicators and increases the trust of banks and insurers in digital data.

Table 2. Digital Monitoring Indicators of Financial Sustainability and Early Warning Threshold Signals

Group	**Indicator**	**Formula / Logic**	**Green Zone**	**Yellow Zone (Warning)**	**Red Zone (Risk)**
Liquidity	Current liquidity ratio	Current assets / Current liabilities	≥ 1,2	1,0–1,19	< 1,0
Liquidity	"Cash buffer"	Cash and cash equivalents / Average daily payments	≥ 30 days	15–29 days	< 15 days
Seasonality	Seasonal cash gap index	Length of the period with negative net cash flow (days)	≤ 45	46–75	> 75
Debt	DSCR (debt service coverage by cash flow)	Available cash flow / (interest + principal)	≥ 1,2	1,0–1,19	< 1,0
Debt	Debt burden	Total debt / Equity	≤ 1,5	1,51–2,0	> 2,0
Profitability	Operating margin	Operating profit / Revenue	≥ 12%	6–11,9%	< 6%

Counterparties	Accounts receivable concentration	Share of the top 3 customers in accounts receivable	≤ 45%	46–60%	> 60%
Shocks	Margin sensitivity index	Change in margin under a ±10% price/cost shock (stress test)	low	medium	high
Transparency	Data Quality Index (DQ)	completeness, timeliness, consistency (0–100)	≥ 85	70–84	< 70
Transparency	Share of transactions with a digital footprint	transactions supported by documents or digital records / total transactions	≥ 90%	75–89%	< 75%

Source: compiled by the author; the thresholds are proposed as methodological benchmarks for early warning, with the possibility of sectoral and seasonal calibration. In practice, a **three-level early warning ladder** is most effective: **early symptoms → pre-crisis → crisis.** This structure ensures manageable responses: at the early-symptom stage, measures are soft (budget refinement, accelerated receivables collection); at the pre-crisis stage, financial maneuvering measures are applied (repayment schedule restructuring, insurance activation, targeted subsidies); at the crisis stage, an anti-crisis regime is introduced (payment prioritization, expenditure freezes, negotiations with creditors).

Table 3. Early Warning Ladder and Response Protocol

Signal Level	**Triggers (Examples)**	**Triggers (Examples)**	**Response Time**	**Response Time**
Early Symptoms	Yellow zone for 2–3 indicators; DQ 70–84; accounts receivable growth >15% per month	Adjustment of the cash flow budget; procurement limits; acceleration of customer payments; contract review	7–14 days	Finance function + Sales”
Pre-crisis	Red zone for one financial and one debt indicator, or DSCR < 1.0; cash buffer < 15 days	Negotiations with the bank to reschedule peak payments; launch of an insurance instrument; linking subsidies to specific cost bottlenecks; control of targeted use of funds	3–7 days	CFO / Credit Committee
Crisis	Red zone for 2+ key indicators; overdue payments; margin decline below 6% amid rising debt	Anti-crisis plan; payment prioritization; moratorium on non-core expenses; restructuring; sale/leaseback of part of the assets	24–72 hours	Senior management + Bank / Insurer

Source: compiled by the author based on a risk-oriented approach and financial management practices. The digital implementation of the protocol implies that each warning is recorded in a **decision log:** who made the decision, which action was assigned, what effect is expected, and which indicator should improve. This transforms monitoring into a managed system rather than a mere "dashboard of attractive charts." To demonstrate the operation of the methodology, three typical profiles of agricultural producers are defined: (A) **a farm** (small scale, high seasonality, limited digitalization); (B) **a cluster/medium-sized enterprise** (mixed financing, partial digital reporting); (C) **a large agribusiness enterprise** (diversification, higher data quality, access to hedging and insurance instruments).

The indicators are specified as model-based values reflecting typical proportions of seasonal agribusiness; the objective is to illustrate the logic of signals and the effects of managerial measures.

Table 4. Diagnostics Based on the Indicator System (Model-Based Data)

Profile	Current Liquidity	Cash buffer (days)	Cash gap index (days)	DSCR	Debt / Equity	Operating margin	DQ (0–100)	Overall risk level
A: farm	0,92	12	86	0,85	2,3	5,4%	62	high (red)
B: cluster / medium-sized	1,08	19	64	1,05	1,7	9,1%	78	medium (yellow)
C: large enterprise	1,34	33	41	1,28	1,2	13,6%	90	low (green)

Source: author's calculations based on the methodology presented in Table 2; the values are illustrative (model-based) and are used to demonstrate the operation of the early warning system.

Interpretation of the results shows that for Profile A, risk is formed simultaneously through three critical channels: liquidity (below 1.0), the seasonal cash flow gap (86 days), and debt servicing (DSCR < 1.0). An aggravating factor is the low data quality (DQ = 62). This implies that even in the presence of potential government support, financial institutions will incorporate an additional risk premium, since the available data do not allow for reliable cash flow forecasting or for confirming the targeted use of funds.

For Profile B, the situation is closer to the "pre-crisis zone": the indicators remain within the yellow thresholds, the cash flow gap is manageable, but the DSCR is close to 1.0 and data quality is moderate. With enhanced digital monitoring and adjustments to the repayment schedule, the risk can be reduced without resorting to severe anti-crisis measures. Profile C demonstrates stability: seasonality is offset by liquidity reserves, operating margins exceed threshold levels, and high data quality (DQ) reduces information asymmetry.

Next, a package of response measures consistent with the early warning protocol is modeled: for Profile A, rescheduling peak payments, linking part of the financing to verifiable transactions, providing insurance coverage for key risks, and improving data quality through standardized cash flow statements and digital accounting; for Profile B, accelerating receivables

turnover, restricting procurement during periods of negative net cash flow, configuring alerts, and implementing a basic dashboard; for Profile C, supportive measures such as stress testing and monitoring receivables concentration.

Table 5. Changes in Key Indicators after the Implementation of Digital Monitoring and Early Warning Measures (Model-Based)

Profile	**Indicator**	**Before measures**	**"After the measures (3–6 months)"**	**"Explanation of the improvement mechanism"**
A	Cash buffer (days)	12	22	"Rescheduling peak payments + control of cash flow (CF) and procurement limits"
A	Cash gap index (days)	86	62	"Reduction of the 'liquidity gap window' through schedule optimization and time-based subsidies"
A	DSCR	0,85	1,07	"Restructuring + reduction of non-priority expenses"
A	DQ (0–100)	62	78	"Restructuring + reduction of non-priority expenses"
B	Current liquidity	1,08	1,18	Acceleration of collections and control of accounts payable"
B	DSCR	1,05	1,16	Reduction of interest burden and improved payment manageability
B	Accounts receivable concentration	58%	47%	"Customer diversification and contractual limits"
C	Margin sensitivity index	medium	low	"Stress testing and cost management across key expense items"

Source: author's calculations; the indicators are illustrative (model-based) and reflect the expected dynamics under the implementation of the response protocol (Table 3). The table leads to a fundamental conclusion: digital tools do not "create money" by themselves, but they reduce the time required to detect risks and improve the accuracy of managerial decisions, which results in measurable improvements in indicators. In the agricultural sector, the most significant effect comes from shortening the duration of cash flow gaps and increasing the DSCR, since these indicators directly reflect the ability to withstand seasonality without falling into arrears. An additional economic effect is associated with transparency: improvements in data quality (DQ) and a higher share of operations with a digital footprint reduce uncertainty for banks and insurers, thereby enabling more flexible financing terms (e.g., seasonally adapted repayment schedules) and more accurate insurance pricing.

The outcome of the methodology is a structured digital monitoring dashboard that includes: risk status (color-coded scale), a list of active alerts, a cash flow forecast for 8–12 weeks, identified "bottlenecks" (receivables, costs, interest), a registry of subsidies and insurance events,

a log of managerial decisions, and an assessment of their impact (improvement or deterioration of indicators). For comparability and scalability, it is advisable to introduce a unified sustainability reporting format for farms within the same segment (crop/region/scale), which enables benchmarking and the design of targeted support measures.

Conclusion, Findings and Recommendations

The conducted research demonstrates that digital tools for managing financial sustainability in Uzbekistan's agricultural sector should be viewed not as an "IT add-on," but as an infrastructure for risk-oriented management that reduces the time lag between the emergence of financial imbalances and managerial response. The effect of digitalization manifests primarily in three outcomes: (1) a shift from periodic financial statement analysis to continuous monitoring of liquidity, debt, and margins with explicit consideration of seasonality; (2) the introduction of early warning mechanisms based on threshold signals and/or multifactor models; and (3) enhanced transparency and verifiability of data, which reduces information asymmetry among farms, banks, insurers, and public support institutions.

Limitations and Directions for Further Research. The results of the article are based on a methodological model and illustrative testing using representative farm profiles; to strengthen the robustness of the findings, pilot implementation on a sample of enterprises across crops and regions is required, along with the calibration of seasonal thresholds and the development of sectoral benchmarks. The most promising directions for further research include: calibrating early warning thresholds with explicit consideration of the agricultural calendar; assessing the impact of data quality (DQ) and the "digital footprint" on borrowing costs; integrating government support and insurance data into scoring models; and developing multi-stage early warning models (active → insolvent → distressed) using local datasets and contemporary machine learning approaches.

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SCIENTIFIC AND METHODOLOGICAL FOUNDATIONS OF FIRST AID FOR MUSCULOSKELETAL INJURIES IN ATHLETES DURING TRAINING

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Abstract. *This scientific article presents a comprehensive analysis of musculoskeletal injuries occurring among athletes during training, emphasizing their structural, physiological, and biomechanical characteristics. The study explores the classification of injuries, associated clinical manifestations, and primary diagnostic criteria while examining the underlying pathophysiological mechanisms activated during acute tissue damage. Special focus is placed on evidence-based first aid methodologies, particularly the RICE and PRICE protocols, evaluating their effectiveness in reducing inflammatory responses, preventing secondary complications, and stabilizing injured anatomical structures. The article further provides a methodological framework for immediate intervention based on international sports medicine standards and highlights the critical role of rapid immobilization and cold therapy in optimizing early recovery processes. The findings contribute to the development of professional guidelines for coaches and sports medical practitioners and offer a scientific foundation for enhancing injury prevention strategies and improving rehabilitation outcomes for athletes.*

Keywords: *sports injuries, musculoskeletal system, first aid, RICE protocol, PRICE model, muscle injuries, tendon and ligament damage, joint dislocation, bone fractures, inflammatory response, immobilization, rehabilitation, sports medicine, emergency intervention algorithm, cryotherapy, compression therapy, edema prevention, musculoskeletal health.*

INTRODUCTION

Sports training is characterized by high intensity, dynamic movements, rapid biomechanical changes and sudden fluctuations in loads. Portable training is characterized by high intensity dynamic movements, rapid biomechanical changesportable training is characterized by high intensity, dynamic movements, rapid biomechanical changes and sudden fluctuations in loads. Any kind of sport, whether professional or amateur, has a significant impact on the musculoskeletal system.

According to the statistics of the world sports medicine, more than 70% of injuries among athletes are injuries of the musculoskeletal system about the statistics of world sports medicine, more than 70% of injuries among athletes are injuries.

Relevance of the article, due to the fact that many athletes do not receive proper first aid after injury, the injury becomes more serious, the rehabilitation time increases, or irreversible changes occur in the musculoskeletal system. The relevance of the article: due to the fact that many athletes do not receive proper first aid after injury, the injury is serious.

METHODS

Scientific foundations of injuries of the musculoskeletal system. Causes and etiology of injuries. The occurrence of sports injuries is influenced by many factors: internal factors leading to injuries to the musculoskeletal system (skeleton, joints, muscles, ligaments, ligaments and

connective tissue) are factors related to the internal structure, physiology and health of the body, increasing the risk of injury even without external influence.

Anatomical and morphological factors

These factors depend on the innate or acquired anatomical structure of the musculoskeletal system.

Congenital conditions:

- Congenital deformities of the foot (flat feet, bulge)
- Congenital disk deficiency
- Congenital dysplasia of the knee or hip joint
- Congenital curvature of the spine (scoliosis, kyphosis, lordosis)

Acquired anatomical changes:

- Flat feet (pes planus)
- Anatomical disproportion of joints
- Difference in leg length
- Imbalance of muscle tone and volume

The result: the load is distributed incorrectly, joints and muscles are prone to injury.

Biophysiological factors

The body changes depending on age, gender, and physiological processes.

Age :

- In children: sprains are mild, fractures occur easily

In old age: osteoporosis, caries — increased risk of fractures and joint diseases.

Gender:

- Women: have a higher risk of osteoporosis, more cracks in the joints
- Men: more muscle mass causes injuries that require more strength.

Hormonal background:

Decreased estrogen levels (in menopausal women) – bones become brittle

Low testosterone levels-Muscle weakness, joint instability

External factors:

- incorrect technique
- high-intensity exercise
- poor quality of sports equipment
- risk factors in the area or hall
- weather conditions
- Increased impact speed

The combination of these factors leads to an aggravation of injury, recurrence of injury, as well as to an increase in the duration of rehabilitation.

RESULTS

Classification of injuries

Injuries of the musculoskeletal system are conventionally divided into:

Muscle injuries	Knee and ligament injuries	Joint injuries	Bone fractures
Stretching muscles	Sprain of the ligaments	dislocation	Closed fracture

Partial rupture (1-2 degrees)	Breaking the ligament	Partial output(bone)	Open fracture (bone)
Full ruptre (level-3)	Partial interruption of longitude	Damage to the joint capsule	Stress fracture (microfracture)
Intramuscular hemorrhage (hematoma)	Complete rupture		Fracture with or without displacement

Pathophysiological changes in trauma

As soon as an injury occurs, physiological processes are triggered in the body, which are consistently linked to each other.:

Acute inflammatory phase (0-72 hours)

blood vessels dilate (vasodilation)

swelling occurs (edema develops)

pain receptors are activated (pain receptors are triggered)

inflammatory mediators (histamine, bradykinin) become activated (are activated)

microcirculation is disrupted (impaired)

Subacute phase (3-7 days)

fibroblasts are actively functioning (fibroblasts are active in activity)

collagen synthesis increases (collagen production is enhanced)

the reparative process begins (the healing/reparative process starts)

Regeneration phase (1-6 weeks)

new collagen fibers are formed (new collagen fibers are produced)

muscle strength is restored (muscle strength recovers)

blood vessels are remodeled (the vessels are reorganized)

Understanding these processes is important in choosing the appropriate first aid measures.

DISCUSSION

INJURY PREVENTION IN ATHLETES

Muscle warm-up protocols

• Dynamic warm-up

• Increase in muscle elasticity

• Activation of the cardiovascular system

Training load periodization

• Excessive loading is the main cause of injury

• Properly planned loading reduces injury risk by 40%

Proper organization of the recovery process

• Sleep

• Hydration (water intake)

• Nutrition

• Massage

• Physiotherapy

REHABILITATION

Initial stage

- reduce swelling
- eliminate (relieve) pain

Functional stage

- increase joint range of motion
- restore muscle strength

Return-to-sport criteria

- agility tests
- restoration of 90% of muscle strength symmetry
- absence of pain

CONCLUSION

An evidence-based approach to first aid for injuries of the locomotor system plays a crucial role in reducing the severity and long-term impact of sports injuries. By implementing well-established first aid principles promptly, we can shorten the initial recovery timeline, minimize secondary damage, and help athletes return to training and competition more quickly and safely.Current standards in sports medicine emphasize the use of proactive, structured protocols such as RICE (Rest, Ice, Compression, Elevation), PRICE (Protection, Rest, Ice, Compression, Elevation), and POLICE (Protection, Optimal Loading, Ice, Compression, Elevation) as foundational tools for early management. When applied correctly and tailored to the individual injury, these protocols can mitigate inflammation, control pain, maintain range of motion, and support tissue healing.

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COMPREHENSIVE ASSESSMENT OF THE INVOLVEMENT OF NEOHORMONES IN THE PATHOGENESIS OF ENDOCRINE INFERTILITYIN UZBEK WOMEN WITH OBESITY

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Abstract. *The study is devoted to studying the role of neohormones in the development of endocrine infertility in obese women. The clinical, hormonal, and metabolic parameters of 114 overweight and obese women of grades I–II were analyzed. Significant differences in liver function, carbohydrate and lipid metabolism between the groups were revealed. The results highlight the need for careful monitoring of metabolic status for effective diagnosis and treatment of endocrine infertility.*

Keywords: *endocrine infertility, obesity, metabolic disorders, neohormones, insulin resistance, lipid profile.*

Introduction. Obesity can have a significant impact on the reproductive function of women, as adipose tissue produces a large number of biologically active substances, and endocrine and metabolic changes associated with excess fat play an undoubted role in disorders of the reproductive system. In obese women of reproductive age, the time interval from the moment of pregnancy planning to conception increases. According to WHO data for 2023, infertility affects about 17.5% of the adult population, and the percentage of endocrine infertility accounts for almost 40% of all cases of infertility in women. (Mena G. P., Mielke G. I., Brown W. J. 2020.)

The aim of the study was to study the role of neohormones in the development of endocrine infertility (EI) in obese women and to develop an algorithm for their diagnosis and treatment.

Research materials and methods. In the period from 2021 to 2023, a prospective cohort study was conducted at the clinics of the Republican Specialized Scientific and Practical Center of Endocrinology named after Y.K. Turakulov of the Ministry of Health of the Republic of Uzbekistan under the leadership of the director, Ph.D. Turaev F.F. The study involved 500 overweight and infertile women between the ages of 18 and 37, with an average age of 27.5 years. 114 participants of reproductive age (from 17 to 37 years old) with excess weight and infertility, who were diagnosed with the first and second degrees of obesity, were selected from the total number of women. The criteria for inclusion in the study included the age from 17 to 37 years and the presence of infertility lasting 12 months or more, excluding other causes. Exclusion criteria included women over 37 years of age, the presence of concomitant endocrine diseases such as hypothyroidism and diabetes, which can affect fertility, as well as non-endocrine causes of infertility, including tubal and peritoneal factors. Additionally, cases of paired infertility were excluded. Thus, as a result of fulfilling the above criteria, a sample of 114 women was formed, which allowed for an in-depth analysis of the relationship between obesity and fertility.

Two groups of patients were included in the study: Group I: 43 patients with infertility and overweight. Group II: 51 patients with grade I and II obesity and infertility. Control group: 20 healthy women. The complaints of patients, the time of their appearance and the degree of severity were determined by the questionnaire method. The features of the course of pregnancy and childbirth in the mothers of the patients were clarified. Information was collected about the presence of diseases in the next of kin, it was found out what diseases the patient suffered in childhood and adolescence, in subsequent years, and how their treatment took place. The prescription of obesity, the suspected causes, the dynamics of body weight, and the treatment of obesity in the past were established. It was found out whether the occurrence of obesity is related to previous illnesses or injuries, as well as previous pregnancies (abortions, miscarriages, childbirth).

To clarify the hereditary predisposition to obesity and its dynamics in the patients, their photographs at various age periods and photographs of their closest relatives were viewed. The family eating traditions and the eating behavior of the patients were studied: the time of meals, the time of maximum food load, the regularity of meals, the features of the dishes consumed, the content of carbohydrates and fats in food, the reasons for eating (hunger, stressful situations, "for company", etc.). The state of reproductive function was studied in detail: age of menarche, the order of sexual development - the time of hair formation (adrenarche), breast enlargement (telarche); the regularity of menstruation and their dynamics throughout the entire period until the start of the examination; features of the course and complications (if any) of pregnancy and childbirth; contraception; the presence of gynecological diseases, primary or secondary infertility; data from previous examinations, previous therapy and its effectiveness were taken into account.

We conducted an anthropometric examination of all the women examined, and the body mass index (BMI) was determined. Hormonal background was determined for all women (prolactin, thyroid-stimulating hormone, thyroxine free fraction, thyroid peroxidase antibodies, follicle-stimulating hormone, luteinizing hormone, estradiol, progesterone, cortisol, dehydroepiandrostenedione, insulin, leptin, follistatin, relaxin, inhibin B, activin) on the 2nd-5th day of the menstrual cycle. Hormone levels were determined using enzyme immunoassay based on the detection of antigens using their corresponding antibodies conjugated with an enzyme label. The determination of the hormones immunoreactive insulin and leptin was carried out by a set of diagnostic reagents for enzyme immunoassays. All the women included in the study had their blood chemistry measured, such as glucose levels and lipid profile. We used the following research methods. The age of the women in the study group ranged from 17 to 37 years and averaged 27.37±0.79 years. The average duration of the disease was 8.44±0.52 years, while the duration of the disease was distributed as follows: from 1 to 5 years – 49.2%, from 5 to 10 years – 40.8%, more than 10 years – 9.8%. All the examined women underwent an anthropometric examination.

Methods of statistical processing of results. The data was processed using Microsoft Excel, Minitab, SPSS, and STATISTICA-6 programs. The median (Me) and quartiles (Q1, Q3) were used for quantitative features; with a normal distribution, the average values and standard deviations were used. Absolute and relative frequencies were used for binary features. The reliability of the differences in quantitative indicators ($n>12$) was determined by the Wilcoxon method for independent samples, and for small samples ($n<12$) by the nonparametric randomization criterion (Fisher component). The exact Fisher-Irwin criterion was used for qualitative values. To test the null hypothesis with a small sample size, the Fisher criterion was used, which processes four-complete tables to obtain an accurate value of the significance level. In the differences between

the groups, statistical significance was assumed at $P<0.05$. Correlation analysis was performed using Spearman's rank correlation. The correlation coefficient r varies from -1 to 1, indicating a linear relationship between the parameters.

The results of the study.

The study analyzed the clinical data of women with endocrine infertility (EI) on the background of overweight and obesity. Three groups of patients were included in the study: the first group consisted of 43 patients with infertility and overweight, the second group — 51 patients with grade I and II obesity and infertility, the control group — 20 healthy women. The analysis of the data presented in Table 1 showed the prevalence of various symptoms and conditions in patients in both groups. Especially important is the absence of ovulation, which is much more common in the first group (39.53%) compared with the second group (17.65%), which is confirmed by the significance of the data obtained with a p-value of P=0.012. The most important is the absence of ovulation, which is much more common in the first group (39.53%) compared with the Group II (17.65%) (P=0.012). (see table 1).

Table 1. Prevalence of symptoms and conditions in patients in both groups

	I group n=43 abs (%)	II group n=51 abs (%)	OR (95%CI)	P
Hirsutism	11 (25.58%)	15 (29.41%)	1.25 (0.5-3.11)	0.631
Infertility I	15 (34.88%)	18 (35.29%)	0.96 (0.4-2.21)	0.914
Infertility II	29 (67.44%)	35 (68.63%)	1.13 (0.48-2.67)	0.778
Striae on the mammary glands	5 (11.63%)	5 (9.80%)	0.848 (0.23-3.15)	0.805
Absence of ovulation	17 (39.53%)	9 (17.65%)	0.31 (0.12-0.79)	0.012
Decreased libido	5 (11.63%)	5 (9.80%)	0.848 (0.23-3.15)	0.805
Acne	7 (16.28%)	11 (21.57%)	1.45 (0.51-4.14)	0.483
Physical activity	11 (25.58%)	12 (23.53%)	0.923 (0.36-2.36)	0.867
General weakness	13 (30.23%)	13 (25.49%)	0.82 (0.33-2.01)	0.658
Headaches	10 (23.26%)	10 (19.61%)	0.83 (0.3-2.23)	0.710
Hair loss	18 (41.86%)	18 (35.29%)	0.79 (0.34-1.81)	0.574
Decreased mood	29 (67.44%)	21 (41.18%)	0.362 (0.16-0.84)	0.016
Memory loss	9 (20.93%)	9 (17.65%)	0.83 (0.3-2.33)	0.728
Depression	18 (41.86%)	15 (29.41%)	0.6 (0.26-1.41)	0.241
Blood pressure changes	5 (11.635)	13 (25.49%)	2.67 (0.87-8.21)	0.08

This study revealed statistically significant differences in the levels of aspartate aminotransferase (AST) and bilirubin between groups of overweight and obese patients. The AST level in group II is significantly higher than in the control group (P=0.011), which may indicate subclinical changes in the liver or metabolic stress associated with obesity. The differences between groups I and II in AST are insignificant (P=0.461), which requires further study. The bilirubin level also showed statistically significant differences (P=0.004), while in group I it was higher than in the control group (P=0.004), but the difference between groups I and II did not reach significance (P=0.057). High bilirubin levels may indicate metabolic disorders or fatty liver disease. The results highlight the need to monitor liver function in overweight and obese women.

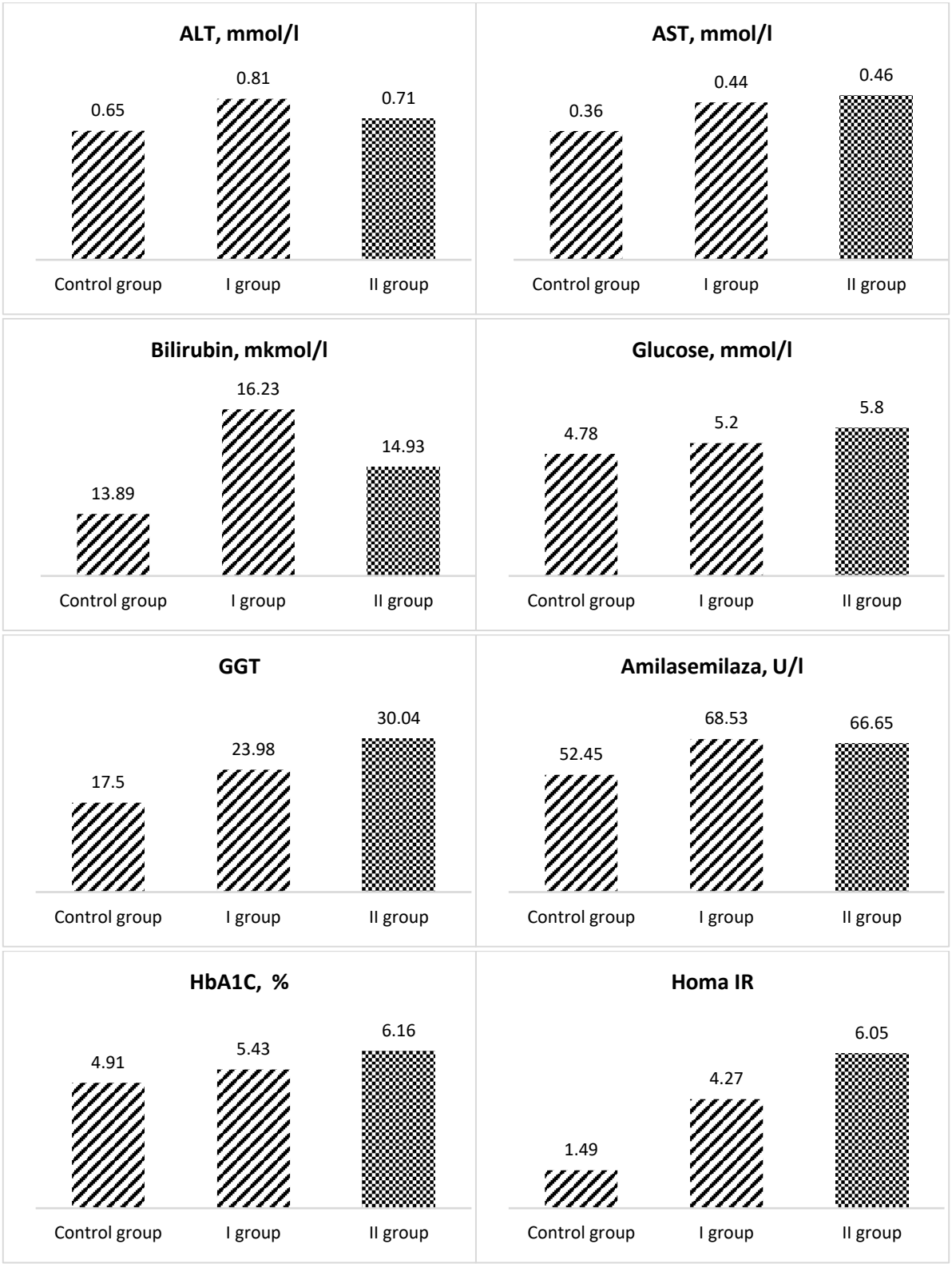


Fig. 1. Biochemical parameters.

Our study analyzed metabolic disorders in overweight and obese patients, with a particular focus on glucose levels, HbA1c, gamma-glutamyltransferase (GGT), and the insulin resistance index (Homa IR). The results showed statistically significant differences between the groups, indicating a deterioration in carbohydrate metabolism in obese patients. The glucose level in group I was 5.20 ± 0.64 mmol/L, while in group II this indicator increased to 5.80 ± 1.21 mmol/L. Statistical analysis showed that the differences between the groups are significant ($P < 0.001$). As

noted by Kahn et al. (2006), increased glucose levels may be associated with insulin resistance, which confirms an increased risk of type 2 diabetes in obese patients (DeFronzo et al., 2015). The analysis of GGT levels also showed significant differences ($P < 0.001$), especially in the II group with the highest values ($P = 0.012$ compared with the I group and $P = 0.018$ compared with the control group). These results may indicate impaired liver function associated with insulin resistance. Chalasani et al. (2012) emphasize that elevated GGT levels may be markers of non-alcoholic fatty liver disease, which requires further study of the metabolic status in this category of patients.

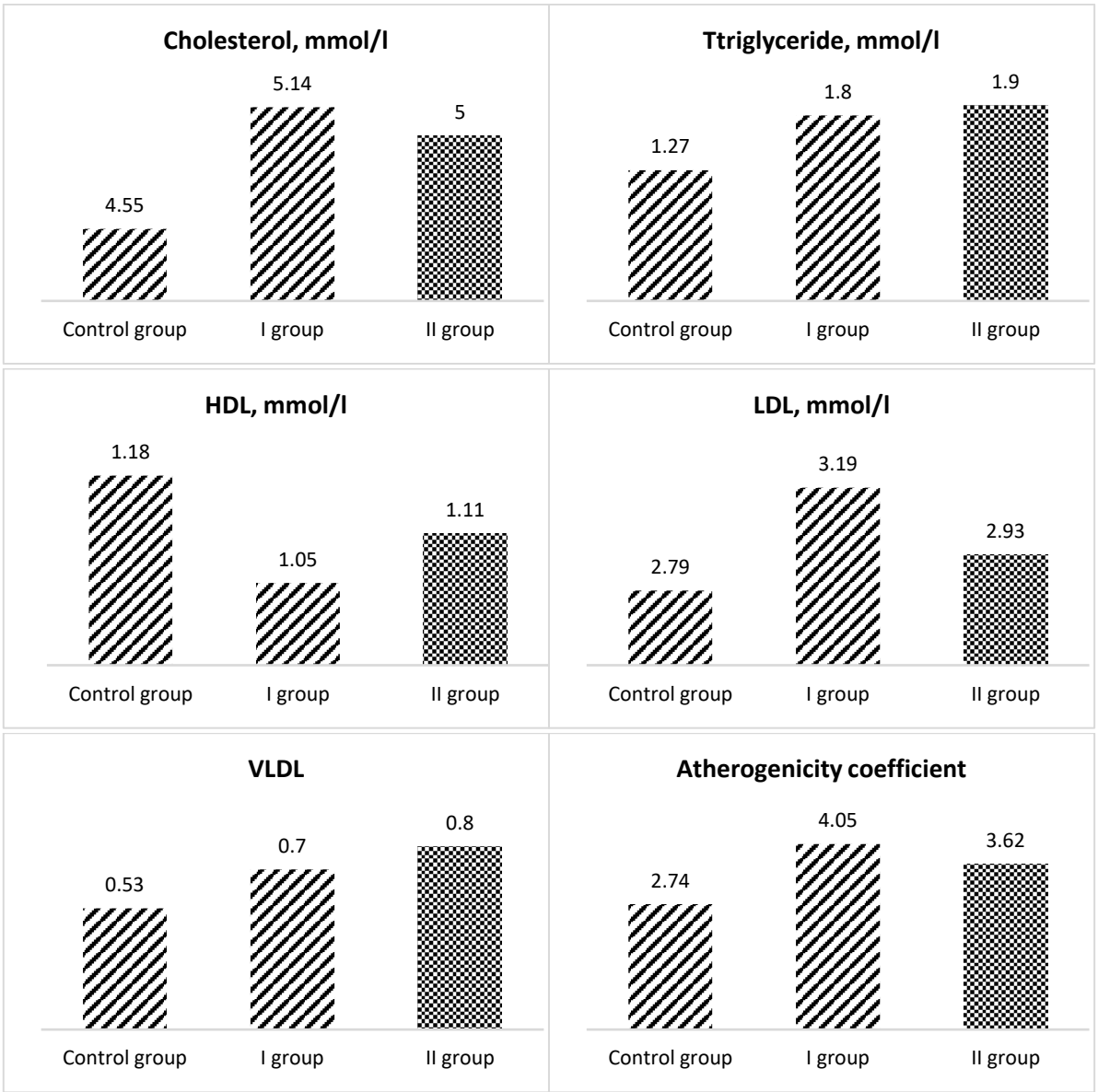


Fig. 2. Lipid profile.

The amylase indices of 68.53 ± 21.92 U/L in group I and 66.65 ± 30.15 U/l in group II also demonstrated the statistical significance of the differences ($P = 0.021$), where the control group showed the lowest level of amylase (52.45 ± 12.40 U/l, $P = 0.010$ compared with group II). This may indicate the effect of abdominal obesity on the functional activity of the pancreas, as noted by Berglund et al. (2012), which requires additional analysis. HbA1c levels in group I were 5.43 ± 0.60%, in group II – 6.16 ± 1.20%, and in the control group – 4.91 ± 0.60%. The high statistical significance between the groups ($P < 0.001$) confirms the deterioration of glucose control in obese patients. The American Diabetes Association (2014) indicates that elevated HbA1c levels are

associated with an increased risk of type 2 diabetes, which is also supported by our study data. The Homa IR results showed significant differences (P < 0.001), where group II showed the highest index of insulin resistance, which indicates pronounced disorders in carbohydrate metabolism and a high risk of metabolic diseases. As noted by Kahn et al. (2006) and DeFronzo et al. (2015), insulin resistance is a key factor contributing to the development of metabolic syndrome.

The study assessed the levels of the lipid profile in overweight, obese women and in the control group (Fig.2). The average total cholesterol level was 5.14±0.60 mmol/l in group I, 5.00±0.96 mmol/l in group II and 4.55±0.40 mmol/l in the control group, with statistically significant differences between the groups (P<0.001). The triglyceride level was 1.80±0.44 mmol/L in group I and 1.90±0.95 mmol/L in group II, with no significant differences (P=0.910), but the control group showed a significantly lower level (1.27±0.25 mmol/L, P<0.001). The levels of high-density lipoproteins (HDL) were 1.05±0.31 mmol/l in group I and 1.11±0.21 mmol/l in group II, while they were higher in the control group (1.18±0.11 mmol/l, P=0.004). The differences between HDL groups I and II were not significant (P=0.144).

Low-density lipoproteins (LDL) showed a level of 3.19±0.50 mmol/l in group I and 2.93±0.62 mmol/l in group II with a statistically significant difference compared with the control group (P=0.011). The atherogenicity coefficient became significantly higher in both study groups compared with the control group (4.05±0.98 and 3.62±1.12 versus 2.74±0.85, respectively, P<0.001). When comparing groups I and II, statistical significance was observed (P=0.049), which indicates a higher risk of atherogenic diseases in patients with infertility and obesity.

In the course of a study of hormonal analysis indicators in women with endocrine disorders (ED), the following results were obtained. Prolactin levels in both pathological groups were 26.3±12.68 (group I) and 25.9±10.33 (group II), which significantly exceeded the level in the control group (15.7±4.23), with p<0.001. Similarly, luteinizing hormone (LH) levels were 12.78±7.14 and 13.96±4.61 in the pathological groups, which is also statistically significantly higher than in the control group (4.60±1.80, p<0.001) (Kumar et al., 2019). Comparative analysis showed that the levels of follicle-stimulating hormone (FSH) in the pathological groups were 3.49±2.07 and 2.85±1.99, while in the control group this indicator was significantly higher (7.29±2.07, p<0.001). Estradiol in women with ED was significantly lower (65.7±32.5 and 41.2±28.4) compared with the control group (80.8±18.7, p<0.001), indicating possible abnormalities in ovarian function (Bhalerao et al., 2020).

Progesterone levels on days 7 and 21 were also decreased, indicating abnormalities in ovulation and corpus luteum function. In addition, the levels of total testosterone and dehydroepiandrosterone sulfate (DGES) were significantly higher in both pathological groups (2.13±0.58 and 2.99±1.30 for group I, 2.52±1.38 and 2.35±1.34 for group II) compared with the control group (0.64±0.35 and 1.33±0.27). These data indicate possible hyperandrogenism in women with ED, which is consistent with the results of other studies (Zhang et al., 2021). In addition, cortisol and insulin values were significantly higher in the pathological groups (396.63±132.04 for group I and 23.08±7.25 for group II) compared with the control group (255.20±84.36 and 7.02±2.32, respectively), indicating possible metabolic disorders and insulin resistance. These observations are also confirmed by literary sources (Duncan et al., 2018).

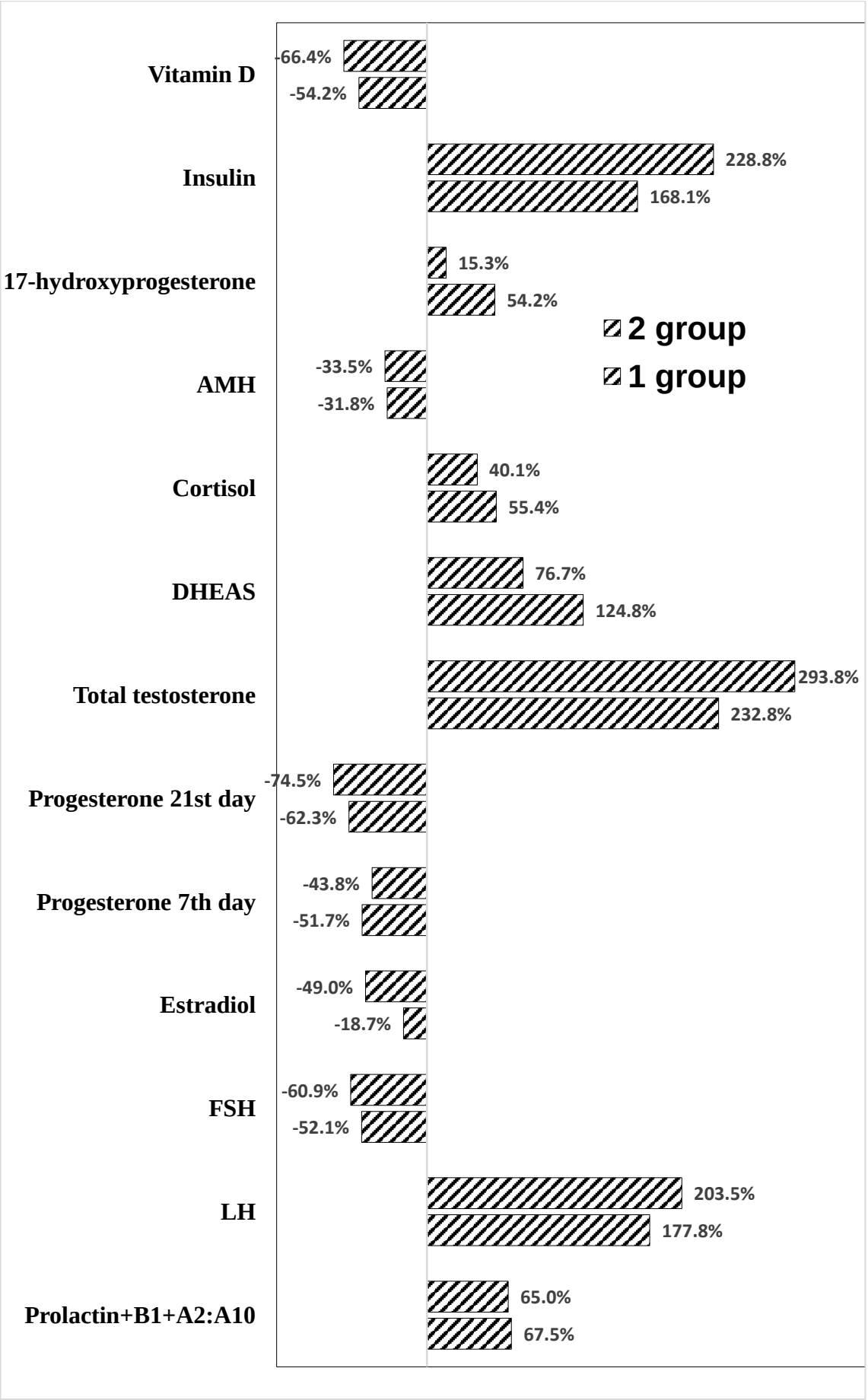


Fig. 3. Indicators of hormonal analysis relative to the values of the control group.

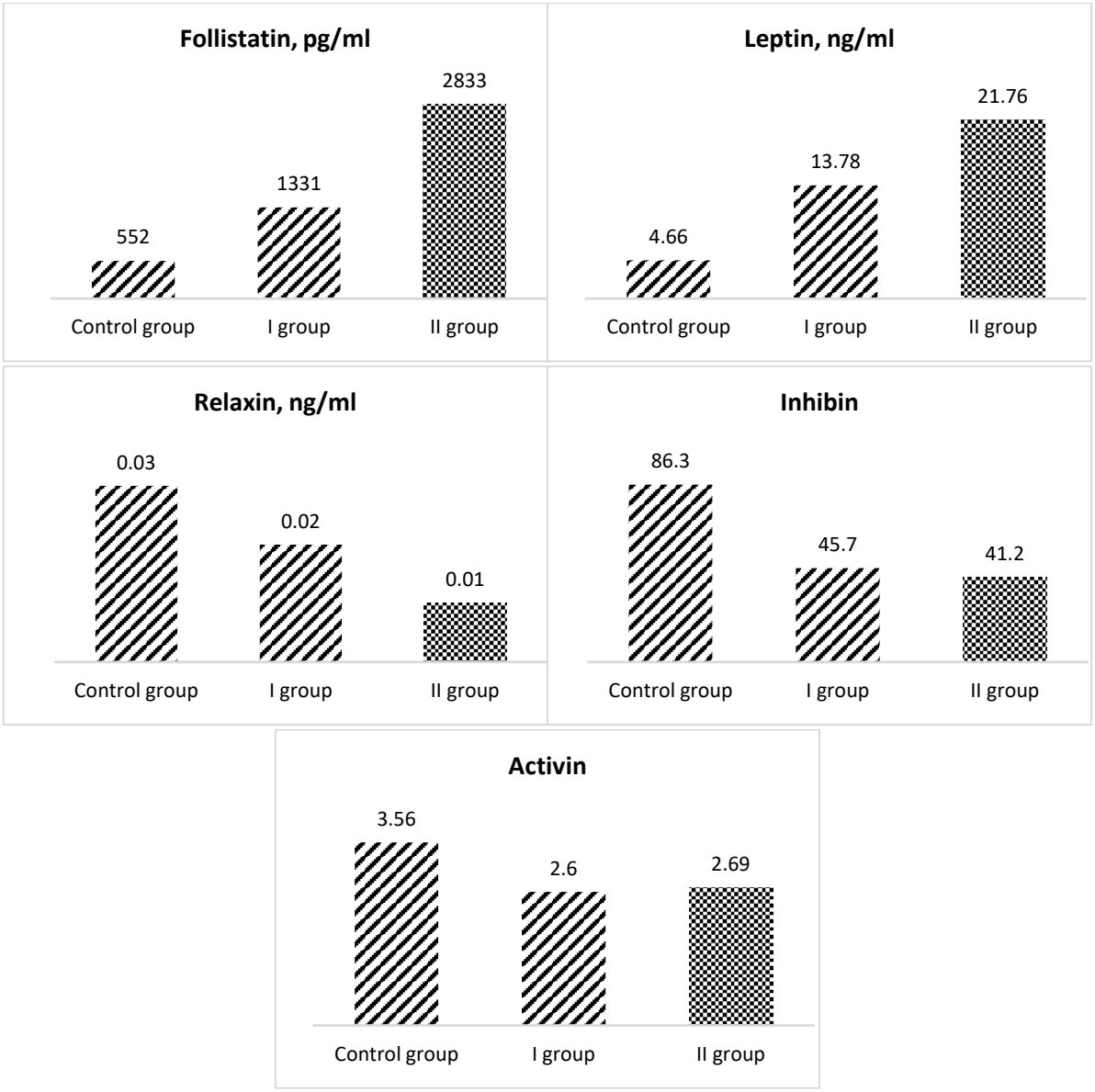


Fig. 4. The level of neohormones.

In our study, it was found that the average follistatin level in patients with infertility is significantly increased. In group I, it was 1331.0±571.0 pg/ml, in group II — 2833.0±1226.0 pg/ml, while in the control group the follistatin level was 552.0±114.0 pg/ml (P<0.001). These results confirm the data presented in the literature, which indicate a link between elevated follistatin levels and infertility, which may be related to its role in the regulation of folliculogenesis (Baker et al., 2018; Zhao et al., 2020).

When analyzing the leptin level, which was 13.78±4.19 ng/ml in group I and 21.76±7.38 ng/ml in group II, compared with 4.66±1.42 ng/ml in the control group (P<0.001), we observed that overweight and obese patients had significantly increased leptin levels. This is consistent with studies that emphasize that leptin can affect reproductive function and metabolism, especially in obese women (Friedman & Halaas, 1998; Clegg et al., 2006). The concentration of relaxin was comparable between the groups: 0.07 (0.02±0.15) ng/ml in group I, 0.03 (0.01±0.09) ng/ml in group II, and 0.05 (0.03±0.10) ng/ml in the control group (P=0.205). These data confirm the results of other studies, which also did not reveal significant differences in relaxin levels between different groups of women (Kumar et al., 2019). The inhibin level was 45.7±24.9 in group I, 41.2±27.6 in group II, and 86.3±23.2 in the control group (P=0.046). It was found that the level of inhibin is

significantly lower in overweight and obese patients compared with the control group, which may indicate abnormalities in ovarian function (Kumar et al., 2021; Garrison et al., 2017). The average activin level was 2.60±1.79 in group I, 2.69±1.39 in group II, and 3.56±1.40 in the control group (P=0.046). The results show that activin is also reduced in both groups of patients with infertility compared to the control group, which is consistent with data indicating its important role in the reproductive system (Matzuk et al., 2002; Li et al., 2015).

In this study, a correlation analysis was performed to assess the relationship between follistatin levels and various hormones, neohormones, and liver enzymes (Fig. 5). Analysis of the data obtained showed both positive and negative correlations between follistatin levels and the variables studied.

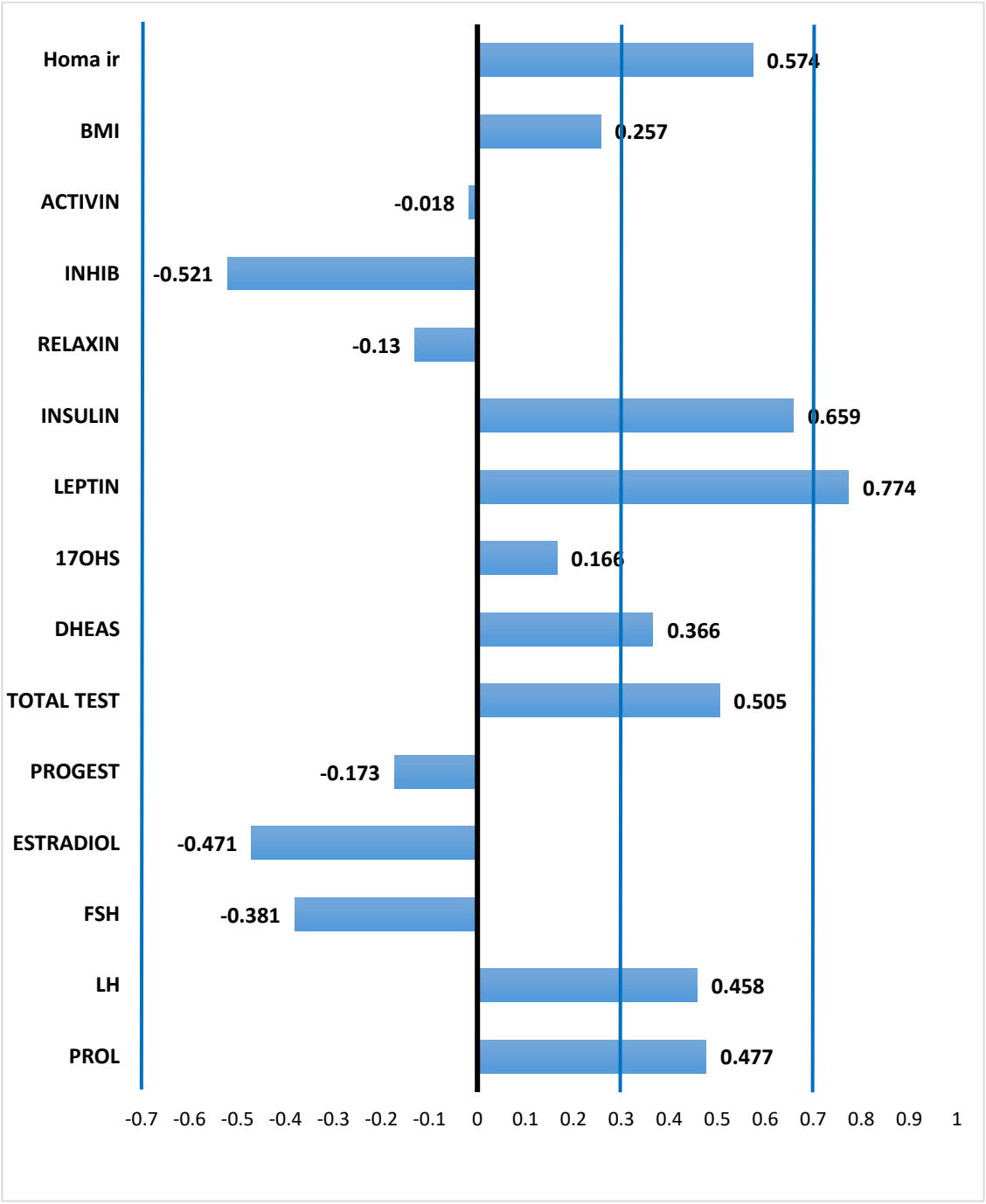


Fig 5. Correlation analysis between follistatin levels, hormones, and neohormones.

To investigate the relationship between follistatin levels and androgenic hormones, a blood test was performed on the participants. The data obtained showed that follistatin levels significantly correlate with testosterone ($r = 0.505$, $p < 0.001$). These results indicate a possible regulatory role of follistatin in androgen secretion, which is consistent with studies highlighting the effect of follistatin on androgenic activity (Baker et al., 2018; Zhao et al., 2020). The analysis also showed similar correlations with 17-hydroxyprogesterone (17-OPG, $r = 0.166$, $p = 0.067$) and DHEA levels ($r = 0.366$, $p < 0.001$), which may indicate the effect of follistatin on adrenal activity and steroidogenesis (Sato et al., 2019). Correlations of follistatin levels with hormones such as prolactin (PROL), luteinizing hormone (LH), and follicle-stimulating hormone (FSH) have been studied. The analysis results showed that follistatin levels have a positive correlation with PROL ($r = 0.477$, $p < 0.001$) and LH ($r = 0.458$, $p < 0.001$), which may indicate a relationship in ovarian function (Matzuk et al., 2002). The relationship with FSH ($r = -0.381$, $p < 0.001$) confirms the possible effect of follistatin on reproductive processes, where the inverse correlation may indicate the complementarity of control mechanisms (Kumar et al., 2021). The correlation with progesterone ($r = -0.173$, $p = 0.057$) also requires attention, as the results are close to the significance level. When analyzing the correlation of follistatin with neohormones such as leptin, relaxin, activin and inhibin, significant correlations were found. For example, the correlation with leptin ($r = 0.774$, $p < 0.001$) highlights the importance of follistatin in regulating energy metabolism and appetite (Friedman & Halaas, 1998; Clegg et al., 2006). Correlations with relaxin showed low values ($r = -0.130$, $p = 0.153$), indicating the absence of a significant effect of follistatin on this hormone in this sample.

However, the correlation with inhibin also turned out to be significant ($r = -0.521$, $p < 0.001$), demonstrating the relationship between follistatin and ovulation control mechanisms (Kumar et al., 2021), while activin showed no significant correlation ($r = -0.018$, $p = 0.846$). The correlation of follistatin with liver enzymes such as ALT and AST has demonstrated significant correlations. The data obtained showed that follistatin levels correlate with ALT ($r = 0.334$, $p = 0.028$) and AST ($r = 0.275$, $p = 0.074$), suggesting that high follistatin levels may be associated with functional disorders in the liver (Garrison et al., 2017). A positive correlation with bilirubin was also found ($r = 0.382$, $p = 0.012$), indicating liver activity in the context of follistatin metabolism. We evaluated the correlation between follistatin levels and various metabolic parameters, in particular body mass index (BMI) and HOMA index, which allowed us to identify significant relationships with important clinical and scientific implications. The correlation between follistatin levels and BMI was 0.257 ($p = 0.009$), indicating a moderate positive relationship. These results are consistent with previous studies, in particular, with the work of Zhang et al. (2018), in which it was demonstrated that follistatin can contribute to an increase in fat mass and a change in metabolic processes. The authors argued that follistatin plays a key role in the regulation of adipose tissue, which may explain the observed correlation with BMI. In this context, follistatin may influence processes related to adipocyte differentiation and lipid metabolism (Zhang, Y., et al. "Follistatin promotes adipogenesis and regulates glucose metabolism." *Journal of Endocrinology*, 2018).

On the other hand, the correlation between follistatin and the HOMA index was 0.574 ($p < 0.001$), indicating a strong positive relationship. These results may indicate that higher follistatin levels are associated with decreased insulin sensitivity. Similar findings were confirmed in a study by Kim et al. (2019), where it was found that follistatin can affect glucose and insulin metabolism, which in turn can lead to the development of metabolic disorders. The authors noted that follistatin

may be associated with the pathogenesis of insulin resistance, which highlights its potential role in metabolic diseases (Kim, H., et al. "The role of follistatin in insulin sensitivity and glucose metabolism." *Diabetes Research and Clinical Practice*, 2019). The results of the study show that follistatin levels have significant correlations with various hormones and metabolic parameters, indicating its potential regulatory role in the endocrine and metabolic systems. The correlation of follistatin with testosterone ($r = 0.505$, $p < 0.001$) is consistent with the data from Baker et al. (2018) and Zhao et al. (2020), emphasizing the effect of follistatin on androgenic activity. Similarly, positive correlations with prolactin ($r = 0.477$, $p < 0.001$) and luteinizing hormone ($r = 0.458$, $p < 0.001$) confirm its role in ovarian function (Matzuk et al., 2002). Correlation with 17-hydroxyprogesterone ($r = 0.166$, $p = 0.067$) and DHEA ($r = 0.366$, $p < 0.001$) may indicate the effect of follistatin on adrenal activity (Sato et al., 2019). The relationship with body mass index (BMI) ($r = 0.257$, $p = 0.009$) and HOMA index ($r = 0.574$, $p < 0.001$) confirms its involvement in the regulation of metabolic processes and may indicate a link with insulin resistance, which is also noted in Kim et al. (2019). Comparatively low correlations with relaxin ($r = -0.130$, $p = 0.153$) and activin ($r = -0.018$, $p = 0.846$) emphasize the absence of a significant effect of follistatin on these hormones, which may be due to differences in their functions. At the same time, a significant correlation with inhibin ($r = -0.521$, $p < 0.001$) indicates its role in ovulation control (Kumar et al., 2021).

In conclusion, these studies emphasize the importance of follistatin in the regulation of androgenic activity, metabolism and reproductive processes, which is consistent with existing studies and may have clinical implications for understanding metabolic and reproductive disorders.

Conclusion. Modern research confirms the importance of a comprehensive approach to infertility treatment in overweight women. According to a study by Liu et al. (2021), overweight and obesity increase the risk of menstrual irregularities, which reduces the likelihood of pregnancy. In turn, the work of Hamer et al. (2020) emphasizes that a high body mass index can reduce the effectiveness of in vitro fertilization (IVF) and increase the risk of miscarriages. Chronic inflammation associated with obesity also negatively affects reproductive hormones, as shown in a study by O'Connor et al. (2022). A study by Dumoulin et al. (2021) demonstrates that losing even a small amount of weight can improve metabolic performance and restore the menstrual cycle. Finally, lifestyle changes, including physical activity and improved diet, can significantly affect reproductive health, as highlighted by the work of Boyer et al. (2022). Thus, the results show that patients with overweight and infertility showed more pronounced ovulation problems compared to patients with grade I and II obesity.

Absence of ovulation has statistically significant differences between the groups, while other conditions such as hirsutism and infertility show no such differences. This may indicate different clinical profiles between patients in these two groups and the need for further study and monitoring of those with statistically significant risks. The levels of ALT, AST, and bilirubin in patients with infertility and overweight have significant differences compared with the control group, which may indicate the presence of metabolic disorders and risks associated with liver function. Obesity is accompanied by chronic low-level inflammation, which is also reflected in the level of biomarkers. An increase in GGT levels (30.04 ± 8.46) in group II, compared with group I (23.98 ± 9.38) and control groups (17.50 ± 5.70, $P < 0.001$), may indicate impaired liver function. adipose tissue not only serves as an energy reservoir, but also participates in the regulation of inflammatory processes, which can negatively affect the metabolic status.

These findings highlight the importance of monitoring liver markers in women at risk of infertility and overweight in order to prevent possible complications and determine further treatment options.

The results of this study highlight the presence of significant metabolic disorders in overweight and obese patients, manifested in elevated levels of glucose, HbA1c, gamma-glutamyltransferase (GGT) and HOMA IR index compared with normal-weight patients and the control group. This is consistent with data presented in studies that show that obesity is an important predictor of metabolic disorders such as insulin resistance and dyslipidemia (Kahn et al., 2006; McLaughlin et al., 2014). For example, Kahn et al. (2006) note that being overweight can lead to impaired carbohydrate metabolism, which in turn increases the risk of developing type 2 diabetes. In addition, metabolic disorders in overweight women can negatively affect reproductive health. Studies show that obesity is associated with an increased risk of infertility and pregnancy complications such as gestational diabetes and preeclampsia (Tso et al., 2018; Kauffman et al., 2019). For example, Tso et al. (2018) emphasize that overweight women have a higher risk of ovulation disorders, which can lead to fertility problems. In the course of the hormonal analysis study, significant deviations in the levels of key hormones were revealed in the women of the main group compared with the control group. Prolactin and luteinizing hormone (LH) levels in the pathological groups significantly exceeded the control values ($p<0.001$), which is consistent with the data of Kumar et al. (2019), emphasizing the link between elevated levels of these hormones and endocrine disorders.

Decreased levels of follicle-stimulating hormone (FSH) and estradiol in group 1 women also indicate possible abnormalities in ovarian function, which is confirmed by the work of Bhalerao et al. (2020), who describe similar changes in the hormonal background in patients with reproductive disorders. In addition, the noted high levels of total testosterone and dehydroepiandrosterone sulfate (DGES) in both pathological groups indicate the presence of hyperandrogenism, which is consistent with the results of Zhang et al. (2021), which also revealed elevated androgen levels in women with infertility. Elevated cortisol and insulin values in pathological groups ($p<0.001$) may indicate metabolic disorders and insulin resistance, which is confirmed by studies by Duncan et al. (2018), indicating a link between endocrine disorders and metabolic disorders. Thus, the results of the study emphasize the need for a comprehensive assessment of hormonal status and metabolic profile in obese women for more effective management of their condition. The findings highlight the importance of hormonal monitoring in women with endocrine disorders, which can help in the diagnosis and treatment of concomitant metabolic disorders. Neohormones such as follistatin and leptin play a key role in regulating metabolism and reproductive function. Elevated follistatin and leptin levels in overweight and obese patients may indicate a link between overweight and reproductive problems, consistent with other studies highlighting the effects of obesity on fertility (Mazzoccoli et al., 2019). Low levels of inhibin and activin may indicate abnormalities in follicular activity, which is also supported by studies showing that these hormones play an important role in regulating ovulation and folliculogenesis (Hirsch et al., 2020).

The results of the study, showing that follistatin and leptin levels are significantly higher in group II ($p<0.001$), indicate a deterioration in reproductive function in obese patients, which is consistent with the conclusions of other authors about the negative impact of excess weight on reproductive health (Franco et al., 2021). A comparative analysis of relaxin levels, which showed no statistically significant differences ($p=0.205$), may indicate the stability of this marker in the

context of overweight, which is also emphasized in the literature (Kumar et al., 2018). Thus, the results of our study indicate significant differences in the levels of a number of neohormones between patients with infertility and the control group. This may be important for understanding the pathogenesis of infertility and developing new approaches to its treatment.

The results of the study show that follistatin levels have significant correlations with various hormones and metabolic parameters, indicating its potential regulatory role in the endocrine and metabolic systems. The correlation of follistatin with testosterone ($r = 0.505$, $p < 0.001$) is consistent with the data from Baker et al. (2018) and Zhao et al. (2020), emphasizing the effect of follistatin on androgenic activity. Similarly, positive correlations with prolactin ($r = 0.477$, $p < 0.001$) and luteinizing hormone ($r = 0.458$, $p < 0.001$) confirm its role in ovarian function (Matzuk et al., 2002). Correlation with 17-hydroxyprogesterone ($r = 0.166$, $p = 0.067$) and DHEA ($r = 0.366$, $p < 0.001$) may indicate the effect of follistatin on adrenal activity (Sato et al., 2019). The relationship with body mass index (BMI) ($r = 0.257$, $p = 0.009$) and HOMA index ($r = 0.574$, $p < 0.001$) confirms its involvement in the regulation of metabolic processes and may indicate a link with insulin resistance, which is also noted in Kim et al. (2019). Comparatively low correlations with relaxin ($r = -0.130$, $p = 0.153$) and activin ($r = -0.018$, $p = 0.846$) emphasize the absence of a significant effect of follistatin on these hormones, which may be due to differences in their functions. At the same time, a significant correlation with inhibin ($r = -0.521$, $p < 0.001$) indicates its role in ovulation control (Kumar et al., 2021).

In conclusion, these studies highlight the importance of follistatin in regulating androgen activity, metabolism, and reproductive processes, which is consistent with existing research and may have clinical implications for understanding metabolic and reproductive disorders. Thus, neohormones such as follistatin can be useful both in the diagnosis and treatment of infertility and obesity, but their use requires further study and validation in clinical practice. They play an important role in the regulation of metabolism and reproductive function, and their levels can serve as indicators of health and metabolism, which contributes to a personalized approach to therapy.

Changes in metabolic parameters in overweight and obese women highlight the complex relationship between these conditions and hormonal disorders. The findings confirm the need for monitoring and intervention to reduce the risk of metabolic diseases, especially in the context of infertility. Significant deviations in hormonal and biochemical status in women with infertility on the background of obesity require further research and the development of individual approaches to therapy. More research is needed to better understand the relationship between obesity, hormonal levels, and infertility, focusing on the pathophysiology and correlations between biomarkers and reproductive health. A comprehensive treatment approach, including hormone therapy and weight loss programs, can increase the chances of conception for overweight women.

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SUBCHORIONIC HEMATOMA IN EARLY GESTATION, THE RISK OF FETAL GROWTH RESTRICTION AND ADVERSE PERINATAL OUTCOMES

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Abstract. *Early gestational bleeding is a common obstetric complication and is increasingly recognized as a clinical marker of impaired implantation and placental dysfunction. One of the most frequent ultrasound findings in this context is sub chorionic hematoma (SCH), which has been associated with a spectrum of adverse perinatal outcomes. Accumulating evidence suggests that SCH reflects abnormal placentation processes that may persist beyond the first trimester and contribute to fetal growth restriction, preterm delivery, placental abruption, and other complications. This review synthesizes current evidence on the epidemiology, pathophysiology, prognostic significance, and clinical implications of SCH and early pregnancy bleeding, with particular emphasis on fetal growth restriction and perinatal outcomes.*

Keywords: *sub chorionic hematoma, early pregnancy bleeding, placental dysfunction, fetal growth restriction, perinatal outcomes.*

Introduction

Bleeding during early pregnancy remains one of the most frequent reasons for obstetric consultation and occurs in approximately 15–25% of all gestations [6,9]. Although many pregnancies with early bleeding progress to term, increasing evidence indicates that such bleeding is not always a benign event and may reflect abnormal implantation or early placental instability [7,10]. Sub chorionic hematoma is the most common sonographic finding associated with first-trimester bleeding [2,3,8]. While often detected incidentally, SCH has attracted growing attention as a potential marker of placental dysfunction [1,7]. The clinical significance of SCH remains controversial, with studies reporting heterogeneous associations with miscarriage, preterm birth, fetal growth restriction (FGR), and placental abruption [1,9-11]. Sub chorionic hematoma is defined as an accumulation of blood between the chorionic membrane and the uterine wall resulting from partial detachment of trophoblastic tissue [2,5]. Reported prevalence varies widely, ranging from <1% to >20%, depending on diagnostic criteria, gestational age at detection, population characteristics, and ultrasound resolution [1-4].

According to World Health Organization data, the prevalence of growth-restricted newborns varies considerably by region, ranging from over 30% in parts of Central Asia to less than 7% in developed European countries. In the United States, fetal growth restriction is diagnosed in 10–15% of births, and severe intrapartum hypoxia is observed in approximately one-third of affected infants. In the Russian Federation, reported rates range from 2.4% to 17% [15]. Infants with fetal growth restriction account for nearly one-third of all low birth weight newborns. Among term infants, growth restriction occurs in approximately 67 per 1,000 live births, increasing to nearly 180 per 1,000 among preterm neonates. In many cases, reduced fetal size is accompanied by delayed development of individual organs, particularly parenchymal structures.

In asymptomatic women, SCH is detected in approximately 1.7–3.1% of pregnancies, whereas among women presenting with threatened miscarriage, prevalence may reach 20% [1,3,8]. Sonographically, SCH typically appears as a crescent-shaped hypoechoic or anechoic area adjacent to the gestational sac in the first trimester [4,8].

The mechanisms behind SCH formation are still not fully understood. Current hypotheses propose mechanical or vascular disruption at the chorionic–decidual interface, resulting in low-pressure bleeding from marginal placental vessels [2,27]. Growing evidence supports viewing SCH as an early sign of impaired placentation [7,10]. Normal placental development requires adequate trophoblastic invasion and remodelling of spiral arteries [7]. Defective placentation has been identified in the majority of early pregnancy failures and is strongly associated with later complications such as hypertensive disorders, placental abruption, spontaneous preterm birth, and fetal growth restriction [7,11,17]. Premature exposure of placental tissues to maternal circulation may induce excessive oxidative stress before sufficient antioxidant defences are established, contributing to placental injury and pregnancy loss [20].

Numerous studies report associations between SCH and adverse pregnancy outcomes, including spontaneous miscarriage, stillbirth, placental abruption, and preterm delivery [1,3,8-11]. Meta-analyses confirm a consistent association between SCH and pregnancy loss, while links with preterm birth and FGR are less consistent [1,9,10]. Hematoma size has been proposed as an important prognostic factor. Several investigations demonstrate higher risks of miscarriage and placental complications with increasing hematoma volume, particularly when SCH is diagnosed early in gestation [8,18]. However, other studies report weaker associations after adjustment for confounding variables [6,10].

The potential impact of SCH on pregnancy prognosis appears to be influenced by multiple factors, including hematoma size, gestational age at diagnosis, and placental function. Adverse outcomes such as placental abruption, preterm delivery, and early pregnancy loss have been reported in association with SCH across multiple studies [7,10–16]. Some investigators have emphasized the importance of hematoma volume, suggesting that specific measurement methods demonstrate stronger correlations with first-trimester outcomes than others [17]. Both the presence and size of SCH have been linked to an increased likelihood of miscarriage, intrauterine growth restriction, recurrent vaginal bleeding, placental abruption, preterm delivery, and fetal growth impairment [1,6–8,14,18–20]. A large meta-analysis including over 1,700 women with SCH and more than 70,000 controls identified a significantly higher risk of spontaneous abortion, stillbirth, placental abruption, preterm birth, and preterm premature rupture of membranes in pregnancies complicated by SCH, although no association was observed with small-for-gestational-age infants or preeclampsia [10].

The location of the hematoma does not appear to significantly influence overall pregnancy outcome, although posteriorly located SCH has been more strongly associated with fetal distress [1,29]. Use of anticoagulant or antiplatelet therapies, including low-dose ASA, heparin, and thrombolytic agents, has been associated with an increased risk of SCH formation in early pregnancy, while progesterone therapy has not consistently demonstrated protective effects against early pregnancy loss [38–40]. Importantly, vaginal bleeding itself—independent of SCH—has been identified as an independent predictor of adverse maternal and neonatal outcomes, including shortened gestational duration, low Apgar scores, and increased neonatal intensive care unit admission [6,9,19].

Fetal growth restriction represents one of the most clinically significant consequences of placental insufficiency [12,13]. Impaired uteroplacental blood flow leads to chronic fetal hypoxia and metabolic disturbances, resulting in reduced fetal growth potential [12]. Epidemiological data demonstrate substantial regional variation in FGR prevalence, ranging from >30% in parts of Central Asia to <7% in developed European countries [15]. In pregnancies complicated by early bleeding and SCH, the risk of delivering growth-restricted or low birth weight infants is consistently elevated [9-11,18]. Low-dose acetylsalicylic acid (ASA) improves uteroplacental perfusion through inhibition of platelet aggregation and has demonstrated efficacy in reducing the risk of preeclampsia and preterm birth in high-risk populations [21,23-25]. Its role in pregnancies complicated by SCH, however, remains controversial.

Although low-dose ASA is routinely recommended for women at high risk of preeclampsia [24], emerging evidence suggests that its use during the first trimester may increase the likelihood of SCH formation. Based on these observations, some authors recommend postponing the initiation of prophylactic ASA therapy until the second trimester in women with a history of preeclampsia. Current guidelines from the U.S. Preventive Services Task Force advise low-dose ASA (81 mg) for women with specific risk factors, including prior preeclampsia, multifetal gestation, chronic hypertension, diabetes, renal disease, and autoimmune disorders [31]. While cost-effectiveness analyses support widespread ASA prophylaxis, these models do not fully account for the potential increase in SCH-related morbidity [32].

Enhanced endometrial and subendometrial vascularity has been observed in women with successful pregnancies compared to those who miscarry, providing a physiological rationale for ASA use in selected populations [33]. Nevertheless, routine administration of ASA in assisted reproduction cycles is not recommended due to insufficient evidence of benefit and a potential risk of harm [22,34–36]. Maternal age, gestational age at diagnosis, and hematoma size have all been identified as independent factors influencing SCH prevalence [36]. Some studies suggest that first-trimester ASA use may increase the likelihood of SCH formation [22,24], prompting debate regarding optimal timing of prophylaxis. Current guidelines recommend ASA for women at high risk of preeclampsia, although SCH-specific recommendations are lacking [24]. Given the heterogeneity of published data, risk assessment in pregnancies complicated by SCH should be individualised [1,10]. Serial ultrasound monitoring allows evaluation of hematoma evolution and early detection of placental complications [8,18]. Although no specific preventive therapy for SCH exists, enhanced surveillance may facilitate the timely management of emerging obstetric risks.

Conclusion

Subchorionic hematoma and early pregnancy bleeding are associated with a modest but reproducible increase in the risk of adverse perinatal outcomes, including pregnancy loss, preterm delivery, placental abruption, and fetal growth restriction. The strongest and most consistent association is observed with placental abruption, supporting the concept of SCH as a marker of abnormal placentation. Integration of sonographic findings, biochemical markers, and clinical risk factors is essential for individualised counselling and management. Further prospective studies are needed to refine prognostic criteria and optimise preventive strategies in early gestation. Overall, while the association between SCH and adverse perinatal outcomes appears modest for some endpoints, such as pregnancy loss and preterm delivery, a stronger relationship has been consistently observed with placental abruption. Given the heterogeneity of available data, risk assessment should be individualized, taking into account hematoma characteristics and additional

maternal risk factors. Future clinical research comparing different approaches to evaluating hematoma size and location may further improve prognostic accuracy and perinatal care.

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CARBOHYDRATE METABOLISM PARAMETERS IN PATIENTS WITH MASLD DEPENDING ON THE PRESENCE OF RENAL DYSFUNCTION

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Abstract. *Objective: To investigate carbohydrate metabolism parameters in patients with metabolic dysfunction–associated fatty liver disease (MAFLD) depending on the presence of renal dysfunction. The study assessed kidney functional status in young patients with metabolic dysfunction–associated fatty liver disease (MAFLD). A total of 105 patients aged 18–45 years with ultrasound-confirmed hepatic steatosis were included and divided into two groups: MAFLD (n = 81) and MAFLD + chronic kidney disease (CKD) (n = 24). Patients with MAFLD and renal dysfunction demonstrated significantly higher levels of fasting glucose, insulin, HbA1c, and metabolic indices—HOMA-IR, TyG, and METS-IR—compared with MAFLD patients without renal impairment. The integral indices of insulin resistance showed significant correlations with eGFR and albuminuria: HOMA-IR, TyG, and METS-IR were inversely associated with eGFR and positively associated with the albumin-to-creatinine ratio (A/Cr). Young patients with concomitant MAFLD and CKD exhibit a marked exacerbation of metabolic disturbances, including increases in HOMA-IR, TyG, and METS-IR, indicating more pronounced insulin resistance. Integral insulin resistance indices—HOMA-IR, TyG, and METS-IR—demonstrate significant correlations with eGFR and albuminuria.*

Keywords: *insulin resistance, CKD, HOMA-IR, TyG, METS-IR.*

Introduction

Metabolic dysfunction–associated steatotic liver disease (MASLD) is one of the most prevalent chronic liver diseases and is currently regarded as a key component of the cardiometabolic continuum [1–3]. The transition from the term non-alcoholic fatty liver disease (NAFLD) to MASLD emphasizes the dominant role of metabolic dysfunction, insulin resistance, and systemic inflammation in disease pathogenesis [1]. Contemporary studies demonstrate that the presence of MASLD significantly increases the risk of developing chronic kidney disease (CKD), with the magnitude of risk closely correlating with the severity of hepatic fibrosis and the degree of metabolic impairment [2–4].Given the close interrelationship between MASLD, insulin resistance (IR), and renal dysfunction, the assessment of carbohydrate metabolism parameters and integrated indices of insulin resistance in patients with MASLD according to the presence of CKD represents a highly relevant research objective with substantial prognostic and clinical significance. Aim of the work to evaluate parameters of carbohydrate metabolism in patients with MASLD depending on the presence of renal dysfunction.

Materials and Methods

The study included 105 young adult patients (aged 18–45 years) with ultrasound-confirmed hepatic steatosis. Inclusion criteria were the absence of alcohol abuse, previously diagnosed chronic kidney disease, diabetes mellitus, and arterial hypertension. Stratification based on renal

function revealed that 22.9% of patients (n = 24) with hepatic steatosis exhibited impaired renal function, defined by reduced estimated glomerular filtration rate (eGFR) and increased albumin-to-creatinine ratio (ACR), corresponding to CKD stages G1–G2, A2 according to KDIGO criteria. All patients with MASLD were divided into two groups according to renal functional status: Group 1 (MASLD) – 81 patients with preserved renal function; Group 2 (MASLD + CKD) – 24 patients with varying degrees of renal dysfunction. Integrated indices of insulin resistance were calculated: HOMA-IR (Homeostasis Model Assessment of Insulin Resistance), TyG (Triglyceride–Glucose Index), and METS-IR (Metabolic Score for Insulin Resistance) using the following formulas:

- **HOMA-IR** = [fasting glucose (mmol/L) × fasting insulin (μIU/mL)] / 22.5
- **TyG** = ln [triglycerides (mg/dL) × glucose (mg/dL) / 2]
- **METS-IR** = ln [2 × glucose (mg/dL) + triglycerides (mg/dL)] × BMI / ln (HDL-cholesterol)

All data were entered into Microsoft Excel spreadsheets. For parametric variables, mean values and standard errors were calculated. Correlation analysis was performed using Pearson's correlation coefficient, with statistical significance determined accordingly.

Results and Discussion

The results demonstrated moderate disturbances of carbohydrate metabolism in patients with MASLD. Mean fasting glucose levels remained within reference ranges but were higher than in healthy controls, reflecting a tendency toward reduced tissue insulin sensitivity (Table 1). In the presence of CKD, fasting glycemia increased significantly to 5.61 ± 0.24 mmol/L ($p < 0.05$), indicating impaired glucose tolerance.

A parallel significant increase in fasting insulin levels was observed in MASLD patients ($p < 0.05$) and was even more pronounced in the MASLD + CKD group ($p < 0.01$) compared with controls. Correspondingly, elevated HbA1c levels in both MASLD and MASLD + CKD groups ($p < 0.01$) confirmed a trend toward chronic hyperglycemia and disturbances in carbohydrate homeostasis. Although absolute values of glycemic parameters formally remained within normal ranges, their elevation relative to healthy individuals indicates early metabolic alterations characteristic of subclinical insulin resistance. These findings are consistent with contemporary data describing early insulin resistance in MASLD [1,5].

In patients with MASLD and concomitant renal dysfunction, all pathological trends were amplified, including higher glucose and insulin levels, reflecting progressive metabolic imbalance. Statistically significant differences between the two clinical groups underscore the mutual aggravation of renal dysfunction and hepatic steatosis in the development and progression of metabolic syndrome. These observations reflect more profound insulin resistance associated with chronic kidney disease, driven by persistent low-grade inflammation and impaired insulin clearance and utilization [10–11].

Table 1.

Parameters of carbohydrate metabolism in patients with MASLD according to renal function status

Parameter	MASLD (n = 81)	MASLD+ CKD (n = 24)	Control group (n = 20)
Fasting glucose, mmol/L	5,20 ± 0,25	5,61 ± 0,24*	4,40 ± 0,16
Fasting insulin, μIU/mL	8,22 ± 3,74*	14,4 ± 2,14**#	5,50 ± 2,10
HbA1c, %	5,3 ± 0,18*	5,7 ± 0,14**	4,6 ± 0,11

Note: Statistical significance was assessed using Student's *t*-test: $p < 0.05$; ** $p < 0.01$ versus the control group;

In recent years, increasing attention has been focused on the non-invasive assessment of metabolic disturbances using integrated indices such as HOMA-IR (Homeostasis Model Assessment of Insulin Resistance), TyG (Triglyceride–Glucose Index), and METS-IR (Metabolic Score for Insulin Resistance). The HOMA-IR index is widely used to quantify the degree of insulin resistance, reflecting reduced tissue sensitivity to insulin. It allows indirect evaluation of the effectiveness of insulin–receptor interaction and pancreatic β-cell function.

In the control group, the mean HOMA-IR value was 1.07 ± 0.15, corresponding to physiological insulin sensitivity. In patients with MASLD, the index was significantly elevated to 1.91 ± 0.42 ($p < 0.001$), indicating the development of early insulin resistance, although values remained within borderline limits (< 2.5). In the presence of CKD, HOMA-IR increased further to 3.72 ± 0.14 ($p < 0.001$), reflecting overt insulin resistance caused by impaired insulin homeostasis and reduced renal insulin clearance. Thus, patients with concomitant MASLD and CKD exhibited an almost two-fold increase in HOMA-IR compared with isolated MASLD, highlighting the amplification of metabolic dysfunction in the setting of renal impairment.

The TyG index is a direct surrogate marker of insulin resistance, reflecting the interplay between lipid and carbohydrate metabolism. In the control group, TyG was 7.30 ± 0.08, which is within the normal range (< 8.5). In patients with MASLD, TyG increased significantly to 8.77 ± 0.10 ($p < 0.001$), indicating subclinical insulin resistance even when individual biochemical parameters remain within reference limits. In the MASLD + CKD group, TyG reached 9.09 ± 0.09 ($p < 0.001$), reflecting severe dysregulation of glucose–lipid metabolism and correlating with an increased risk of cardiovascular complications.

METS-IR is an integrated metabolic index reflecting the degree of insulin resistance and overall metabolic impairment. This index shows a strong correlation with insulin sensitivity assessed by the euglycemic clamp technique (gold standard). In the present study, healthy individuals demonstrated a mean METS-IR value of 30.2 ± 1.1, consistent with normal insulin sensitivity. In patients with MASLD, METS-IR was significantly higher at 40.7 ± 1.2 ($p < 0.001$), indicating metabolic imbalance and enhanced tissue lipid infiltration. In patients with combined MASLD and CKD, METS-IR reached 54.8 ± 1.4 ($p < 0.001$), exceeding control values by nearly 1.8-fold. This finding reflects severe metabolic decompensation characteristic of patients with chronic renal dysfunction and advanced metabolic syndrome.

Table 2.

Integrated indices of carbohydrate metabolism in patients with MASLD according to renal function status

Parameters	MASLD (n = 81)	MASLD+CKD (n = 24)	Control group (n = 20)
HOMA-IR	1,91 ± 0,42*	3,72 ± 0,14***##	1,07 ± 0,15
METS-IR	40,7 ± 1,2***	54,8 ± 1,4***##	30,2 ± 1,1
TyG	8,77 ± 0,10***	9,09 ± 0,09***#	7,30 ± 0,08

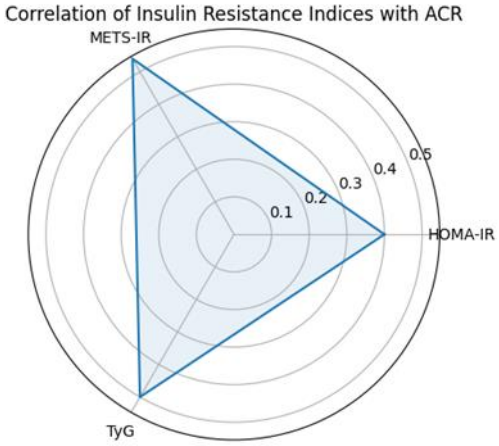
Note: Statistical significance was assessed using Student's *t*-test: $p < 0.05$; ** $p < 0.01$ versus the control group;

Correlation Analysis

A correlation analysis was performed to evaluate the associations between insulin resistance indices and renal functional parameters in patients with MASLD. The data demonstrated significant correlations between integrated metabolic indices (HOMA-IR, METS-IR, and TyG) and key markers of renal function, including estimated glomerular filtration rate (eGFR) and the albumin-to-creatinine ratio (ACR).

A statistically significant inverse correlation was identified between HOMA-IR and eGFR ($R = –0.31$; $p < 0.05$), as well as between METS-IR and eGFR ($R = –0.31$; $p < 0.01$). The TyG index, reflecting combined glucose–lipid dysregulation, showed an even stronger negative association with eGFR ($R = –0.41$; $p < 0.05$), suggesting higher sensitivity to early metabolic disturbances affecting renal function.

A significant positive correlation was observed between insulin resistance indices and ACR levels (Figure 1). HOMA-IR correlated moderately with ACR ($R = +0.40$; $p < 0.01$), whereas stronger associations were observed for METS-IR ($R = +0.54$; $p < 0.01$) and TyG ($R = +0.50$; $p < 0.01$), indicating a close relationship between metabolic dysregulation and early renal injury in patients with MASLD.



Elevated HOMA-IR in patients with MASLD, particularly in the MASLD + CKD group, is consistent with large-scale studies demonstrating an independent association between HOMA-IR, albuminuria, and reduced eGFR [11,12]. According to Li et al., a HOMA-IR threshold > 2.5 is associated with an increased risk of CKD [13], supporting the pivotal role of insulin resistance in early nephron injury.

The TyG index exhibited pronounced intergroup differences and high diagnostic value. Its elevation in MASLD + CKD patients aligns with findings by Wang Z. and Li X., reporting associations between TyG, microalbuminuria, and declining eGFR [14,15]. Recent cohort studies have demonstrated that both TyG and METS-IR independently predict CKD onset and progression even in non-diabetic populations [6,10], highlighting METS-IR as a valuable integrated metabolic marker.

The observed inverse correlations between HOMA-IR, METS-IR, TyG and eGFR, together with positive correlations with albuminuria, are consistent with the concept of a “metabolic nephropathic continuum.” These findings indicate that increasing insulin resistance is closely linked to the development of albuminuria, reflecting enhanced glomerular permeability and early glomerular injury [3,4]. The strongest associations with eGFR were observed for METS-IR and TyG, consistent with reports suggesting that these indices may outperform HOMA-IR in assessing cardiometabolic and renal risk [9,10].

Conclusions

Young adults with MASLD exhibit moderate disturbances of carbohydrate metabolism consistent with early-stage insulin resistance. Concomitant CKD is associated with a significant amplification of metabolic abnormalities, including elevated HOMA-IR, TyG, and METS-IR, indicating more pronounced insulin resistance. Integrated insulin resistance indices demonstrate significant correlations with eGFR and albuminuria, supporting their potential utility as non-invasive markers for early identification of renal dysfunction and cardiometabolic risk in patients with MASLD.

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THE WORLDWIDE IMPACT OF RESPIRATORY SYNCYTIAL VIRUS INFECTION IN CHILDREN: PROGRESS AND ONGOING CHALLENGES IN CONTEMPORARY PEDIATRICS

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Abstract. *Respiratory syncytial virus (RSV) infection is one of the leading causes of acute respiratory diseases among neonates and young children worldwide. Its high transmissibility, pronounced seasonality, and severity of clinical manifestations, including bronchiolitis and pneumonia, make RSV a significant public health concern. The long-standing absence of specific antiviral therapies has limited etiological treatment options, resulting primarily in supportive and symptomatic care. In recent years, substantial progress has been made in disease prevention, including the introduction of long-acting monoclonal antibodies (nirsevimab), the registration of vaccines for use in pregnant women (Abrysvo, Arexvy), and the development of innovative platforms, including mRNA technologies, offering new prospects for reducing RSV-related morbidity and mortality. Particular attention is given to infants in the first six months of life and high-risk groups, including preterm neonates, children with congenital heart defects, bronchopulmonary dysplasia, and immune system disorders. Modern diagnostic approaches combine clinical criteria with highly sensitive laboratory methods, such as rapid RSV antigen tests and PCR. The integration of contemporary preventive strategies, enhancement of epidemiological surveillance, and rational use of healthcare resources are key directions in combating RSV infection and reducing its global burden.*

Keywords: *respiratory syncytial virus (RSV), young children, monoclonal antibodies, maternal vaccination, mRNA vaccines, bronchiolitis, prevention and immunization, epidemiology, diagnosis, laboratory methods.*

Introduction

Respiratory syncytial virus (RSV) remains one of the principal causes of acute respiratory illness in neonates and young children worldwide, posing a significant public health concern. The virus is characterized by high transmissibility, distinct seasonal patterns, and a broad clinical spectrum, ranging from mild upper respiratory infections to severe lower respiratory tract conditions, including bronchiolitis and pneumonia. RSV infection is associated with considerable morbidity and mortality, particularly in infants under six months of age, preterm neonates, and children with underlying medical conditions, such as congenital heart defects, chronic pulmonary disorders, and immunodeficiencies. On a global scale, RSV contributes to millions of pediatric hospitalizations each year, with a substantial proportion of cases leading to severe complications or death. The socioeconomic impact of RSV is notable, encompassing direct medical costs, extended hospital stays, parental work absenteeism, and long-term sequelae, including recurrent wheezing and an elevated risk of developing bronchial asthma.

Despite extensive research efforts, effective etiological treatments and universally available vaccines have historically been lacking, resulting in a management approach that remains largely supportive and symptomatic.Recent developments in RSV prophylaxis, including the introduction of long-acting monoclonal antibodies (e.g., nirsevimab), maternal immunization strategies (Abrysvo, Arexvy), and novel vaccine platforms such as mRNA-based vaccines, offer promising avenues to reduce RSV-related morbidity, hospitalization rates, and mortality. Concurrently, the adoption of rapid and sensitive diagnostic methods, including antigen-based rapid tests and PCR assays, has enhanced the timely detection and clinical management of RSV infections. The present study aims to systematically review and integrate data from 27 recent publications (2022–2025) to assess the epidemiology, clinical presentation, diagnostic strategies, and preventive measures for RSV infection in neonates and young children, with a particular focus on high-risk groups. Furthermore, the review emphasizes recent advancements in prophylactic interventions and their potential role in mitigating the global burden of RSV disease.

Study objective. The aim of this study is to systematically review and analyze the epidemiology, clinical characteristics, diagnostic approaches, and effectiveness of modern preventive strategies for respiratory syncytial virus (RSV) infection in neonates and young children worldwide, based on data from 27 published studies. Special emphasis is placed on high-risk populations, including infants during the first six months of life, preterm neonates, children with congenital heart disease, bronchopulmonary dysplasia, and immune system deficiencies.

Materials and methods. This study represents a systematic literature review aimed at evaluating the epidemiology, clinical manifestations, diagnostic approaches, and preventive strategies for respiratory syncytial virus (RSV) infection in neonates and young children. The review focuses on high-risk populations, including infants during the first six months of life, preterm neonates, children with congenital heart defects, bronchopulmonary dysplasia, and immune system disorders. A comprehensive literature search was conducted across major scientific databases, including PubMed, Scopus, Web of Science, and Google Scholar, covering the period from 2022 to 2025. The search strategy employed keywords such as “RSV infection,” “respiratory syncytial virus,” “infants,” “neonates,” “monoclonal antibodies,” “maternal vaccination,” “mRNA vaccines,” “bronchiolitis,” “prevention,” “diagnosis,” and “epidemiology.” In total, 27 peer-reviewed studies were selected based on the following inclusion criteria:Original research articles, systematic reviews, or meta-analyses published between 2022 and 2025, studies reporting on RSV epidemiology, clinical features, laboratory diagnostics, preventive interventions, or outcomes in children under five years of age, articles available in English with full-text access. Exclusion criteria included case reports, letters to the editor, and studies with incomplete or non-reproducible data.

Relevant data were extracted from each study, including: study population characteristics (age, gestational age, comorbidities, high-risk status), epidemiological findings (incidence, seasonality, RSV subtypes A and B), clinical outcomes (hospitalizations, complications, mortality), diagnostic approaches (rapid antigen tests, PCR, laboratory biomarkers), preventive strategies (monoclonal antibodies, maternal vaccination, novel vaccine platforms including mRNA technologies).

Results. The extracted information was systematically tabulated and qualitatively analyzed to identify common trends, risk factors, and evidence-based recommendations. Comparative

analysis across studies allowed assessment of RSV-related morbidity, hospitalization rates, and the impact of preventive interventions. Being a literature-based study, the findings are inherently limited by the quality, heterogeneity, and reporting standards of the included studies. Variation in study design, population demographics, and regional epidemiology were considered when interpreting the results.

Respiratory syncytial virus (RSV) is among the leading etiological agents of acute respiratory infections in neonates and young children worldwide. The extent of its global spread and the severity of its clinical manifestations are comparable to those of the most serious infectious diseases in pediatric practice. In terms of hospitalization rates among neonates and infants, RSV consistently ranks among the leading causes [1,2,25]. According to estimates by the World Health Organization, more than 33 million cases of RSV infection are reported annually worldwide, over 3 million of which require inpatient care, while tens of thousands result in fatal outcomes, predominantly among infants within the first six months of life [25]. Of particular concern is the fact that, until recently, effective etiological therapies and universally applicable vaccine-based preventive strategies were lacking.

For a prolonged period, particular concern was associated with the lack of effective etiological therapies and a universally applicable vaccine against respiratory syncytial virus (RSV), rendering it a persistent challenge even for healthcare systems in economically developed countries. RSV infection is characterized by pronounced seasonality and high transmissibility, which facilitates rapid spread among pediatric populations, including outbreaks in maternity wards and within household settings [25,26]. Severe clinical manifestations, notably bronchiolitis and pneumonia, are frequently accompanied by the development of respiratory failure, apnea, and hypoxemia, often necessitating intensive care. Importantly, even mild or subclinical infections may be associated with long-term adverse outcomes, including an increased risk of bronchial asthma, chronic obstructive lung diseases, and airway hyperreactivity later in life.

The socio-economic burden of RSV infection remains substantial and is driven by high healthcare and hospitalization costs, prolonged recovery periods, temporary loss of parental work capacity, and long-term adverse health consequences for affected children. Collectively, these factors impose a considerable strain on healthcare systems [3,4,5,7]. These circumstances underscore the need for the development and implementation of comprehensive preventive strategies, including active immunization, the use of monoclonal antibodies for passive protection, and the strengthening of epidemiological surveillance systems.

Recent reviews and epidemiological studies confirm that the global burden of RSV infection remains exceedingly high, particularly among infants and young children. According to the World Health Organization, RSV infection in children under five years of age results annually in approximately 3.6 million hospitalizations and nearly 100,000 deaths, with about half of these fatalities occurring in infants younger than six months. The burden is especially severe in low- and middle-income countries, which account for more than 97% of RSV-associated mortality [8,24,25]. Additional evidence highlights the substantial healthcare expenditures and resource utilization associated with the management of infants with RSV infection, further emphasizing the considerable economic impact of the disease [20].

In recent years, progress has been achieved in the prevention of RSV infection, including the licensing of long-acting monoclonal antibodies (e.g., nirsevimab) and the development and implementation of maternal vaccination strategies. These advances offer new opportunities to reduce the global burden of RSV disease [12]. The highest epidemiological and clinical burden

continues to be observed among infants during the first six months of life, as well as among high-risk groups, including preterm infants and children with congenital heart disease, chronic lung conditions, or immune system disorders [14,19,21].

Numerous studies have demonstrated that the clinical manifestations of RSV infection are influenced by viral load, the genetic variability of circulating strains (RSV-A and RSV-B), and host-related factors, including age, the functional maturity of the immune system, and genetic susceptibility [8,10,12,21,23,25]. An incomplete and short-lived immune response to RSV predisposes individuals to recurrent infections, thereby amplifying the overall disease burden and potentially contributing to the development of recurrent wheezing and bronchial asthma [16].

RSV infection exhibits marked seasonal patterns: in temperate climates, incidence peaks during the winter months, whereas in tropical regions, increased activity is observed during the rainy season [6,18]. However, prolonged implementation of non-pharmaceutical interventions, such as mask wearing, social distancing, and school closures, has led to significant disruptions in the traditional seasonal circulation of the virus [17]. The COVID-19 pandemic substantially altered the epidemiology of RSV, with a marked decline in incidence observed across many countries during 2020 and the first half of 2021. This phenomenon has been attributed to widespread public health measures, including mobility restrictions and infection control interventions [12]. For example, in Australia, RSV incidence during the winter season of 2020 declined by nearly 98% compared with previous years. Following the relaxation of these restrictions, RSV circulation resumed but with altered seasonal dynamics, including delayed, atypical, and even summer outbreaks reported in several regions [15,26].

Timely and accurate diagnosis of respiratory syncytial virus infection (RSV) in children is critical for effective disease control and the rational management of patients. An optimal diagnostic approach combines clinical assessment with laboratory methods, ensuring a balance between diagnostic accuracy and practical feasibility. While clinical criteria play a central role, etiological confirmation through virological testing remains a critical component of patient management [13]. Underestimation of the importance of laboratory verification often results in inappropriate prescription or escalation of antibacterial therapy in cases of viral etiology, contributing to antimicrobial resistance and inefficient use of healthcare resources.

In this context, the implementation of accessible, rapid, and highly sensitive diagnostic methods, including RSV antigen rapid tests and molecular PCR assays, represents a priority in contemporary pediatric practice [24,25,26]. Therapeutic options for RSV infection remain limited, highlighting the paramount importance of preventive measures. Current international guidelines emphasize prevention as the most effective strategy to reduce RSV-related morbidity and mortality. Previous attempts to develop active vaccines have not provided sufficient protection, particularly in infants and preterm children. Significant progress has been achieved through passive immunization using monoclonal antibodies. Palivizumab (Synagis), a humanized IgG antibody targeting the RSV F protein, exhibits strong neutralizing activity against circulating RSV strains of subtypes A and B [11]. Palivizumab has been shown to reduce hospitalizations and severe outcomes in high-risk pediatric populations, including preterm infants, patients with bronchopulmonary dysplasia, and those with congenital heart disease.

Recent years have seen active research into new long-acting monoclonal antibodies (e.g., nirsevimab) and innovative vaccine platforms for maternal and infant immunization, offering new avenues for RSV prevention [5,16]. Management of RSV infection remains primarily supportive;

as specific antiviral therapies are currently unavailable. Ribavirin, although available as an inhaled formulation abroad, has limited use due to potential toxicity [9,22].

The management of RSV-associated bronchiolitis in children remains a subject of debate. Contemporary meta-analyses indicate that bronchodilators do not reduce disease duration or hospitalization rates, and therefore are not recommended for routine use [17]. Systemic corticosteroids and leukotriene receptor antagonists have not demonstrated clinical benefit and may cause adverse effects, including growth suppression and decreased bone mineral density. Antibiotics are effective only in the presence of secondary bacterial infection, and physiotherapy is primarily reserved for children with chronic pulmonary conditions. Supportive care, including adequate hydration and oxygen therapy to maintain saturation ≥92%, remains the cornerstone of treatment [26].

Vaccination remains the principal strategy for RSV prevention, aimed at inducing durable immunity and reducing the risk of severe complications. Maternal immunization is of particular importance, providing protection to newborns during the most vulnerable period of early life [17]. In recent years, significant progress has been achieved: the U.S. Food and Drug Administration (FDA) has approved two vaccines — Abrysvo (Pfizer) and Arexvy (GSK) — for the prevention of RSV in adults and pregnant women.

Simultaneously, the development of mRNA vaccines and other innovative platforms aimed at providing more effective protection across all age groups continues [21]. Research is actively underway on seasonal prediction models, personalized preventive strategies, and biomarkers of disease severity, offering new opportunities for clinical practice and RSV epidemiological control [26].

Conclusion. Respiratory syncytial virus (RSV) infection remains one of the most pressing challenges in contemporary pediatrics and public health. Its high transmissibility, pronounced seasonality, severe clinical manifestations, and frequent complications in neonates and young children contribute to a substantial impact on global health indicators. Despite advances in diagnostics, therapy, and prevention, RSV continues to rank among the leading causes of hospitalization in children under five years with acute respiratory infections. For a long time, the absence of specific antiviral therapies and effective vaccines limited the possibilities for etiological treatment, rendering management predominantly supportive and symptomatic.

In recent years, significant progress has been achieved in RSV prevention: the introduction of long-acting monoclonal antibodies (nirsevimab), approval of vaccines for use in pregnant women (Abrysvo, Arexvy), and the active development of innovative platforms, including mRNA technologies, provide new prospects for reducing RSV-related morbidity and mortality. Preventive strategies should prioritize infants during the first six months of life and high-risk populations, including preterm infants, children with congenital heart disease, bronchopulmonary dysplasia, and immune deficiencies. Strengthening epidemiological surveillance, improving laboratory diagnostics, rational utilization of healthcare resources, and integrating modern preventive approaches at the national level are key measures in combating RSV infection. Contemporary advances in vaccinology and monoclonal antibody therapy offer novel opportunities to reduce the global burden of RSV. Their widespread implementation, combined with comprehensive preventive programs and international epidemiological monitoring, has the potential to significantly improve outcomes in the most vulnerable pediatric populations.

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SOME ASPECTS OF ALLERGIC RHINITIS (LITERATURE REVIEW)

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Abstract*. The article describes the etiology, clinical picture, differential diagnosis and the significant role of doctors in improving the quality of medical care for patients with this disease is noted. Allergic rhinitis is an atopic disease characterized by sneezing, nasal congestion, watery discharge, and nasal itching. It is caused by an IgE-mediated immune response to inhaled allergens: an immediate-phase reaction develops first, followed by a late-phase reaction associated with the action of leukotrienes.*

Keywords*: allergic rhinitis, etiology, epidemiology, differential diagnosis and treatment of allergic rhinitis.*

Introduction. It is widely acknowledged that allergic rhinitis (AR) is a common condition affecting patients of all ages. It contributes to the development of significant functional impairment, decreased work capacity, and limitations of daily activities, as well as leads to social problems, negatively impacting sleep, learning, professional activity, general well-being, and quality of life [26]. AR is an atopic disorder and presents with a complex of symptoms including nasal congestion, watery discharge, sneezing, postnasal drip, and nasal itching. The disease affects approximately one in six people and is characterized by high prevalence, leading to decreased work capacity and increased healthcare costs. Previously, AR was considered a pathological process affecting exclusively the nasal airways. However, the concept of "unity of the airways" considers it a component of the body's systemic allergic response associated with concomitant conditions such as bronchial asthma and atopic dermatitis, which share common pathogenetic mechanisms [9-4].

Depending on the course of the disease, AR is divided into seasonal (intermittent) and year-round (persistent): approximately 20% of cases are seasonal, 40% are year-round, and another 40% of patients exhibit a combination of both [23]. In addition to nasal manifestations, patients with AR often experience allergic conjunctivitis, dry cough, Eustachian tube dysfunction, and chronic sinusitis. It has been extensively argued that AR is treatable with various therapeutic methods, with topical glucocorticosteroids considered first-line drugs.[18]

Non-IgE-mediated hyperreactivity can develop as a result of eosinophilic infiltration and structural changes in the nasal mucosa. As a result, the mucosa becomes hypersensitive to nonspecific irritants, such as tobacco smoke and cold air, leading to sneezing, rhinorrhea, and nasal itching [17]. There is evidence suggesting the possible involvement of genetic factors in the development of allergic rhinitis, but high-quality studies in this area are limited. In monozygotic twins, the concordance rate for the development of allergic rhinitis is 45–60%, while in dizygotic twins it is approximately 25%. Furthermore, a link between allergic reactions and certain regions of chromosomes 3 and 4 has been identified [25].

Epidemiological data indicate that the prevalence of allergic rhinitis based on physician diagnosis is approximately 15%, while among patients with nasal symptoms, this figure can reach

30%. It is known that the peak incidence of allergic rhinitis is observed in the second to fourth decades of life, followed by a gradual decline [25]. In the pediatric population, the incidence of allergic rhinitis also remains high, making it one of the most common chronic diseases in children. According to the International Study of Asthma and Allergies in Childhood, symptoms of rhinoconjunctivitis associated with allergic rhinitis are detected in 14.6% of children aged 13-14 years and in 8.5% of children aged 6-7 years [18]. Seasonal allergic rhinitis is more common in children, while persistent allergic rhinitis is more common in adults [2].

According to a 2023 statistical review, 3.6% of adults were forced to miss work, and 36% experienced decreased productivity due to allergic rhinitis. Economic research indicates that the majority of indirect costs are associated with lost productivity due to allergic manifestations [1]. Risk factors for the development of allergic rhinitis include a strong family history of atopy, male gender, the presence of allergen-specific IgE, total serum IgE levels above 100 IU/mL before the age of 6 years, and higher socioeconomic status [25]. Studies conducted among young children have revealed an increased likelihood of developing AR in those who were introduced to complementary foods or formula early and/or were heavily exposed to tobacco smoke during the first year of life [23].

Many studies have examined the possible link between environmental pollution and the development of allergic rhinitis; however, a convincing quantitative correlation has not yet been established. However, factors that potentially have a protective effect on the development of AR have been identified. For example, the role of breastfeeding is actively debated: despite the lack of definitive evidence of its preventive effect on AR, it remains recommended due to its numerous proven benefits and the absence of negative consequences.

There is no reliable evidence that avoiding contact with pets in childhood prevents the development of allergic rhinitis; on the contrary, it is assumed that early contact with animals may contribute to the development of immune tolerance. In recent years, interest in the so-called "farmer effect" in the context of allergic diseases has increased. The results of eight meta-analyses on children in the first year of life living in rural areas demonstrated a reduction in the risk of developing allergic rhinitis by approximately 40% compared to the urban population. [27]

The number of diagnostic approaches exist for assessing allergic rhinitis. A thorough history and physical examination remain the most common and accessible method for establishing a diagnosis. A positive clinical response to a trial of intranasal glucocorticosteroids may provide additional confirmation of the diagnosis. Definitive confirmation of allergic rhinitis is achieved either by measuring allergen-specific IgE in the serum or by skin allergy testing [26]. The American Academy of Otolaryngology guidelines emphasize that allergy testing is appropriate for patients who do not respond to empirical treatment or when identifying a specific allergen is necessary for targeted therapy [18]. Serum testing does not require the participation of specially trained personnel and does not require prior discontinuation of antihistamines, thereby avoiding deterioration in the patient's quality of life.

Skin allergy testing, in contrast, requires a qualified specialist, but its results can be obtained almost immediately. To more accurately identify the causative allergens in patients with seasonal manifestations of the disease, testing is recommended during the period of peak symptom severity [26]. Skin tests are known to have slightly higher sensitivity compared to serum methods and are more cost-effective. However, skin allergy testing has a number of contraindications, including uncontrolled or severe bronchial asthma, unstable cardiovascular disease, pregnancy, and the concomitant use of β-blockers. Furthermore, H2-receptor antagonists, tricyclic

antidepressants, and the anti-IgE monoclonal antibody omalizumab can interfere with skin test results, and therefore it is recommended to temporarily discontinue them before testing.[27].

It should be noted that radiographic examination is generally not used to diagnose allergic rhinitis and is used primarily to exclude other conditions, particularly rhinosinusitis [23,27]. Treatment is based on minimizing exposure to triggers, especially in patients with seasonal symptoms, although complete avoidance of allergens is not always possible. Preventive measures aimed at reducing exposure to household allergens, such as dust mites, animal hair and dander, and upholstered furniture, are possible; however, such interventions often require significant lifestyle changes and may be unacceptable to the patient. If removing the pet from the home is not possible, limiting its presence to one room to reduce exposure to allergens is considered an acceptable option. It should be noted that complete elimination of cat dander from a living space may take up to 20 weeks, even after removing the pet. Using hypoallergenic bedding, washing linens in hot water, and using vacuum cleaners with high-efficiency particulate air (HEPA) filters can significantly reduce the severity of symptoms [25].

Drug treatment for allergic rhinitis includes antihistamines, intranasal glucocorticosteroids, leukotriene receptor antagonists, and allergen-specific immunotherapy. Intranasal corticosteroids can be used either as monotherapy or in combination with oral antihistamines in patients with mild, moderate, and severe manifestations of the disease. Studies have demonstrated that intranasal corticosteroids are superior to antihistamines in their ability to reduce inflammation of the nasal mucosa and improve its condition.

Therefore, topical intranasal steroids are considered first-line therapy for allergic rhinitis [28]. The most common nasal sprays include beclomethasone, budesonide, fluticasone propionate, mometasone furoate, and triamcinolone acetonide. Proper technique for using nasal sprays is crucial for achieving maximum therapeutic effect and reducing the risk of adverse reactions, so patients should receive detailed instructions on their use. These medications should be used regularly, as the maximum effect develops within a few days. It is recommended to insert the spray into the nostril and point it laterally, toward the corresponding eye, to minimize contact of the spray with the nasal septum. The most common adverse events are nasal irritation and nosebleeds, which can be prevented with proper spray technique [24].

Although oral and injectable glucocorticosteroids can reduce the symptoms of allergic rhinitis, they are not recommended for routine use due to the significant risk of systemic side effects. [27]. First-generation antihistamines include diphenhydramine, chlorpheniramine, and hydroxyzine, while fexofenadine, loratadine, desloratadine, and cetirizine represent the second generation of these agents. Both groups of medications effectively reduce the symptoms of allergic rhinitis. However, first-generation antihistamines have a pronounced sedative effect due to their ability to penetrate the blood-brain barrier. They also interact with muscarinic receptors, which can lead to side effects such as dry mouth, urinary retention, constipation, and tachycardia.

Second-generation antihistamines are characterized by greater selectivity for H1 receptors, less sedative effects, and a longer half-life of 12 to 24 hours compared to first-generation medications. Fexofenadine causes virtually no drowsiness, while loratadine and desloratadine can cause sedation when used in high doses. Cetirizine, in turn, has the greatest sedative potential among second-generation antihistamines. It should be noted that no single drug has a clear advantage over the others, as they all demonstrate comparable efficacy and safety profiles for relieving allergic rhinitis symptoms [25].

Topical antihistamines, such as azelastine, have a rapid onset of action and are superior to oral formulations in reducing nasal symptoms. They are recommended as first- or second-line therapy for allergic rhinitis and can be used in combination with intranasal glucocorticosteroids, providing a synergistic therapeutic effect [27]. Leukotriene receptor antagonists (LTRAs), including montelukast and zafirlukast, can be used to treat allergic rhinitis; however, they are inferior in efficacy to intranasal glucocorticosteroids [20]. These drugs are most often used as part of combination therapy in patients with severe disease or in those with an inadequate response to standard therapy.

In cases where allergen avoidance measures and combination drug therapy do not produce a satisfactory clinical effect, it is advisable to consider allergen-specific immunotherapy. The most common methods are subcutaneous (ASIT) and sublingual (SLIT) immunotherapy. Treatment typically begins with weekly administration of gradually increasing doses for 6–8 months, followed by a maintenance regimen lasting 3–5 years. Patients typically experience a long-lasting protective effect, allowing for subsequent discontinuation of therapy [18]. It is well known that oral decongestants, such as pseudoephedrine, can reduce the severity of symptoms; however, their continuous daily use is not recommended due to potential side effects. Intranasal vasoconstrictors, such as xylometazoline, are alpha-adrenergic agonists and act directly on the nasal mucosa, causing vasoconstriction.

Long-term use of nasal decongestants carries a high risk of developing rebound nasal congestion, known as rhinitis medicamentosa, and therefore their use should not exceed one week [27]. Sodium cromoglycate (cromolyn) effectively reduces symptoms such as sneezing, runny nose, and itching, making it a reasonable treatment option. Surgical treatment is indicated for patients with nasal polyposis, inferior turbinate hypertrophy causing intractable nasal congestion, or chronic paranasal sinus disease refractory to medical treatment [12,25,29]. Budesonide is the only glucocorticosteroid approved for use in pregnant women with symptoms of allergic rhinitis [18]. The monoclonal antibody omalizumab may be an effective treatment option for patients with AR; however, its high cost limits its widespread use [3]. Nasal saline solutions may also be used in combination with other treatments: isotonic solutions are more commonly used in adults, while hypertonic solutions may be more effective in children [27].

Differential diagnosis of allergic rhinitis includes exclusion of other types of rhinitis not associated with allergies. These include vasomotor rhinitis, infectious rhinitis, pregnancy rhinitis, hormonally induced rhinitis, nonallergic rhinitis with eosinophilia (NARES), chemical rhinitis, drug-induced rhinitis, as well as autoimmune, granulomatous, and vasculitic rhinitis, nasal polyposis, nasopharyngeal neoplasms, cerebrospinal fluid leakage, and sickle cell anemia. Children, especially those under 2 years of age, should also be examined for congenital causes of nasal congestion, such as choanal atresia and immunodeficiencies [23, 26, 27].

According to clinical guidelines by E.R. Terenkova and D.V. Terenkov, desloratadine for seasonal allergic rhinitis is recommended to be started 1–2 weeks before the expected pollen season. The drug is also indicated for perennial allergic rhinitis as a baseline therapy for mild cases. For moderate to severe forms of allergic rhinitis, intranasal glucocorticosteroids are prescribed in combination with desloratadine or other second-generation antihistamines. The selection and combination of baseline therapy medications is individualized, taking into account the severity of symptoms, drug tolerability, and the patient's lifestyle. Long-term experience with desloratadine demonstrates its high efficacy in both seasonal and perennial allergic rhinitis. The drug has a high

safety profile and can be combined with other medications, making it an advantage among other antihistamines used to treat allergic rhinitis [26,30].

Chronic rhinosinusitis, although distinct from allergic rhinitis, can develop as a complication of the latter. It is characterized by inflammation of the nasal cavity with symptoms of congestion or discharge persisting for more than three months. Chronic rhinosinusitis often leads to the development of nasal polyps, which arise from long-term inflammation of the paranasal sinus mucosa. Nasal polyps are typically benign and occur symmetrically on both sides; the presence of unilateral polyps requires further investigation to rule out malignancy. The incidence of polyps in the population is approximately 4% and is more common in men. Treatment includes topical steroids and nasal irrigation with saline. Surgical removal is considered only in patients who do not respond to drug therapy.[18,23]

It is also known that sensitization to allergens in allergic rhinitis can alter the immunological parameters of the adenoids, which can lead to adenoid hypertrophy.[22] Eustachian tube dysfunction is commonly seen in patients with allergic rhinitis and manifests as ear congestion, otalgia, and ear fullness. Approximately 10 to 40% of patients with allergic rhinitis also have concomitant asthma, with studies showing that asthma is more common in patients with moderate to severe persistent rhinitis. Data from numerous studies confirm that allergic rhinitis is an independent risk factor for the development of asthma, especially if the disease is diagnosed in infancy. Other possible associated complications include otitis media with effusion, chronic cough, and eosinophilic esophagitis, although the extent of the association of these conditions with allergic rhinitis requires further clarification [27–30].

Conclusion

Exacerbations of rhinitis or asthma, as well as the development of anaphylaxis, can be triggered by allergen-specific desensitization (allergy shots). Therefore, staff in departments providing such therapy must have a high level of training in the diagnosis and treatment of severe allergic reactions, as well as have access to emergency medications, especially epinephrine, and airway management equipment. [6, 8]

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HEPATIC DYSFUNCTION AND COVID-19: A REVIEW OF THE LITERATURE AND AN ASSESSMENT OF THE PROBLEM

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Abstract. *This article analyzes research studies on the clinical manifestations, pathogenesis and effective treatment of extrathoracic lesions of coronavirus infection. Recent studies have shown that the pathogenetic mechanisms of liver damage in COVID-19 may include various factors, including direct viral damage, a severe systemic inflammatory response, hypoxia, drug-induced toxic injury, and activation of preexisting liver disease. The degree of liver dysfunction can vary from asymptomatic elevations of serum transaminases and/or bilirubin to severe hepatocellular failure. Inflammatory and toxic damage can develop both in the acute phase and in the post-infection phase during the rehabilitation period.*
Keywords: *coronavirus Disease 2019, enzyme-linked immunosorbent assay, non-alcoholic fatty liver disease, Post-COVID-19 Functional Status, liver dysfunction.*

Introduction. It has long been recognized that the clinical significance and long-term consequences of COVID-19-associated liver injury are not fully understood. Therefore, determining the severity of structural and functional liver damage in patients who have recovered from COVID-19 and developing methods for its correction are pressing issues in modern medicine. It should be noted that from 2019 to 2022, extensive work was undertaken in our country to improve the healthcare system and refine diagnostic, treatment, and prevention methods for somatic diseases. To advance healthcare services to a new level, important tasks have been identified "...aimed at improving the efficiency, quality, and accessibility of medical care, supporting a healthy lifestyle, and disease prevention, including through the development of a medical standardization system, the implementation of high-tech diagnostic and treatment methods, and effective models of home care and medical examination.". In this regard, in recent years, as healthcare has reached a new level, the diagnosis of post-COVID syndrome, COVID-19-associated liver injury, and the development of medical treatment principles have become particularly important, improving quality of life, and reducing disability and mortality.

According to international studies in recent years, COVID-19 viruses affect not only the respiratory system but also parenchymal organs (Jin X et al, 2020; Huang C, et al, 2020). In a systematic review, "Coronavirus disease (COVID-19) and the liver," published in September 2020, the cumulative prevalence of acute liver injury was 23.7 cases (16.1-33.1) per 100 COVID-19 patients (Kumar-M P. et al, 2020). In another meta-analysis, the incidence of liver injury ranged from 19% to 53%. Moreover, the incidence of liver damage is higher in patients with severe disease (74.4%) compared to patients with moderate infection (43.0%), and elevated levels of ALT, AST, and bilirubin are associated with a long period of hospitalization (Fan J-G., 2020; Wang D. et al., 2019). A number of studies have shown that liver damage is more prevalent in patients with severe infection compared to moderate infection (Jiehao C. et al., 2020, Li L. et al., 2020). Epidemiological studies have demonstrated that increased levels of ALT, gamma-glutamyl aminotransferase (GGT), and bilirubin associated with COVID-19 are more pronounced in men compared to women (Cai Q. et al., 2020) and

in young patients compared to older ones (Phipps MM. et al., 2020). In children, hyperenzymemia is less common than in adults, as are pulmonary involvement and severe cases of the disease (Xu Y. et al., 2020).

Research studies on the pathophysiology of COVID-19-associated liver injury have shown that COVID-19 has both direct and indirect effects on the hepatobiliary system. Liver biopsy revealed the detection of viral RNA in the parenchyma, confirming direct viral liver injury (Gu J, Han B, Wang J. 2020). Viral liver injury is characterized by hepatomegaly with dark red ballooning of hepatocytes, lobular necrosis, infiltration of neutrophils, lymphocytes, and monocytes in the portal system, sinusoidal dilation, and vascular congestion with microthrombosis (Zhang C., et al., 2020; Li J, Fan JG., 2020). A group of researchers (Zhou Z., et al, 2020; Zhong P, Xu J. et al, 2020; Wrapp D. et al, 2020) demonstrated that SARS-CoV2 infection depends on the lock-and-key binding of the viral S protein and the ACE receptor type 2, where the S protein acts as the key, and that the SARS-CoV2 S protein has a 10-20-fold higher affinity for the membrane ACE receptor type 2 compared to SARS-CoV.

The presence of angiotensin-converting enzyme 2 (ACE) receptors in cholangiocytes, which act as a key receptor for SARS-CoV2 particles, confirms the retrograde model of liver parenchyma injury after biliary tree invasion (Galanopoulos M. et al, 2020; Tan Y-J et al, 2004). Scientists have found that the expression of ACE-2 receptors in cholangiocytes is 20 times higher than in hepatocytes (Chai X. et al, 2020; Guo A-X. et al, 2020; Hamming I et al, 2004). SARS-CoV2 infection disrupts the barrier and transport function (bile acid transport) of cholangiocytes, leading to toxic damage to cholangiocytes by bile acids (Zhao B. et al, 2020). A number of studies have shown that liver damage in the context of COVID-19 involves a systemic inflammatory response, viral replication, and drug-induced injury. A direct association has been demonstrated between systemic inflammation involving ferritin, IL-2, and C-reactive protein (CRP), liver injury, and hepatotoxicity (Banks RE et al, 2020; Gauldie J. et al, 2021), as well as a strong association between the level of IL-6, acute-phase mediators of inflammation, and AST activity in peripheral blood serum (Drexler JF. et al, 2021).

It is well established that scientific and clinical studies on the timely diagnosis of liver damage in coronavirus infection emphasize the importance of determining blood biomarkers such as albumin concentration in peripheral blood, ALT, AST, GGT, LDH, and others (Chai X, Hu L et al, 2020; Gholizadeh P et al, 2020). A retrospective study conducted in the United States and including more than 1800 patients with COVID-19 revealed an increase in ALT, AST, and alkaline phosphatase (ALP) upon admission in 41.6%, 66.9%, and 13.5% of patients, and in the middle of hospitalization in 61.6%, 83.4%, and 80% of patients, respectively (Hundt MA et al, 2020). According to some researchers, bilirubin concentration in patients with COVID-19 can increase to 2 times the normal value, but jaundice is a rare symptom (Cai Q. et al, 2020; El Ouali S, Romero-Marrero C et al, 2020; Jaza L. et al, 2020). It has been established that the severity of COVID-19 correlates with an increase in the activity of ALT, AST, and alkaline phosphatase in the peripheral blood serum and a decrease in albumin concentration (Cai Q, Huang D. et al, 2020; Hundt MA, Deng Y. et al, 2020; Mantovani A, Beatrice G. et al, 2020).

In recent years, Karimov M.M., Muminov D.K., Daminov B.T., Alyavi A.L., and Gadaev A.G. have been conducting research in Uzbekistan aimed at early diagnosis and optimization of therapy for patients with various clinical variants of post-COVID syndrome. An analysis of the current state of the problem revealed that impaired structural and functional liver function in COVID-19 patients is widespread and potentially detrimental in the late post-infection period.

Further study of the severity of these abnormalities, identification of factors that contribute to liver damage progression, and development of methods for their correction are urgent issues.

Aim of research: To analyze contemporary research articles to examine the functional and structural state of the liver in patients who have recovered from COVID-19.

Research methods: The study included research articles using databases such as PubMed, ResNet, eLibrary, Scopus, and Web of Science. The search was conducted using the English keywords "Coronavirus Disease 2019" and "Liver dysfunction," which identified relevant studies on this issue.

Epidemiology of COVID-19-associated liver injury. COVID-19, which has caused a pandemic that has spread worldwide over the past 3 years, is also associated with infection by the SARS-CoV2 virus [1, 2; pp. 250-256]. Early symptoms of COVID-19 include fever, cough, myalgia, and general weakness. Severe infection, observed in 15-20% of patients, is characterized by shortness of breath and can progress to acute respiratory distress syndrome (ARDS) and multiple organ failure (MOF) [3; pp. 497-506]. In addition to respiratory syndromes, SARS-CoV2 can cause liver damage, accompanied by manifestations of cytolytic and cholestatic syndromes. Pathogenetic mechanisms of liver damage in COVID-19 can be various factors - direct viral damage, severe systemic inflammatory response, hypoxia, drug-induced toxic damage, as well as activation of pre-existing liver pathology [4; pp. 1278-1281, 5; pp. 18-24]. The degree of liver dysfunction can vary from an asymptomatic increase in serum transaminases and/or bilirubin to severe hepatocellular failure [6; pp. 1231-1240].

If liver damage persists, there is a high risk of chronicity of the pathology and progression of hepatobiliary dysfunction in the future, after recovery from COVID-19. In sepsis, the liver is one of the most important organs regulating metabolic processes and the activity of the systemic inflammatory response. It is believed that metabolic liver dysfunction against the background of sepsis is associated with the progression of pathology to MOF [7; p.335-337]. Patients with metabolic liver dysfunctions, especially with autoimmune lesions or against the background of post-transplant immunosuppression, demonstrate an increased risk of infection due to disruption of the normal functioning of the immune system. Patients with liver cirrhosis have a high risk of decompensation against the background of systemic bacterial, fungal or viral infection [8; pp.220-245]. Hepatobiliary symptoms in patients with COVID-19 can be observed against the background of respiratory symptoms or without them. Hepatobiliary symptoms are associated with a worse clinical prognosis and an increased risk of mortality [9; pp.521-523]. Clinical and biochemical manifestations of liver damage should be carefully monitored taking into account the previous functional state of the organ and the therapy used for the infection [10,26].

In a systematic review published in September 2020, the cumulative prevalence of acute liver injury was 23.7 cases (16.1-33.1) per 100 COVID-19 patients [11; pp. 711-722]. In another meta-analysis, the incidence of liver injury was 19% (1-53%). Hypoalbuminemia (26.3-30.9 g/L) was more common in patients with severe infection (6%). The incidence of elevated serum alanine, aspartame aminotransferase (ALT and AST) and bilirubin levels was 18% (13-25%), 21% (14-29%) and 6% (3-11%), respectively [12; pp. 667-678]. Elevated levels of ALT, AST and bilirubin are associated with a prolonged period of hospitalization. Liver damage is more prevalent in patients with severe compared to moderate infection [13]. In fatal COVID-19 cases, the incidence of clinically evident liver dysfunction is 58%-78% [27,28].

Conclusion

It is generally recognized that increased levels of ALT, gamma-glutamyl aminotransferase (GGT), and bilirubin associated with COVID-19 are more pronounced in men compared to women [12,26] and in younger patients compared to older ones [13; pp. 807-817]. Hyperfermentemia is less common in children than in adults, as are lung damage and severe cases of the disease. Moreover, this also applies to children with pre-existing liver pathology [14; pp. 1547-1551, 15; pp. 1663-1665, 16; pp. 689-696]. Children under 18 years of age are less likely to show signs of liver damage compared to adults: 10% [17; p. 1561, 18] versus 18% [19; pp. 1518-1519, 20, 21, 22, 23, 24], although the difference is not statistically significant [25; pp. 667-678].

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SURGICAL APPROACHES TO INFERIOR OBLIQUE MUSCLE OVERACTION IN ATYPICAL STRABISMUS: A LITERATURE REVIEW

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Abstract. *Inferior oblique muscle overaction (IOOA) is one of the most frequent motility disorders associated with atypical strabismus, particularly in V-pattern deviations. This condition significantly affects ocular alignment, binocular vision, and quality of life, while also complicating surgical planning and influencing postoperative stability. Several surgical approaches have been developed to correct IOOA and are currently performed by strabismus surgeons. The aim of this article is to summarize the modern surgical techniques used in the management of IOOA based on a literature review. Recent publications, reports, guidelines, and textbooks were analyzed. According to the review, weakening procedures-including recession, myectomy, myotomy, and anterior transposition-are the most widely employed surgical methods. Each technique has its own advantages and limitations, and evidence suggests that surgical success depends on the severity of IOOA, the type of atypical strabismus, and the individual anatomy of the patient. Moreover, combined surgical approaches are increasingly utilized to improve both functional and cosmetic outcomes. In conclusion, although surgical management of IOOA in atypical strabismus is effective, it remains a complex challenge. An individualized approach tailored to each patient is essential for achieving optimal results. Future long-term follow-up studies will play a crucial role in establishing standardized surgical guidelines for IOOA correction.*

Keywords: *inferior oblique muscle overaction, atypical strabismus, surgical management, V-pattern.*

Introduction. Strabismus, defined as both a cosmetic and functional disorder of binocular vision and the oculomotor system, represents a significant ophthalmologic as well as social problem. The prevalence of strabismus in the general population is estimated to range between 2% and 5% [1]. Atypical forms of strabismus are relatively uncommon but clinically significant disorders of ocular motility, often presenting with complex deviations that cannot be explained by simple horizontal or vertical misalignment. Among these, V-pattern strabismus associated with inferior oblique muscle overaction (IOOA) is one of the most frequently observed variants in pediatric ophthalmology. IOOA is clinically characterized by overelevation of the eye in adduction and is reported to occur in approximately 70% of patients with esotropia and 30% of those with exotropia [2]. According to Chang B.L. and Yang S.W. (1988), inferior oblique overaction is considered the most frequent type among all extraocular muscle overactions [3,5].

The presence of this condition may cause abnormal ocular alignment, impair binocularity, and influence psychosocial development in children. From a surgical standpoint, IOOA remains a challenging problem. Although multiple procedures such as recession, myectomy, myotomy, and anterior transposition of the inferior oblique muscle have been introduced, there is still no universal consensus regarding the optimal surgical method [4]. Each approach has distinct advantages and limitations, and the choice largely depends on the degree of muscle overaction, the type of

associated strabismus, and individual anatomical variations (Parks, 1972; Mims, 1993). Furthermore, atypical forms of strabismus are often accompanied by additional motility disorders, which complicate surgical planning and may affect postoperative stability. Therefore, a comprehensive analysis of the existing literature is essential to identify the most effective strategies for managing IOOA in atypical strabismus. The present review aims to summarize current knowledge on surgical approaches for inferior oblique overaction, to compare their reported outcomes, and to underline the importance of individualized surgical planning in achieving optimal functional and cosmetic results.

Materials and Methods. A comprehensive literature search was conducted to identify studies related to inferior oblique muscle overaction (IOOA) and its surgical management in atypical strabismus, particularly V-pattern deviations. The search was performed electronic databases, including Google Scholar, Science Direct, Scopus and PubMed, covering the period from 1980 to 2025. Keywords used were: “inferior oblique muscle overaction”, “IOOA”, “V-pattern strabismus”, “atypical strabismus”, “oblique muscle surgery” “recession” “myectomy”, “anterior transposition”. Only peer-reviewed articles, clinical studies, systematic reviews, and case series published in English and Russian were included. The references of the included studies were also screened to identify additional relevant publications. This approach ensured that the review summarized the most relevant and up-to-date evidence available on surgical strategies for inferior oblique overaction in atypical strabismus.

Results and Discussion. Frequency in the Literature and Clinical Characteristics. Inferior oblique muscle overaction (IOOA) is one of the most frequent ocular motility disorders associated with strabismus. Its prevalence varies depending on the underlying type of deviation and patient population. Several studies have demonstrated a strong relationship between IOOA and horizontal deviations such as esotropia and exotropia, where it contributes to the development of characteristic motility patterns. According to Wilson M.E. and Parks M.M., IOOA was observed in 72% of patients with congenital esotropia at a mean age of 3. 6 years, in 34% of patients with accommodative esotropia at a mean age of 5.2 years, and in 32% of patients with intermittent exotropia, also at a mean age of 5.2 years [3]. These findings highlight that IOOA is not confined to a single form of strabismus but can occur across different subtypes, with particularly high prevalence in congenital esotropia. In atypical strabismus, IOOA most commonly presents in association with V-pattern deviations, both in exotropia and esotropia. In these cases, the deviation decreases in downgaze and increases in upgaze, reflecting the dominant role of the inferior oblique muscles.

IOOA is also frequently encountered in dissociated vertical deviation (DVD), where excessive inferior oblique activity produces an upward and outward drift of the eye. In skew deviation and paretic strabismus, such as trochlear nerve (cranial nerve IV) palsy, weakness of the superior oblique muscle often leads to compensatory IOOA [5]. Additionally, it may occur in more complex atypical patterns, such as A-V, Y, or other irregular motility deviations, where imbalances between multiple extraocular muscles contribute to overelevation in adduction. From a symptomatic perspective, patients may complain of diplopia (double vision), especially in upward and outward gaze, due to abnormal ocular alignment. They can also exhibit limitation of ocular motility, visible strabismus with outward deviation of the eye, and asthenopia or headaches related to muscular strain. To minimize diplopia and visual discomfort, many adopt a compensatory head posture, which can become habitual and affect daily functioning [6]. Taken together, the literature demonstrates that IOOA represents a frequent and clinically significant feature of atypical

strabismus. Its manifestations extend beyond simple overelevation and involve a wide spectrum of motor and sensory dysfunctions, which must be carefully considered in diagnostic evaluation and in planning surgical correction.

Surgical approaches. The surgical treatment of inferior oblique overaction (IOOA) in atypical strabismus represents one of the most debated areas in pediatric ophthalmology. The goal is to restore ocular alignment, minimize abnormal motility patterns such as V-pattern or dissociated vertical deviation (DVD), and improve binocular vision. Over the past decades, various weakening techniques have been described, each with distinct advantages, limitations, and long-term stability profiles. Coats D.K. and Olitsky S.E. (2007) proposed that the choice of weakening procedure for IOOA should be tailored to the degree of overaction: +1 – observation (marginal or complete myotomy may be considered), +2 – recession (tenotomy, myectomy, or complete myotomy), +3 – recession (tenotomy, myectomy), +4 – myectomy (recession or anterior transposition). In cases of significant residual overaction after myectomy or recession, denervation or extirpation may be performed [7,8]. Similarly, Plager D.A. and Buckley E.G. (2004) emphasized that surgical correction of IOOA is primarily indicated in the presence of a pronounced V-pattern: +1 – rarely requires surgery, +2 – occasionally requires surgery, +3 – often requires surgery, and +4 – always requires surgery, with no alternative to surgical treatment [8].

1. Myectomy and Myotomy. Inferior oblique weakening can be achieved through myectomy, which entails excision of a muscle segment, or myotomy, which involves simple transection of the muscle. Both techniques are regarded as straightforward, commonly performed, and effective surgical options, often producing an immediate decrease in inferior oblique overaction. Despite their technical simplicity, long-term results may be inconsistent, largely due to unpredictable muscle reattachment, which can lead to residual overaction or late recurrence [Del Monte & Parks, 1983]. Myectomy is generally indicated for pronounced inferior oblique overaction or in cases associated with dissociated vertical deviation, whereas myotomy is more frequently selected for less severe involvement. Several modified techniques, collectively referred to as edge or marginal myotomy—including I-, Z-, and W-shaped incisions—have been introduced as alternative approaches. Among these, Z-myotomy has received particular interest for the management of mild inferior oblique overaction (+1 to +1.5) [9]. Originally described by De Decker and Kueper in 1973, this method consists of creating two longitudinal cuts along opposite borders of the muscle while preserving its original insertion. The procedure is relatively brief, technically uncomplicated, and carries a low risk of scleral perforation or vortex vein injury, as scleral suturing is not required. Previous studies have demonstrated that Z-myotomy provides sufficient weakening in small-angle yet symptomatic cases, where more aggressive procedures such as recession or myectomy could increase the risk of overcorrection [10]. Nevertheless, both myectomy and myotomy are associated with potential limitations, particularly undercorrection or recurrence over time. Consequently, in complex or atypical forms of strabismus, many surgeons favor combining these procedures with horizontal rectus muscle surgery to enhance surgical outcomes.

2. Inferior Oblique Recession. Inferior oblique recession is regarded as a standard surgical strategy in the treatment of inferior oblique overaction (IOOA) due to its consistent effectiveness and broad clinical acceptance. The principle of this technique is not direct muscle weakening through cutting or removal, but rather functional attenuation achieved by relocating the site of muscular attachment. By shifting the insertion to a position posterior and lateral to that of the

inferior rectus muscle, the vertical elevating force and excyclotorsional contribution of the inferior oblique are substantially diminished, improving ocular alignment.

The extent of muscle displacement is individualized and determined by the severity of overaction observed during clinical assessment. Minimal inferior oblique hyperactivity is typically corrected with a small recession of around 6 mm, while intermediate cases require a greater posterior shift of approximately 10 mm. In situations characterized by pronounced overaction, the recession may be increased to nearly 14 mm. These measurements function as flexible reference values and are routinely modified to accommodate patient-specific anatomical differences and the degree of functional imbalance [11, 12].

In standard practice, recession is usually performed at distances of 10 mm, 12 mm, or 14 mm. During the procedure, the muscle hook is passed beneath the inferior rectus insertion with the globe rotated upward to optimize exposure. Importantly, the eye should not be rotated inward or outward, as this may alter the relative position of the muscle edge. A 10-mm recession positions the anterior edge 3 mm posterior and 2 mm temporal to the lateral border of the inferior rectus insertion; a 12-mm recession places it 6–8 mm posteriorly; while a 14-mm recession locates it 8–10 mm posteriorly and close to the lateral border of the inferior rectus muscle. In the latter case, suturing over the muscle is sometimes necessary due to the proximity of the inferotemporal vortex vein, which poses a potential risk of injury[13].

A specific modification, Fink's recession, involves posterior displacement of the inferior oblique along its anatomical course. In this technique, the anterior border of the new insertion is positioned 6 mm inferior and posterior to the inferior end of the lateral rectus insertion, corresponding to an approximate 8-mm recession. This method provides a predictable and physiologic weakening effect while maintaining the natural vector of the muscle's action [14]. Overall, recession remains the most widely practiced and versatile weakening procedure for IOOA, with advantages of stable alignment, graded weakening potential, and applicability in both isolated overaction and atypical strabismus patterns.

3. Anterior Transposition (Anteriorization). The concept of weakening the inferior oblique (IO) muscle through transposition was first mentioned in the 1940s, although the term transposition at that time was largely applied to traditional recession procedures in cases of marked IO overaction.

A novel approach was introduced in 1981 by Elliot and Nankin, who described anterior transposition for severe bilateral IO overaction [15]. The principle consists of relocating the IO insertion from its natural posterior position to the anterior segment of the globe, thereby changing its plane of action and converting the muscle configuration into a J-shape. In this technique, the Lockwood ligament and the neurovascular bundle act as the axis of rotation. Later, Wright (2007, 2015) proposed a graded anterior transposition depending on the degree of overaction:

+1 IOOA: 4 mm posterior and 3 mm lateral to the inferior rectus insertion,

+2 IOOA: 3–4 mm posterior,

+3 IOOA: 1–2 mm posterior,

+4 IOOA: directly adjacent to the inferior rectus insertion [16, 8].

Several modifications have been described to optimize outcomes and reduce complications:

Full anterior transposition – indicated for severe IOOA with DVD;

Graded anterior transposition – allows individualized weakening;

Modified anteriorization – anterior fibers placed close to the inferior rectus, posterior fibers slightly posterior, minimizing AES;

J-shaped anterior transposition – mainly used for marked bilateral IOOA with DVD.

In clinical practice, anterior transposition is especially valuable for IOOA associated with DVD, where recession alone is often insufficient. However, in V-pattern strabismus, this technique is less advantageous, as other weakening procedures such as recession or myectomy usually provide more stable outcomes [17, 18].

4. Combined Techniques. In recent years, combined surgical approaches have been increasingly applied in the management of inferior oblique muscle (IO) overaction. The primary objective of these techniques is not only to weaken the overacting muscle but also to address associated ocular motility disorders that frequently coexist. The most widely used combinations include:

IO anterior transposition + inferior rectus surgery – indicated in cases of dissociated vertical deviation (DVD), hypertropia in upgaze, and V-pattern deviations. This approach provides better alignment by correcting both vertical deviation and motility imbalance.

IO recession + lateral rectus recession – most commonly applied in V-pattern exotropia, where IO overaction contributes to the pattern deviation and is effectively managed in combination with weakening of the horizontal rectus.

Anteriorization combined with myotomy or partial myectomy – reserved for severe IO overaction, particularly when standard anterior transposition is insufficient. This method further reduces the excessive pulling force of the IO muscle.

Bilateral combined procedures – frequently indicated in bilateral IO overaction with DVD, where symmetric correction ensures improved ocular alignment and preservation of binocular function [19].

In 2015, Tomarchio S. introduced an innovative surgical method known as the equatorial scleral anchor technique. In this procedure, the IO muscle is sutured 11 mm posterior to its insertion at the Gobin point, without detachment of the muscle belly. This modification, considered an anteroposition of the IO with scleral fixation near the equator, has demonstrated favorable outcomes in patients with mild to moderate IO overaction, while minimizing the risks associated with belly dissection [20].

Furthermore, a novel combined surgical approach has been developed for the management of bilateral asymmetric IO overaction. This technique incorporates inferior oblique belly transposition in one eye and contralateral IO recession in the other, aiming to achieve balanced weakening of both oblique muscles. Clinical evidence suggests that this strategy provides effective correction and functional improvement in asymmetric IOOA cases.

The advantage of combined techniques lies in their ability to simultaneously correct complex or atypical forms of strabismus by addressing multiple contributing factors. However, the main limitation remains the increased surgical extent, which can complicate the prediction of postoperative muscle balance and long-term alignment stability [21].

Long-Term Outcomes and Complications. Long-term evaluation of inferior oblique (IO) weakening procedures demonstrates that while most patients achieve satisfactory ocular alignment, the stability of results and the risk of recurrence remain significant considerations. Reoperation rates are not negligible, particularly in cases with severe or asymmetric IO overaction, or when atypical strabismus patterns such as dissociated vertical deviation (DVD) and V-pattern are present [22].

Surgical weakening of the IO is also associated with several important complications. Recurrence of IO overaction is one of the most common, frequently requiring secondary intervention. In the case of IO transposition procedures, the absence of reliable surgical dosing methods often leads to overcorrection of hypertropia, whereas recession and other weakening techniques may produce an insufficient corrective effect. Persistent IO overaction immediately after surgery has been attributed to incomplete dissection of muscle fibers at their scleral insertion, particularly in patients with broad or anatomically variant insertions, such as double or triple fiber bundles. If unrecognized, these anomalies can significantly reduce surgical effectiveness.

The anatomical complexity of the IO muscle and its proximity to vortex veins increase the risk of intraoperative hemorrhage during both recession and transposition procedures. Reports also describe severe retrobulbar hemorrhage that can threaten vision. Furthermore, dissection in the posterior pole carries the risk of damaging Tenon's capsule, which may result in orbital fat prolapse, scarring, and subsequent restriction of ocular motility.

Even after apparently successful transposition, recurrence of hypertropia may occur. This has been linked to chronic stretching of the posterior temporal muscle fibers between the neurofibrovascular bundle and the new insertion site, leading to posterior retraction after suture absorption and weakening of the corrective effect. Additionally, traumatic handling of the muscle fibers during dissection may predispose to slippage.

Among the most serious complications of IO transposition is the development of anti-elevation syndrome (AES). This condition manifests as restriction of elevation in abduction of the operated eye and paradoxical overelevation of the contralateral eye in adduction. The mechanism is believed to involve overstretching of the distal IO fibers and neurofibrovascular bundle during anterior displacement. In some cases, this overstretching may even produce transient paresis of the oculomotor nerve branches, clinically evident as temporary postoperative pupillary dilation [15].

Despite the extensive literature on IO weakening procedures, no single technique has been universally recognized as the method of choice. Future directions should emphasize individualized approaches, including the use of cyclodeviation assessment, advanced diagnostic imaging, and mathematical modeling of IO biomechanics. Development of refined dosing systems would allow surgeons to balance surgical efficacy with safety, minimize iatrogenic complications, and achieve more consistent long-term functional outcomes [23].

Discussion. The present analysis highlights the complexity of surgical management of inferior oblique muscle (IO) overaction, particularly in cases associated with dissociated vertical deviation (DVD), V-pattern strabismus, and other atypical ocular motility disorders. Anterior transposition of the IO has emerged as one of the most widely applied procedures, providing effective weakening of IO overaction and offering substantial benefits in controlling DVD. Various modifications of this technique, including graded anterior transposition and differential positioning of anterior and posterior fibers, have been developed to improve surgical predictability and outcomes.

In recent years, combined surgical approaches have gained increasing importance. For example, IO anterior transposition combined with inferior rectus surgery, or IO recession combined with lateral rectus recession, has been shown to enhance alignment in complex forms of strabismus. These procedures are particularly effective in bilateral IO overaction with asymmetry, where symmetric correction helps restore ocular alignment and maintain binocular function. However, the broader surgical extent involved in combined techniques introduces challenges,

including the risk of overcorrection and the difficulty of predicting postoperative muscle balance [24, 25].

Long-term follow-up studies generally report positive surgical outcomes, with the majority of patients demonstrating adequate correction of hypertropia and improved ocular motility. Despite these encouraging results, certain challenges persist, including ongoing or recurrent inferior oblique overaction, residual vertical deviation, and suboptimal surgical correction. These limitations have been attributed to several factors, such as individual anatomical variability of the inferior oblique muscle, insufficient release at the insertion site, or gradual elongation of posterior muscle fibers after anterior transposition, which may lead to a progressive decline in the effectiveness of the procedure over time [15, 8].

In summary, anterior transposition of the inferior oblique muscle continues to represent a fundamental surgical option for managing inferior oblique overaction. Nonetheless, optimal surgical decision-making requires an individualized approach that takes into account the severity of overaction, coexistence of dissociated vertical deviation, the presence of V-pattern strabismus, and any accompanying horizontal deviations. Further investigations employing standardized assessment protocols, modern imaging techniques, and biomechanical analysis are necessary to refine surgical strategies, minimize recurrence rates, and enhance long-term functional outcomes.

Conclusion. Inferior oblique muscle overaction (IOOA) in the context of atypical strabismus remains one of the most complex and debated issues in pediatric ophthalmology. A wide spectrum of surgical techniques has been described, including myotomy, myectomy, recession, anterior transposition, and various combined approaches. Each of these methods has its own advantages and limitations, and none can be considered universally applicable.

Recession and myectomy are simple and widely practiced procedures, providing predictable weakening in mild to moderate IOOA. Anterior transposition, particularly in graded or modified forms, has demonstrated high effectiveness in severe IOOA and cases associated with dissociated vertical deviation, though it requires careful consideration of postoperative motility. Combined approaches are increasingly employed in complex and asymmetric forms of strabismus, allowing simultaneous correction of multiple deviations.

Despite these advances, long-term outcomes indicate that recurrence, residual overaction, or insufficient correction may still occur. Therefore, the choice of surgical technique must be individualized, taking into account the degree of overaction, type of strabismus pattern, and anatomical variations of the inferior oblique muscle.

Overall, contemporary evidence highlights that successful management of IOOA requires a tailored approach, supported by accurate preoperative assessment and careful intraoperative technique. Further research, particularly long-term prospective studies, is essential to refine surgical methods and improve functional as well as cosmetic outcomes for patients with atypical strabismus.

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RETROSPECTIVE ANALYSIS OF CONGENITAL HEART DEFECTS AND POSTOPERATIVE COMPLICATIONS IN EARLY CHILDHOOD CARDIAC SURGERY

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Abstract. *Congenital heart defects (CHDs) are among the most common congenital anomalies in children and are associated with significant morbidity and mortality. Early surgical correction is often required to restore normal cardiac function; however, these procedures can be complicated by postoperative adverse events, including acute kidney injury (AKI), which may prolong hospitalization, increase intensive care unit (ICU) stay, and elevate in-hospital mortality. Both maternal health and prenatal conditions, such as iron deficiency anemia, infections, and obstetric complications, as well as perioperative factors, can influence the development of CHDs and impact postoperative outcomes. This retrospective study analyzed 110 children aged 6 months to 3 years who underwent cardiac surgery for CHDs. Maternal history, perioperative data, and postoperative outcomes were assessed, and patients were categorized based on the occurrence of postoperative AKI. Logistic regression analysis was performed to identify independent risk factors associated with AKI. The findings highlight that maternal and prenatal factors, including viral and TORCH infections, threatened miscarriage, and chronic urogenital infections, significantly contribute to the risk of CHDs. Perioperative factors, such as low body weight, hypotension, and prolonged surgery, were identified as independent predictors of postoperative AKI. These results underscore the importance of comprehensive evaluation of maternal history and careful perioperative management to reduce complications and improve recovery in children undergoing cardiac surgery for CHDs.*

Keywords: *congenital heart defects, pediatric cardiac surgery, maternal health, prenatal risk factors, acute kidney injury, postoperative complications.*

Introduction

Congenital heart defects (CHDs) are the most prevalent type of congenital malformations in children and continue to be a major cause of morbidity and mortality globally. Surgical correction of CHDs in early childhood is frequently associated with perioperative and postoperative complications, including acute kidney injury (AKI), which can lead to prolonged hospitalization, extended ICU stays, and increased in-hospital mortality. Therefore, identifying factors related to CHDs and predictors of postoperative complications is essential for improving patient outcomes.

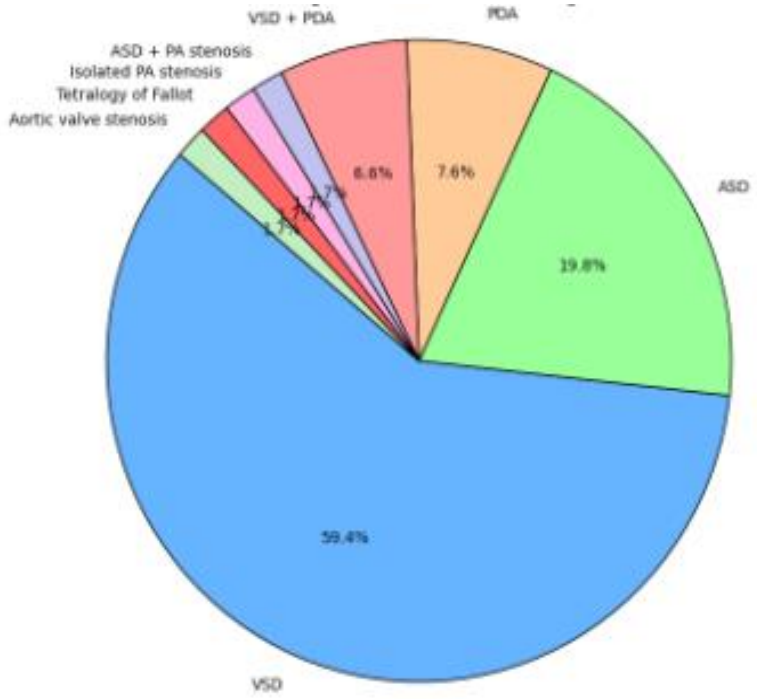
Maternal health and prenatal conditions play a critical role in the development of CHDs. Factors such as iron deficiency anemia, obstetric complications, chronic or acute infections, and metabolic disorders can adversely affect fetal cardiac development, resulting in structural anomalies such as ventricular septal defect, atrial septal defect, and Tetralogy of Fallot. Notably, infections occurring during the first trimester, including viral and TORCH infections, as well as

persistent urogenital infections, have been linked to a higher risk of CHDs in offspring. Additionally, a complicated obstetric history, including spontaneous miscarriages and threatened miscarriage, further increases this risk.

Beyond maternal and prenatal influences, perioperative factors also contribute to adverse postoperative outcomes like AKI. Low body weight, hypotension, prolonged surgical procedures, and extended cardiopulmonary bypass have been recognized as independent risk factors for the development of AKI in pediatric patients undergoing cardiac surgery. Despite improvements in surgical techniques and perioperative management, postoperative AKI remains a frequent and serious complication, highlighting the importance of thorough evaluation of both maternal history and preoperative risk factors to optimize surgical outcomes. This study aims to examine clinical, maternal, and perioperative factors and to identify independent predictors of postoperative AKI in children undergoing cardiac surgery for CHDs in early childhood. Study objective. The aim of this study was to analyze the clinical characteristics, perioperative factors, and maternal history associated with congenital heart defects in children, and to identify independent risk factors for the development of postoperative acute kidney injury (AKI) following cardiac surgery in early childhood.

Picture No.1

Distribution of congenital heart defects among 110 children



Materials and methods. A retrospective analysis of medical records was conducted in the Department of Pediatric Cardiac Surgery at the Specialized Scientific and Practical Medical Center of Cardiology and Cardiac Surgery of the Aral Region. The study included 110 children with congenital heart defects who underwent surgical interventions between 2022 and 2025. The patients' ages ranged from 6 months to 3 years, with a mean age of 21 ± 8.7 months. Of these, 57 children (63.3%) were boys and 53 (36.7%) were girls. In this study, particular attention was paid to maternal history, including complaints, occupational hazards, and the presence of chronic diseases (age at disease onset, duration, and medication use), as well as gynecological history

(previous illnesses, outcomes of prior pregnancies, course of the current pregnancy, gestosis, medication use during the current pregnancy, and details of the current delivery).

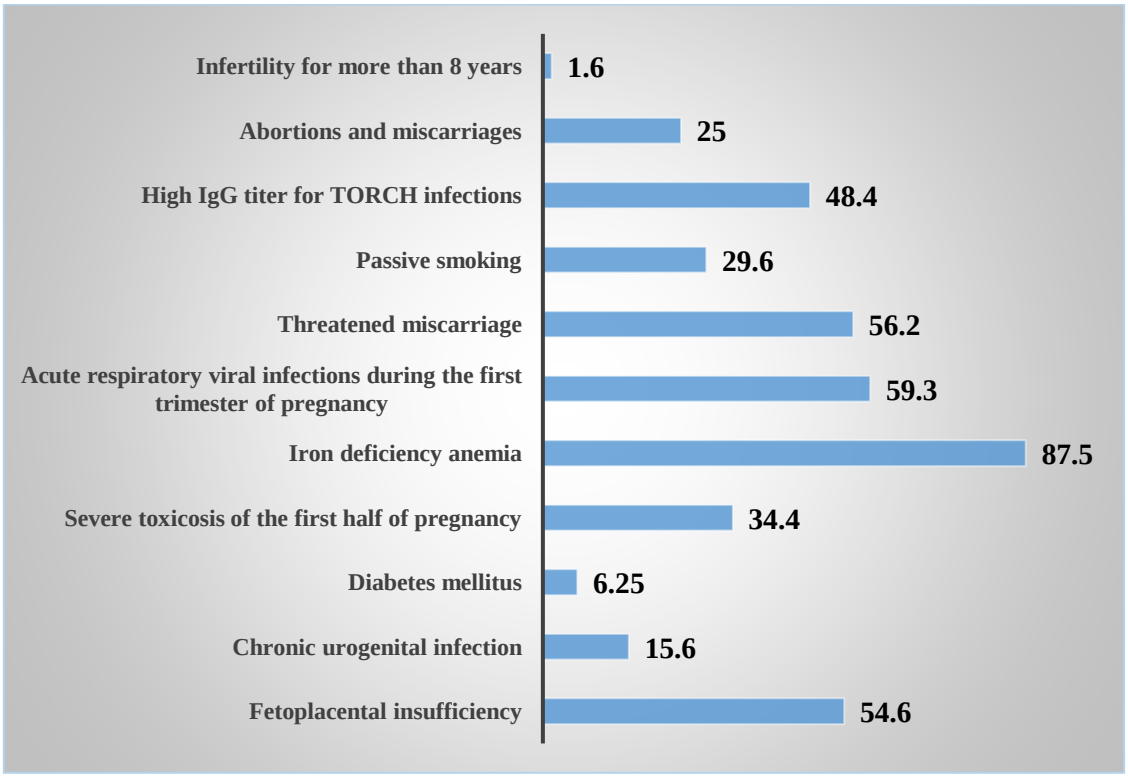
The use of mechanical ventilation during surgery was also recorded. Patients were divided into two groups based on the occurrence of postoperative acute kidney injury (AKI): the AKI group (n = 90) and the non-AKI group (n = 20). Clinical data were compared between the two groups, including demographic characteristics (sex, age, weight), preoperative, intraoperative, and postoperative parameters, duration of mechanical ventilation, length of hospital stay and intensive care unit (ICU) admission, treatment costs, and in-hospital mortality. Logistic regression analysis was performed to identify risk factors for postoperative AKI.

Results and Discussion. During the period 2022–2025 in the Khorezm region of the Republic of Uzbekistan, among 110 children who underwent surgery for congenital heart defects, ventricular septal defect (VSD) was identified in 63 children (57.3%). Atrial septal defect (ASD) was diagnosed in 21 children (19.1%), and patent ductus arteriosus (PDA) in 8 children (7.3%). A combination of VSD and PDA was found in 7 children (6.4%). The least common defects included ASD with pulmonary artery stenosis, isolated pulmonary artery stenosis, Tetralogy of Fallot, and aortic valve stenosis, each accounting for 1.6% of cases (pic.1).

During the analysis of maternal anamnesis data of children born with congenital heart defects, factors were identified that may have influenced the development of anatomical abnormalities of the cardiac structures during the intrauterine period (Figure 2).

Figure 2.

Characteristics of the maternal medical history of children born with congenital heart defects (%)



According to the data presented, the majority of mothers (87.5%) experienced the current pregnancy against the background of iron deficiency anemia, which is known to cause chronic hypoxia and fetal growth restriction. A complicated obstetric history, including spontaneous miscarriages and abortions, was noted in 25% of mothers, threats of miscarriage in early gestation

in 56.2%, and fetoplacental insufficiency in 54.6%. Previous studies have demonstrated that a history of early spontaneous miscarriages increases the risk of congenital heart defects in the fetus, such as Tetralogy of Fallot by 1.5-fold and atrial septal defect by 2-fold. Additionally, 59.3% of expectant mothers suffered from acute viral infections during the first trimester, and 48.4% showed high IgG titers against TORCH infections (herpes, toxoplasmosis, cytomegalovirus) according to enzyme-linked immunosorbent assay results. It has been established that bacterial and viral infections accompanied by fever during the first trimester increase the risk of congenital heart defects in the fetus by 2–3 times, with the most common defects being ventricular septal defect, aortic coarctation, and pulmonary valve anomalies. Persistent opportunistic and viral infections in the mother have also been identified as significant risk factors for the development of congenital heart defects in children, with herpes and cytomegalovirus infections most frequently causing malformations of the primary and secondary atrial septa during embryonic development.

Previous studies have demonstrated a link between chronic maternal urogenital infections and the risk of congenital heart defects in offspring involving obstruction of the right heart chambers [7]. In our study, 15.6% of mothers had persistent urogenital infections during pregnancy. To assess the significance of these associations, logistic regression analysis was performed. The calculation of odds ratios allowed the identification of the most significant risk factors for the development of congenital heart defects in children, as presented in Table 1.

Table 1.

Factors associated with the development of congenital heart defects in children

Factor	**OR**	**95% CI**	**p-value**
Threatened miscarriage	2.54	1.10–5.88	0.029
High IgG titer for TORCH infections	3.63	1.92–6.87	0.0001
Fetoplacental insufficiency	1.17	1.10–1.25	0.0001
Severe toxicosis in the first half of pregnancy	2.46	1.01–5.97	0.001
Chronic urogenital infection	3.21	1.84–6.25	0.031
Maternal diabetes mellitus	1.16	1.06–1.26	0.0001
Acute respiratory viral infections in the first trimester	4.37	1.35–14.11	0.0001

Note: OR – odds ratio; CI – confidence interval; p – statistical significance

As shown in Table 1, the development of anatomical abnormalities of cardiac structures during the intrauterine period is strongly associated with maternal history characteristics in children with congenital heart defects. According to logistic regression analysis, the most significant risk factors were acute respiratory viral infections in the first trimester of pregnancy (OR 4.37; 95% CI 1.35–14.11), high IgG titers for TORCH infections (OR 3.63; 95% CI 1.92–6.87), and threatened miscarriage (OR 2.54; 95% CI 1.10–5.88).

Compared to the non-AKI group, children in the AKI group had lower body weight [(7.2 ± 4.3) kg vs. (10.9 ± 2.6) kg, P = 0.025] and mean arterial pressure (MAP) [(90.3 ± 20.1 mmHg vs. 110.2 ± 15.6 mmHg, P < 0.001], but longer durations of surgery [(250.3 ± 78.8 min vs. 150.1 ± 54.2 min, P < 0.001], cardiopulmonary bypass [(201.2 ± 49.9 min vs. 70 ± 29.2 min, P < 0.001], and mechanical ventilation. The AKI group also exhibited prolonged mechanical ventilation, longer stays in the intensive care unit, extended hospitalization, and higher in-hospital mortality. Multivariate logistic regression analysis identified lower body weight (OR = 0.589, 95% CI: 0.398–0.802, P = 0.005), lower mean arterial pressure (OR = 0.829, 95% CI: 0.791–0.969, P =

0.001), and longer surgical duration (OR = 3.035, 95% CI: 2.016–1.054, P < 0.001) as independent risk factors for the development of acute kidney injury (AKI).

Conclusion

The study demonstrates that the development of congenital heart defects in children is strongly associated with maternal factors, including iron deficiency anemia, obstetric complications, TORCH infections, acute respiratory viral infections in the first trimester, and chronic urogenital infections. Logistic regression analysis identified acute respiratory viral infections, high maternal IgG titers for TORCH infections, and threatened miscarriage as the most significant risk factors for congenital heart defects. Furthermore, postoperative AKI in children was significantly associated with lower body weight, lower mean arterial pressure, and longer surgical duration. These findings highlight the importance of comprehensive maternal and perioperative assessment to identify high-risk patients and implement strategies aimed at reducing postoperative complications and improving outcomes in pediatric cardiac surgery.

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COMPARATIVE ANALYSIS OF VARICOSE VEIN RECURRENCE RATES AFTER ENDOVENOUS LASER ABLATION OF THE GREAT SAPHENOUS VEIN WITH PRESERVATION VERSUS SIMULTANEOUS ABLATION OF THE ANTERIOR ACCESSORY SAPHENOUS VEIN

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Abstract. *Aim of the research is to evaluate the effect of simultaneous endovenous laser ablation (EVLA) of the anterior accessory great saphenous vein (AAGSV) with a diameter greater than 5 mm, in the absence of baseline reflux, on the recurrence rate of varicose vein disease within one year after EVLA of the great saphenous vein (GSV) trunk. This prospective single-center study included 100 patients (78 women and 22 men) with CEAP clinical classes C2–C4 who underwent EVLA of the GSV between October 2023 and October 2024. Patients were divided into two groups: Group I (n = 50) underwent EVLA of the GSV only; Group II (n = 50) underwent EVLA of the GSV with simultaneous EVLA of the AAGSV (diameter >5 mm, without baseline reflux). A 1470-nm diode laser with a radial fiber (IPG, Russia) was used at a power of 7 W, with a pullback speed of 1 mm/s and a linear endovenous energy density of approximately 70 J/cm. Tumescent anesthesia consisted of 0.03% lidocaine (300–350 mL). Pathological reflux was defined as retrograde flow lasting more than 0.5 seconds on duplex ultrasound. Follow-up was performed at 1, 6, and 12 months. The primary endpoint was clinically significant recurrence of varicose vein disease. At 12 months, recurrence was observed in 10 patients (20%) in Group I and in 2 patients (4%) in Group II (relative risk [RR] = 0.20; 95% confidence interval [CI] 0.05–0.87; p = 0.028). The absolute risk reduction was 16 percentage points, with a number needed to treat (NNT) of 6.25. New reflux in the AAGSV was detected in 18% versus 2% of patients (RR = 0.11; 95% CI 0.015–0.845; p = 0.016). Repeat interventions were required in 12% versus 2% of cases. Patient satisfaction scores were significantly higher in Group II (9.4 ± 0.6 vs 8.1 ± 1.2; p < 0.001). The overall complication rate did not differ between groups (8% vs 10%; p > 0.05). Simultaneous EVLA of the AAGSV with a diameter greater than 5 mm, even in the absence of baseline reflux, is associated with an 80% relative reduction in varicose vein recurrence within one year. This approach does not increase the risk of complications and improves patient-reported outcomes. It may be considered a preventive strategy in patients with anatomically prominent AAGSV.*

Keywords: *varicose vein disease; endovenous laser ablation; anterior accessory great saphenous vein; recurrence; prevention; linear endovenous energy density.*

Introduction

In recent years, endovenous laser ablation (EVLA) has become firmly established as a first-line treatment for incompetence of the great saphenous vein (GSV). According to multicenter studies, the use of 1470-nm lasers with radial fibers provides primary occlusion rates exceeding 95–98% within 12 months after the procedure, remaining above 90% even after 3–5 years of follow-up [5,15]. Despite the high anatomical effectiveness of GSV trunk ablation, recurrence of varicose vein disease is reported in 15–25% of patients within 2–3 years after intervention [1]. One of the most common sources of recurrent venous reflux is the anterior accessory great saphenous vein (AAGSV), which is located in close proximity to the saphenofemoral junction and may serve as an alternative pathway for pathological reflux after exclusion of the main GSV trunk [2].

Previous studies have demonstrated that even in the absence of baseline reflux, an AAGSV diameter greater than 5 mm represents an anatomically significant risk factor for subsequent dilation and reflux development [2,4]. In addition, the AAGSV may act as a “hidden reservoir” of hemodynamic overload following GSV ablation, leading to ascending reflux and clinical recurrence [3]. According to Hamel-Desnos et al. [1], up to 40% of repeat interventions after EVLA are associated with AAGSV incompetence. These findings support the need to reconsider the role of the AAGSV even when no initial reflux is detected. In a study by Dyachkov [4], the simultaneous inclusion of the AAGSV in the ablation protocol when its diameter exceeded 5 mm reduced recurrence rates from 18–22% to 3–5% within 12 months, without an increase in complication rates.

At the same time, current clinical guidelines do not provide unified standards for the management of patients with a dilated but hemodynamically “silent” AAGSV [12]. Most treatment algorithms favor selective ablation only of tributaries with documented baseline pathological reflux. Therefore, the feasibility and effectiveness of prophylactic simultaneous EVLA of the AAGSV with a diameter greater than 5 mm in the absence of reflux remain an open question and require confirmation through comparative clinical data.

Materials and Methods.

Study Design and Setting. A prospective single-center comparative study was conducted at the VarikozOFF Clinic between October 2023 and October 2024. The study aimed to compare the recurrence rates of varicose vein disease after endovenous laser ablation (EVLA) of the great saphenous vein (GSV) with preservation of the anterior accessory great saphenous vein (AAGSV) versus simultaneous ablation of the AAGSV in the absence of baseline reflux but with a diameter greater than 5 mm.

Inclusion Criteria

- age ≥ 18 years;
- CEAP clinical class C2–C4;
- duplex ultrasound–confirmed pathological reflux in the GSV trunk (reflux duration >0.5 s);
- AAGSV diameter >5 mm in the absence of baseline reflux;
- written informed consent to participate in the study.

Exclusion Criteria

- history of deep vein thrombosis;
- active thrombophlebitis;
- CEAP class C5–C6 with active venous ulcers;
- severe comorbid conditions precluding intervention;
- pregnancy or lactation;
- previous intervention on the same limb within 6 months prior to inclusion.

Patient Allocation

Group	Intervention	n
I	EVLA of the GSV (AAGSV preserved)	50
II	EVLA of the GSV with simultaneous EVLA of the AAGSV	50

Table 1. Patients were enrolled consecutively. The groups were comparable in terms of sex, age, CEAP class, and diameters of the GSV and AAGSV.

A total of 100 patients (78 women and 22 men; mean age 46.2 ± 8.7 years) were included and evenly distributed between the two groups.

Ultrasound Examination.

Duplex ultrasound scanning was performed using a 7–12 MHz linear transducer with the patient in the standing position. The GSV diameter was measured at the level of the saphenofemoral junction and in the upper third of the thigh. The AAGSV diameter was assessed 2–3 cm distal to the junction. Pathological reflux was defined as retrograde flow lasting more than 0.5 seconds during proximal compression or the Paran maneuver. Flow velocity was recorded but was not used as a criterion for pathological reflux.

EVLA Procedure. All procedures were performed in an outpatient operating suite under tumescent anesthesia (0.03% lidocaine, 300–350 mL). A 1470-nm diode laser with a radial fiber (IPG, Russia) was used. Laser power was set at 7 W in continuous mode, with a fiber pullback speed of 1 mm/s, resulting in a linear endovenous energy density of approximately 70 J/cm. In Group II, EVLA of the AAGSV was performed using the same protocol up to the level of tributary confluence. Mini-phlebectomy of varicose tributaries was performed when indicated. Postoperatively, class II compression stockings were prescribed for 7–10 days.

Outcome Measures.

Primary endpoint: Clinically significant recurrence, defined as the appearance of new varicose veins in the treated limb combined with newly detected pathological reflux (>0.5 s) in the AAGSV, GSV, or incompetent perforator veins.

Secondary endpoints: -new reflux in the AAGSV;

-need for repeat intervention;

-patient satisfaction score (0–10 points);

-complication rate.

Statistical Analysis

The analysis was performed according to the intention-to-treat (ITT) principle. Categorical variables were compared using the χ^2 test or Fisher's exact test, as appropriate. Continuous variables were analyzed using the Student's t-test. Treatment effectiveness was assessed by calculating relative risk (RR), absolute risk reduction (ARR), and number needed to treat (NNT). Freedom from recurrence was evaluated descriptively using the Kaplan–Meier method. A p-value < 0.05 was considered statistically significant.

Ethical Considerations

The study protocol was approved by the local ethics committee of the VarikozOFF Clinic (Protocol No. 124/89, dated December 18, 2023). Written informed consent was obtained from all participants prior to inclusion in the study.

Results.

Baseline Patient Characteristics. The study groups were comparable with respect to demographic characteristics, CEAP clinical class, and diameters of the GSV and AAGSV, which minimized structural bias and allowed for direct comparison between groups (Table 1).

Table 2. Baseline characteristics of patients (n = 100)

Parameter	Group I (n = 50)	Group II (n = 50)	p
Mean age, years	46.1 ± 8.5	46.3 ± 8.9	0.91
Female / Male	39 (78%) / 11 (22%)	39 (78%) / 11 (22%)	1.00
CEAP: C2 / C3 / C4	27 / 15 / 8	26 / 16 / 8	0.97
GSV diameter at SFJ, mm	7.2 ± 1.4	7.3 ± 1.5	0.78
AAGSV diameter, mm	5.8 ± 0.4	5.9 ± 0.4	0.49
BMI, kg/m²	27.8 ± 2.9	28.1 ± 3.1	0.64

Primary Clinical Outcomes (12 Months)

Table 3. Clinical outcomes at 12-month follow-up

Outcome	Group I	Group II	RR (95% CI)	ARR	NNT	p
Varicose vein recurrence	10 (20%)	2 (4%)	0.20 (0.05–0.87)	16%	6.25	0.028
New AAGSV reflux	9 (18%)	1 (2%)	0.11 (0.015–0.845)	16%	6.25	0.016
Repeat interventions	6 (12%)	1 (2%)	0.17 (0.02–1.30)	10%	10	0.11
Patient satisfaction (0–10)	8.1 ± 1.2	9.4 ± 0.6	—	—	—	<0.001
Overall complication rate	4 (8%)	5 (10%)	—	—	—	0.73

- A clinically significant reduction in the risk of varicose vein recurrence was observed, with an 80% relative risk reduction in Group II compared with Group I (RR = 0.20).
- The absolute risk reduction was 16 percentage points, corresponding to a number needed to treat (NNT) of approximately 6, indicating that one recurrence was prevented for every six patients treated with simultaneous ablation of the AAGSV.
- Patient-reported treatment satisfaction was significantly higher in Group II ($p < 0.001$).
- Importantly, the overall complication rate did not differ significantly between the two groups ($p > 0.05$).

3. Freedom from Recurrence (Kaplan–Meier Analysis).

According to Kaplan–Meier survival analysis, freedom from recurrence at 12 months was significantly higher in Group II (96%) compared with Group I (80%). The difference between the survival curves was statistically significant based on the log-rank test ($p < 0.05$).

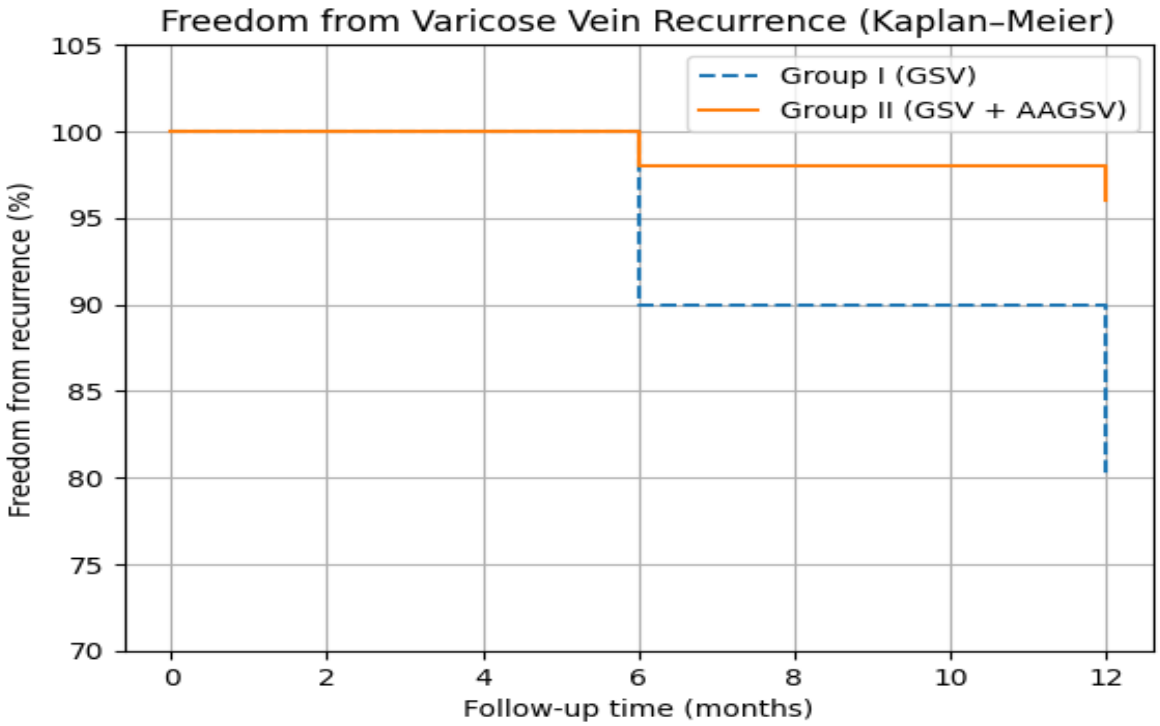


Figure 1. Kaplan–Meier curves of freedom from varicose vein recurrence during 12 months of follow-up after EVLA. The solid line represents patients who underwent GSV ablation with simultaneous EVLA of the AAGSV (Group II), while the dashed line represents patients who underwent EVLA of the GSV alone (Group I). The difference between the curves was statistically significant according to the log-rank test ($p < 0.05$).

Discussion.

The results of the present study demonstrate the clinical relevance of simultaneous ablation of the anterior accessory great saphenous vein (AAGSV) during endovenous laser ablation (EVLA) of the great saphenous vein (GSV). The analysis revealed a significant reduction in the recurrence rate of varicose vein disease in the group undergoing simultaneous AAGSV ablation, which is further supported by the Kaplan–Meier survival analysis. At 12 months, freedom from recurrence reached 96% in the intervention group compared with 80% in the control group ($p < 0.05$).

These findings are consistent with previously published studies highlighting the role of the AAGSV as a frequent source of reflux and disease recurrence following isolated treatment of the main saphenous trunk【1–3】. Failure to address the AAGSV may result in persistent or recurrent venous reflux within the saphenofemoral junction basin, despite technically successful ablation of the GSV【4,5】.

The use of EVLA with a 1470-nm wavelength, a radial fiber, and a standardized pullback speed of 1 mm/s in both study groups ensured a high degree of procedural uniformity. Therefore, the observed differences in clinical outcomes can be attributed primarily to the intervention on the AAGSV rather than to variations in the ablation technique itself.

From a practical perspective, the proposed approach may serve as a step toward standardization of EVLA protocols in patients with anatomically prominent AAGSV, particularly when high-frequency duplex ultrasound enables reliable visualization of the vein in the region of the saphenofemoral junction. The use of tumescent anesthesia at a volume of 300–350 mL with a

low lidocaine concentration (0.03%) further contributed to the safety and reproducibility of the procedure without increasing the complication rate.

Conclusions:

1. Simultaneous ablation of the anterior accessory great saphenous vein (AAGSV) during endovenous laser ablation (EVLA) of the main great saphenous vein (GSV) is associated with a significant reduction in the recurrence rate of varicose vein disease within the first year of follow-up.
2. Kaplan–Meier analysis demonstrated a 12-month freedom from recurrence rate of 96% in patients who underwent AAGSV ablation compared with 80% in patients without AAGSV intervention ($p < 0.05$), highlighting the clinical relevance of a combined treatment approach.
3. The use of a radial laser fiber with a wavelength of 1470 nm, a power setting of 7 W, and a linear endovenous energy density of approximately 70 J/cm², in combination with tumescent anesthesia, ensures high procedural efficacy and safety.
4. Based on the present findings, incorporation of AAGSV ablation into standard EVLA protocols appears justified when anatomical visualization and/or reflux in this vein is present.
5. Further multicenter studies with longer follow-up periods are required to assess long-term outcomes and the durability of the clinical effect.

Nevertheless, this study has several limitations, including a relatively short follow-up period (12 months), a limited sample size, and the absence of stratification according to the severity of chronic venous insufficiency (CEAP classification). Future research should focus on extending follow-up to 3 and 5 years, as well as incorporating assessments of quality of life and aesthetic outcomes using validated instruments such as CIVIQ or AVVQ.

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DRUG-INDUCED HEPATOTOXICITY AND ITS COMORBIDITY WITH SARS-CoV-2 INFECTION

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Abstract. *This article presents an analysis of scientific research focused on the clinical manifestations, pathogenesis, and effective treatment of extrapulmonary complications of coronavirus infection. Recent studies have demonstrated that the pathogenetic mechanisms of liver injury in COVID-19 involve multiple factors, including direct viral damage, a pronounced systemic inflammatory response, hypoxia, drug-induced toxic injury, as well as the activation of pre-existing liver diseases.*

Keywords: *coronavirus Disease 2019; enzyme-linked immunosorbent assay; non-alcoholic fatty liver disease; Post-COVID-19 Functional Status; hepatic dysfunction.*

Introduction

At present, the clinical significance and long-term consequences of COVID-19–associated liver injury remain unclear. Therefore, determining the severity of structural and functional liver disorders in patients who have recovered from COVID-19 and developing methods for their correction represents a relevant issue in modern medicine. Patients with COVID-19 demonstrate a wide spectrum of liver injuries, which may be associated with pre-existing pathology, direct viral damage, inflammatory injury, or the effects of pharmacological agents. Approximately 50% of patients show signs of impaired structural and functional liver status upon hospital admission. During hospitalization, up to 90% of patients exhibit a moderate increase (up to two times the upper limit of normal) in aminotransferase activity in peripheral blood, while in 25% of patients' enzyme levels exceed three times the upper limit of normal [1,2; pp. 727–733]. The most frequently observed symptom is hypoalbuminemia. One of the causes of hepatopathy may be drug-related effects. Responsible agents include antiviral drugs such as umifenovir (arbidol), favipiravir, remdesivir, as well as steroid hormones and anti-inflammatory drugs, including acetaminophen and other nonsteroidal anti-inflammatory drugs [3; pp. 420–422; 4; pp. 475–481].

Drug-induced liver injury is confirmed by the detection of microvesicular steatosis and mild inflammatory changes in the hepatic parenchyma [3; pp. 420–422]. At least 10% of patients demonstrate drug-induced hepatopathy [5; pp. 566–574]. In a meta-analysis by Kulkarni et al., drug-induced liver injury was diagnosed in 25.4% of more than 20,000 patients [6; pp. 584–599]. Antiviral drugs prescribed to patients with severe and critical COVID-19, as well as to those with moderate and mild disease but at risk of viral persistence and adverse outcomes, are all metabolized in the liver and utilize the cytochrome P450 system, the activity of which is reduced in COVID-19 [7; pp. 17, 38].

Favipiravir is an antiviral drug approved in Japan for the treatment of influenza. It is a prodrug whose active metabolite, favipiravir ribofuranosyl-5′-triphosphate, is formed through intracellular phosphorylation. This compound is a purine nucleotide that inhibits RNA-dependent RNA polymerase. The drug is effective against Ebola virus, West Nile fever virus, yellow fever virus, and Lassa fever virus [8; pp. 446–454]. Adverse effects of favipiravir include hyperuricemia

and diarrhea, observed in approximately 20% of patients, while psychiatric disorders, neutropenia, and elevated transaminase levels occur in about 2% of patients. Overall, the drug has an excellent safety profile [9; pp. 45–51]. Another study reports that the use of lopinavir/ritonavir, with or without ribavirin, interferon beta, and/or corticosteroids, is associated with increased transaminase levels in patients with COVID-19 [10; pp. 733–742].

Lopinavir is a protease inhibitor used in the treatment of HIV infection in combination with low doses of ritonavir, another protease inhibitor that prolongs the half-life of lopinavir [11; pp. 1787–1799]. The use of high doses of lopinavir (1200 mg/day, once daily) is associated with pronounced adverse effects, including hepatotoxicity. Therefore, the drug is administered at lower doses (200–400 mg) to enhance the effectiveness of other antiviral agents [12; pp. 2277–2284]. Studies have shown that hospitalized patients receiving lopinavir/ritonavir exhibit elevated levels of gamma-glutamyl transferase (GGT) and bilirubin; thus, this antiviral combination should be used with extreme caution in patients with a history of metabolic liver disease [12; pp. 2277–2284, 39].

Studies indicate that antiviral drugs used in the treatment of COVID-19 play a key role in the development of hepatic dysfunction. In particular, the use of lopinavir/ritonavir is associated with hepatocyte injury and impaired liver function in patients with a non-critical course of infection [13; p. 347]. In 11% of patients, alanine aminotransferase (ALT) levels increased more than threefold, while in 12% of patients' gamma-glutamyl transferase (GGT) levels increased more than threefold. Moreover, the use of this drug combination increases the risk of liver failure fourfold [14; pp. 727–733].

Cytochrome P450 (CYP450) is a superfamily of monooxygenases that mediate clinically significant interactions in various pathological conditions [15; pp. 1267–1293]. There is a hypothesis that the metabolic activity of CYP450 is impaired—predominantly reduced—during COVID-19, leading to decreased clearance of substances and corresponding alterations in the pharmacokinetics of antiviral agents. In addition, liver involvement in the infectious process contributes to an increased risk of complications. In May 2020, remdesivir, previously approved for the treatment of Ebola virus disease, received emergency authorization for use in patients with COVID-19. Remdesivir is also metabolized by cytochrome P450 enzymes, particularly CYP3A4. Other potential therapeutic candidates for COVID-19 include chloroquine [16; pp. 72–73] and colchicine [17; pp. 42–45], which are likewise metabolized by hepatic enzymatic systems. Understanding the interactions between drug molecules and hepatic enzyme systems is essential for predicting both therapeutic efficacy and toxic effects [18; p. 110033]. These patterns necessitate cautious use of anti-cytokine agents and the incorporation of measures aimed at normalizing hepatic metabolic activity into immunomodulatory treatment strategies.

Remdesivir has been shown to reduce the duration of hospitalization in patients with COVID-19 [19; pp. 1813–1826]. Among patients treated with remdesivir, a reversible increase in serum ALT and AST activity has been observed without the development of other pathological changes in liver or kidney function. A significant elevation in ALT and AST levels is diagnosed in 6% of patients, including life-threatening liver dysfunction in 2%, which has led to recommendations to shorten the duration of remdesivir therapy [20; pp. 1827–1837]. Conversely, moderate hepatic dysfunction manifested by an increase in ALT/AST activity up to two times the upper limit of normal in patients without pre-existing liver disease does not tend to progress to acute liver failure. In patients with prior liver pathology, remdesivir therapy should be administered under strict monitoring of liver function [21; pp. 881–883].

A recent placebo-controlled study evaluated the protective effect of intravenous remdesivir in hospitalized patients with severe COVID-19. It was found that patients receiving remdesivir discontinued treatment more frequently than those in the placebo group due to increased transaminase activity and/or elevated bilirubin levels in peripheral blood. Given the frequent association of COVID-19 with hepatic dysfunction, a higher incidence of liver injury was observed in patients treated with remdesivir compared with other therapeutic strategies. Although the drug remains approved for the treatment of COVID-19, its use requires careful and continuous monitoring of liver function [22; pp. 2835–2836].

Other antiviral drugs used in the treatment of patients with severe COVID-19 (used in approximately 50% of cases) include oseltamivir, umifenovir (arbidol), lopinavir, and ritonavir [23; pp. 475–481]. All of these drugs are capable of causing impaired liver function. In addition, ribavirin-induced hemolysis leads to tissue hypoxia, which may also result in increased transaminase activity in peripheral blood. Pre-existing chronic liver diseases (hepatitis B, C, etc.), regardless of whether blood enzyme levels are elevated or not, also predispose patients to the development of drug-induced hepatotoxicity [24; pp. 4753–4762]. Furthermore, in patients with pre-existing liver diseases, the use of nonsteroidal and steroidal anti-inflammatory drugs, traditional (“folk”) remedies, and antibiotics should be undertaken with caution, taking into account and monitoring liver function.

Doxycycline is a broad-spectrum tetracycline antibiotic that chelates zinc used by inflammatory matrix metalloproteinases and also inhibits the activity of SARS-CoV-2 RNA polymerase and the penetration of viral particles into cells. Doxycycline is an inhibitor of viral serine protease and demonstrates high antiviral activity. In addition, doxycycline exhibits anti-inflammatory effects by reducing the activity of nuclear factor kappa B in activated B lymphocytes, which leads to decreased secretion of pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6, and by inducing apoptosis of mast cells [25; pp. 487–488]. Hepatotoxicity has been observed during doxycycline therapy; however, it occurs less frequently than with tetracycline use. Doxycycline is an effective and generally safe drug; nevertheless, it may cause damage to the biliary tract. Moreover, isolated cases of acute liver injury and liver failure have been reported in patients receiving potentially hepatotoxic drugs in combination with doxycycline [26; pp. 483–487].

Azithromycin also exerts toxic effects on the hepatobiliary system, including symptoms and signs of cholestatic hepatitis, such as fever, weakness, jaundice, pruritus, and eosinophilia. There are sporadic case reports of acute liver failure requiring liver transplantation associated with bile duct injury during azithromycin therapy [27; pp. 1171–1178; 28; pp. 683–686].

Tocilizumab is a drug approved for the treatment of rheumatoid arthritis and juvenile rheumatoid arthritis. Although it is not a specific antiviral agent, some researchers have proposed the use of tocilizumab for the management of hyperactivation of the systemic inflammatory response and cytokine storm in patients with COVID-19 [29]. Tocilizumab is a recombinant monoclonal antibody directed against interleukin-6 (IL-6) receptors, blocking the pathogenetic signaling pathway mediated by this cytokine. The most common adverse effects associated with tocilizumab therapy include headache and arterial hypertension. Hepatotoxicity may also occur during tocilizumab treatment, ranging from moderate elevations in liver enzymes to severe drug-induced liver injury [30; pp. 1901–1905].

There is evidence supporting the effectiveness of tocilizumab in patients with COVID-19 in terms of controlling the systemic inflammatory response, even in the presence of a fivefold increase in transaminase levels above the upper limit of normal and a tenfold increase in gamma-glutamyl transferase (GGT) activity. In patients with pre-existing liver disease, liver biopsy is

recommended prior to initiating tocilizumab therapy in order to assess the structural and functional state of the hepatic parenchyma and to reduce the risk of acute liver failure. Some studies have demonstrated the possibility of liver injury associated with a systemic inflammatory response triggered by the administration of antiviral and antibacterial drugs [31; pp. 11–12]. Further studies are required to evaluate the safety and feasibility of using tocilizumab in patients with chronic liver diseases [32; pp. 727–733].

When treating patients with COVID-19, it is necessary to consider the potential for viral and immune-mediated liver injury, the risk of hepatotoxicity associated with administered medications, and the presence of pre-existing liver pathology. For all patients with COVID-19, especially hospitalized and elderly individuals, regular monitoring of serum transaminase activity, bilirubin and albumin concentrations, and coagulation parameters is recommended. If increased levels of lactate dehydrogenase (LDH) and aspartate aminotransferase (AST) are detected in the absence of alanine aminotransferase (ALT) elevation, possible skeletal or cardiac muscle injury should be considered. In patients with previously diagnosed viral hepatitis B or C, discontinuation of antiviral therapy is not recommended in order to avoid viral reactivation during treatment with anti-inflammatory agents and corticosteroids. Pharmacological agents used in the treatment of COVID-19 and their potential hepatotoxic and hepatoprotective properties are presented in Table 1.1. In the presence of signs of severe hepatic parenchymal injury in a patient with COVID-19, thorough evaluation is required to identify underlying liver disease, exposure to hepatotoxic agents, the severity of hypoxic liver injury, and the degree of liver failure. In cases of hypoxic liver injury, circulatory and respiratory support is recommended [33; pp. 217–231]. To reduce the severity of hepatic encephalopathy and decrease ammonia levels in systemic circulation, L-ornithine L-aspartate is used. However, this agent is palliative in nature, as it does not correct hepatic dysfunction but rather masks its manifestations. In the presence of impaired liver function, intestinal dysbiosis and “leaky gut” syndrome may develop, leading to increased endotoxemia and ammonia production. To restore normal intestinal microbiota, the use of pro- and prebiotics is recommended [34]. Administration of silymarin at a dose of 420 mg/day and ursodeoxycholic acid (UDCA) at a dose of 500 mg/day may prevent hepatic dysfunction, particularly in patients with elevated transaminase and bilirubin levels associated with severe COVID-19 [35].

Table 1.1.

Characteristics of drugs used in the treatment of COVID-19 in terms of their hepatotropic effects and evidence base

Drug	**Pharmacological activity**	**Mechanism of action**	**Molecular effects (liver)**	**Molecular effects (lungs)**
Tocilizumab	IL-6 receptor blocker	Decreased expression of TNF-α and IL-10, reduced inflammasome activity, inhibition of monocyte phagocytic activity, suppression of cytokine storm	Moderate elevation of transaminases; drug-induced liver injury	Reduction of inflammatory activity in lung tissue

Remdesivir	Antiviral agent	Inhibitor of RNA-dependent RNA polymerase (adenosine analog)	Increased transaminases and bilirubin	Reduces viral load in lungs, decreases risk of pulmonary hemorrhage, improves lung function
Oseltamivir	Antiviral agent	Neuraminidase inhibitor; inhibits release of viral progeny from infected cells	Elevated transaminases and bilirubin (rare)	Decreased IL-1β, TNF-α, IL-4, interferon-γ
Umifenovir (Arbidol)	Antiviral agent	Inhibits binding of spike protein to ACE2 receptors; blocks viral entry; stimulates immune response	Increased transaminases	Reduced viral attachment to ACE2 receptors
Lopinavir/ Ritonavir	Antiviral agent	Protease inhibitors; impairment of viral entry	Golgi apparatus fragmentation; activation of organelle stress response	Activation of DNA damage response
Bicyclol	Candidate antiviral agent	Direct damage to viral membranes; reduction of host inflammatory response	Decreased transaminases; reduced hepatic triglycerides	Reduced severity of acute lipopolysaccharide-induced lung injury
Ribavirin (+ interferon)	Antiviral agent	Inhibition of viral RNA-dependent RNA polymerase (guanine analog)	Reduced transaminases; decreased histological liver injury; reduced hepatic inflammation	Improved survival in MERS-CoV infection
Favipiravir	Antiviral agent	RNA-dependent RNA polymerase inhibitor	Increased transaminases	Reduced viral load and inflammation in lung tissue
Chloroquine and Hydroxychloroquine	Antimalarial agents	Inhibition of viral binding and entry into cells	Reduced IL-6, TNF-α, NF-κB expression; reduced hepatocyte apoptosis and hepatic inflammation	Reduced lung inflammation, oxidative stress, and pulmonary fibrosis

Probiotics	Live normal microbiota	Preventive effect against bacterial and viral infections	Reduced hepatic inflammation and transaminases; decreased TNF-α; restoration of liver function and parenchyma	Reduced lung inflammation; preventive effect against respiratory infections
N-acetylcysteine	Antioxidant	Precursor of reduced glutathione; mucolytic agent	Reduced lactic acid in liver; improved liver function	ACE inhibition; reduced viral replication and lung inflammation
Glycyrrhizic acid	Natural triterpenoid saponin	Anti-inflammatory, antioxidant, antiviral effects	Reduced oxidative stress; decreased hepatocyte apoptosis	Inhibition of coronavirus replication and cell entry; reduced IL-33
Vitamin E	Fat-soluble vitamin (α-tocopherol)	Antioxidant and immunomodulator	Reduced free radicals; increased glutathione; inhibition of NF-κB; reduced inflammation, fibrosis, and transaminases	Reduced oxidative stress; decreased NO and cyclooxygenase activity; increased T-cell proliferation
Vitamin A	Fat-soluble vitamin (retinol)	Antioxidant and immunomodulator	Reduced transaminases; increased IL-10; inhibition of NF-κB and TNF-α	Reduced IL-1β; decreased oxidative stress; improved lung function
Vitamin D	Fat-soluble secosteroid (cholecalciferol)	Reduces viral entry, replication, and inflammation	Modulation of hepatic inflammation and fibrogenesis	Reduced TNF-α and interferon-γ; increased glutathione

Vitamin C	Water-soluble vitamin (ascorbic acid)	Enzymatic cofactor; antioxidant	Reduced transaminases; increased superoxide dismutase and glutathione; reduced oxidative stress and TNF-α	Reduced TNF-α, IL-1β, IL-8; inhibition of NF-κB; reduced inflammation
Zinc	Dietary trace element	Anti-inflammatory and antioxidant effects	Reduced pro-inflammatory cytokine production; reduced oxidative stress and hepatocyte apoptosis	Reduced lung inflammation; decreased TNF-α, IL-6, IL-1β; increased IL-2
Magnesium	Dietary trace element	Anti-inflammatory and antioxidant effects	Reduced hepatic fibrosis; decreased IL-6 and TNF-α; inhibition of NF-κB pathway; reduced transaminases	Reduced IL-6 and IL-1β; inhibition of NF-κB; decreased COX-2 activity, prostaglandin E2, and oxidative stress
Copper	Dietary trace element	Antiviral activity via viral envelope damage and genome destruction	Increased ceruloplasmin; reduced inflammation and IL-6; increased oxidative stress	Reduced viral replication, release, and cellular entry
Dexamethasone	Corticosteroid hormone	Suppression of excessive inflammatory response	Increased VLDL and HDL; reduced IL-1β, IL-2, TNF-α, interferon-γ; reduced prostaglandin production; prevention of hepatic fibrosis	Reduced inflammation; inhibition of NF-κB; decreased oxidative markers; reduced pulmonary fibrosis and mortality in severe COVID-19

A study evaluating the use of N-acetylcysteine (NAC) [36] demonstrated that this agent reduces the risk of bronchial obstruction and may be safely used in patients with COVID-19 who have glucose-6-phosphate dehydrogenase deficiency. The administration of NAC is associated with an improvement in clinical condition and a reduction in C-reactive protein (CRP) and ferritin

concentrations. Upon discontinuation of the drug, inflammatory marker levels return to baseline values. The use of NAC also reduces the duration of mechanical ventilation and length of hospital stay. In addition, NAC inhibits hemolysis and prevents elevations in liver enzyme levels in patients with glucose-6-phosphate dehydrogenase deficiency. The mechanism of action of NAC includes inhibition of viral infection and attenuation of the cytokine storm. Patients who have undergone liver transplantation, due to their immunosuppressed status, may remain viral carriers for a prolonged period. Moreover, they are predisposed to bacterial superinfection, sepsis, and multiple organ failure, with a high risk of mortality [37,38].

Conclusion. Thus, a review of the available literature indicates that the use of corticosteroids in patients with significant liver injury—whether due to pre-existing liver disease or COVID-19–associated damage—should take into account the underlying pathogenetic mechanisms of hepatic injury. Hormonal therapy is justified in cases of inflammatory liver damage but may be hazardous in the presence of viral-mediated liver injury.

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ASSESSMENT OF QUALITY OF LIFE IN COMBINED POST-BURN CICATRICIAL STRICTURES OF THE PHARYNX, ESOPHAGUS, AND STOMACH

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Abstract. *This article presents an analysis of quality of life in 68 patients who underwent pharyngocoloplasty for combined post-burn cicatricial strictures of the pharynx, esophagus, and stomach. The authors performed a statistical comparative analysis of the results of patients' subjective self-assessment and clinical symptoms using the Visual Rating Scale (VRS), the Hospital Anxiety and Depression Scale (HADS), the Spielberger State–Trait Anxiety Inventory (STAI), and the SF-36 Health Survey over the course of the study.*

Keywords: *pharyngocoloplasty; combined post-burn cicatricial strictures of the esophagus; quality of life assessment.*

Introduction

Quality of life (QoL) is defined as a "characteristic of a person's physical, psychological, emotional, and social functioning based on their subjective perception" [2]. As dissatisfaction with the conditions of modern life increases, the study of quality of life—initially rejected in the contemporary industrial world due to its perceived vagueness and lack of substantive content—now requires active investigation, without which any research aimed at meeting human needs is doomed to failure [3]. The principal surgical components of QoL in such patients are rightly considered to be the degree of dysphagia in relation to the severity of the maximal stricture, as well as the rate of food passage through the gastrointestinal tract and the pace of restoration of normal body weight [9].

The best quality of life has been observed in patients after surgical procedures using the whole stomach to create an artificial esophagus; isoperistaltic small-intestinal reconstruction ranks second; an artificial esophagus constructed from the colon in an antiperistaltic position demonstrated satisfactory results; while the most favorable outcomes were achieved with local reconstructive procedures when the native esophagus was preserved [4]. Self-assessment of one's own condition clearly reflects the level of quality of life, although it varies widely among individuals [6, 7].

Aim of the study. To assess the quality of life of patients in terms of the immediate and long-term effectiveness of standard and newly developed surgical methods for combined post-burn cicatricial strictures of the pharynx, esophagus, and stomach.

Materials and methods. In accordance with the study design, a comparative analysis of the dynamics of quality of life was conducted in 68 patients with combined post-burn cicatricial strictures of the pharynx, esophagus, and stomach, aged 4–85 years (mean age 34.43 ± 0.66 years). All patients underwent inpatient examination and treatment in the Department of Esophageal and Gastric Surgery of the State Institution "Republican Specialized Scientific and Practical Medical

Center of Surgery named after Academician V. Vakhidov" during the period from 2000 to 2023. Quality of life was assessed at the following time points: within the first 24 hours after hospital admission, after completion of treatment, and at 6 months, 1 year, 2 years, and 3 years following treatment.

The patients were divided into two groups: the main group (MG) consisted of 39 patients with combined post-burn cicatricial strictures of the pharynx, esophagus, and stomach who underwent surgery using the method developed by the authors for forming a pharyngocolonic anastomosis during bypass esophageal reconstruction (invention patent IAP No. 05835 "Method for forming a pharyngocolonic anastomosis during bypass coloplasty"); the comparison group (CG) included 29 patients with combined post-burn cicatricial strictures of the pharynx, esophagus, and stomach who underwent surgical correction of cicatricial narrowing of the pharynx and esophagus by creating an anastomosis with an oblique-transverse incision of the esophagus.

A statistical comparative analysis was performed to evaluate the results of patients' subjective self-assessment and clinical symptoms using the Visual Rating Scale (VRS), the Hospital Anxiety and Depression Scale (HADS), the Spielberger State-Trait Anxiety Inventory (STAI), and the SF-36 Health Survey over the course of the study.

Results and discussion. Comparative analysis of the dynamics of overall condition scores according to the VRS demonstrated a statistically significant intergroup difference as early as 6 months after surgical correction of combined post-burn cicatricial strictures of the pharynx, esophagus, and stomach, which persisted throughout the entire period of dynamic follow-up (Table 1).

Table 1. Dynamics of subjective assessment of overall condition according to the VRS in patients with combined post-burn cicatricial strictures of the pharynx, esophagus, and stomach (M ± m).

Follow-up period	MG (n = 39)	CG (n = 29)	p-value
At admission	8.82 ± 0.79	8.91 ± 0.84	0.938029
At discharge	5.36 ± 0.64*	5.89 ± 0.82*	0.612113
After 6 months	3.54 ± 0.35*	4.76 ± 0.45*	0.036111
After 1 year	2.44 ± 0.42*	4.12 ± 0.59*	0.023507
After 2 years	2.28 ± 0.48*	3.94 ± 0.54*	0.024813
After 3 years	2.14 ± 0.41*	3.42 ± 0.47*	0.044174

* Difference compared with the baseline value is statistically significant at **p ≤ 0.05**.

A similar pattern was observed for clinical symptomatology, particularly dysphagia, the dynamics of which also demonstrated a statistically significant intergroup difference beginning at 6 months and persisting until the end of the follow-up period.

Table 2. Dynamics of subjective assessment of dysphagia according to the Visual Rating Scale (VRS) in patients with combined post-burn cicatricial strictures of the pharynx, esophagus, and stomach (M ± m).

Follow-up period	**MG (n = 39)**	**CG (n = 29)**	**p-value**
At admission	8.47 ± 0.94	8.51 ± 0.89	0.975444
At discharge	6.44 ± 0.87	7.09 ± 0.91	0.607400
After 6 months	3.17 ± 0.49*	4.51 ± 0.42*	0.041822
After 1 year	2.51 ± 0.47*	3.92 ± 0.49*	0.041789
After 2 years	2.27 ± 0.41*	3.41 ± 0.37*	0.042993

After 3 years	2.09 ± 0.38*	3.19 ± 0.39*	0.047494

* Difference compared with the baseline value is statistically significant at **$p \leq 0.05$**.

In addition, it should be noted that the onset of statistically significant differences in overall condition scores relative to baseline was comparable between both groups and was already observed at the time of hospital discharge. In contrast, statistically significant differences in dysphagia scores relative to baseline in both study groups emerged only 6 months after discharge from the hospital. Thus, based on the VRS data, we concluded that the method of forming a pharyngocolonic anastomosis during bypass esophageal reconstruction developed by the authors demonstrates greater subjective effectiveness compared with the conventionally used surgical technique (Fig. 1).

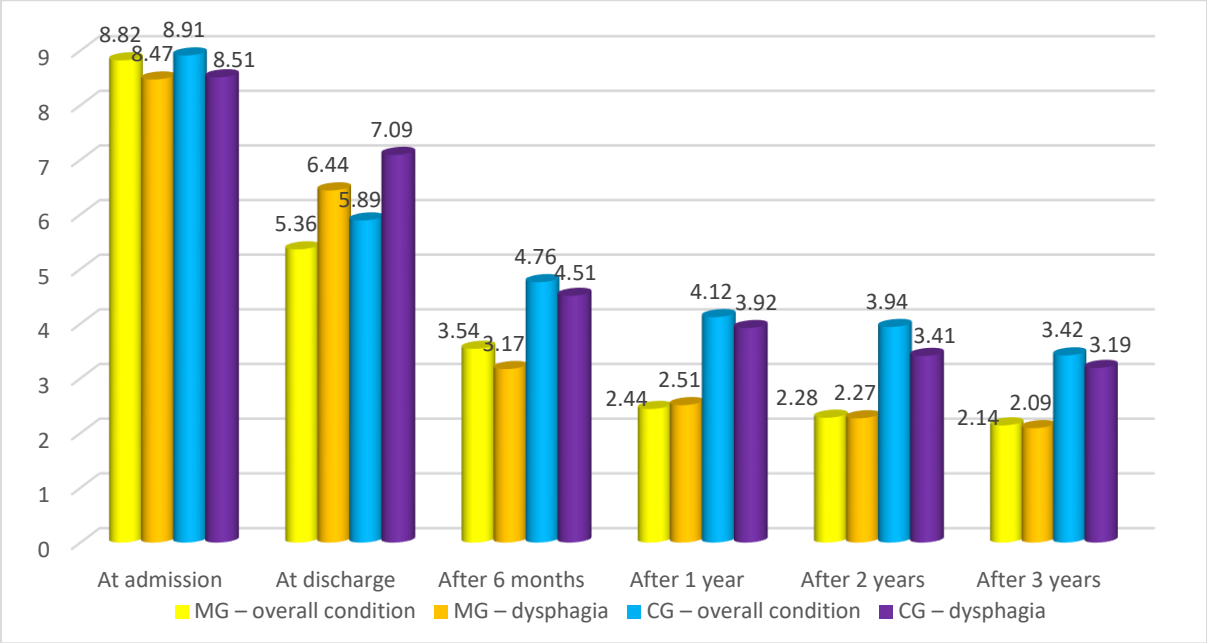


Figure 1. Dynamics of the indicators assessed by the Visual Rating Scale (VRS) in patients.

A comparative evaluation of patients in the study groups was also performed with regard to the dynamics of psychological status using the Hospital Anxiety and Depression Scale (HADS) (Table 6.6). Subclinical anxiety was observed in 32 (82.05%) patients in the main group (MG), while 7 (17.95%) patients had clinically significant anxiety; in the comparison group (CG), these proportions were 26 (89.66%) and 3 (10.34%) patients, respectively, with no statistically significant intergroup difference ($p = 0.597$). According to the depression subscale of the HADS, clinically significant depression was identified in 27 (69.23%) patients in the MG and subclinical depression in 12 (30.77%) patients, whereas in the CG, 23 (79.31%) patients had clinically significant depression and 6 (20.69%) had subclinical depression; no statistically significant intergroup difference was observed ($p = 0.514$).

Thus, the baseline levels of the study groups on the HADS subscales were comparable, with depression being more pronounced; in the majority of patients, it was clinically expressed, although not at the maximum possible severity. At the time of hospital discharge, patients in both groups were characterized by subclinical levels of anxiety and depression according to the HADS. Normalization of anxiety on the HADS anxiety subscale occurred as early as 6 months after surgery, whereas a statistically significantly better psychological state in the main group was observed at 2 years postoperatively; similarly, statistically significant intergroup differences were identified at 2 years of follow-up.

Table 3. Dynamics of scores on the HADS subscales in patients with combined post-burn cicatricial strictures of the pharynx, esophagus, and stomach (M ± m)

HADS – Anxiety

Follow-up period	MG (n = 39)	CG (n = 29)	p-value
At admission	10.85 ± 1.03	10.87 ± 1.08	0.846534
At discharge	7.22 ± 0.71*	7.91 ± 0.82*	0.526918
After 6 months	6.14 ± 0.45*	7.23 ± 0.54*	0.125836
After 1 year	6.02 ± 0.32*	6.98 ± 0.35*	0.047052
After 2 years	5.64 ± 0.38*	6.67 ± 0.34*	0.047509
After 3 years	5.13 ± 0.32*	6.46 ± 0.38*	0.009389

HADS – Depression

Follow-up period	MG (n = 39)	CG (n = 29)	p-value
At admission	10.98 ± 1.07	11.37 ± 1.16	0.805588
At discharge	7.82 ± 0.99*	8.56 ± 1.08	0.615206
After 6 months	6.17 ± 0.47*	7.48 ± 0.56*	0.077814
After 1 year	6.12 ± 0.33*	7.18 ± 0.41*	0.048149
After 2 years	5.64 ± 0.36*	6.73 ± 0.40*	0.046928
After 3 years	5.35 ± 0.34*	6.40 ± 0.39*	0.046517

* Difference compared with baseline is statistically significant at **p ≤ 0.05**.

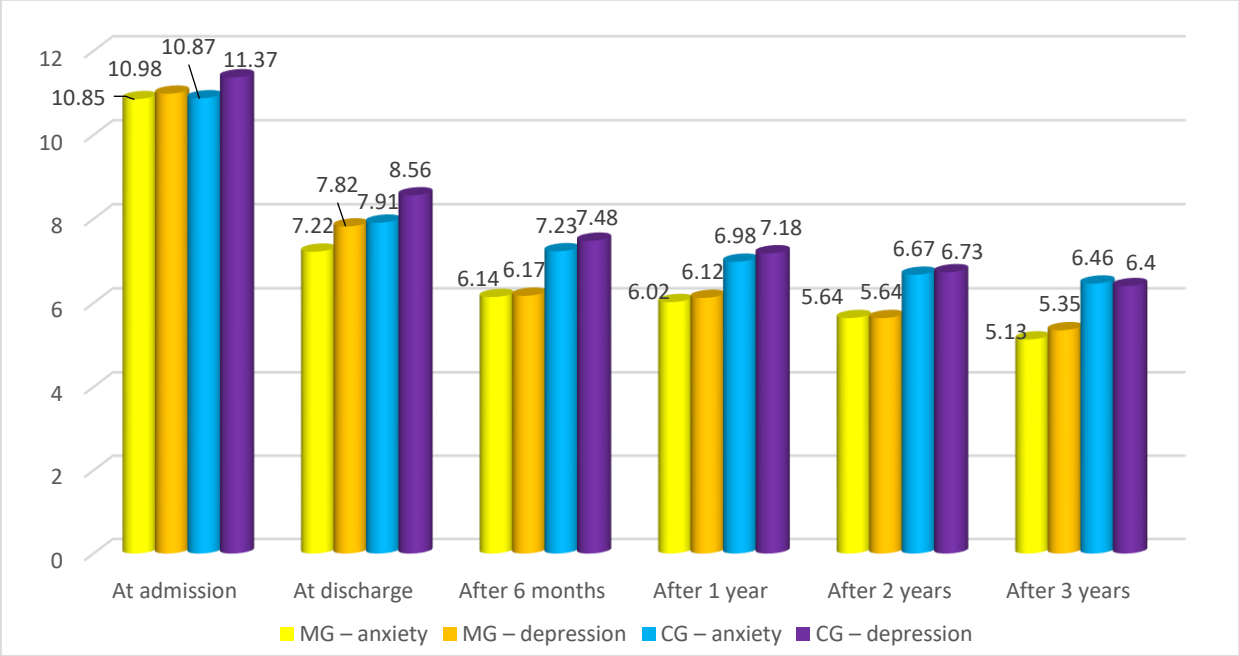


Figure 2. Dynamics of HADS scale indicators in patients of both groups.

According to the HADS depression subscale, normalization of patients' condition in the main group (MG) was observed at 6 months, whereas in the comparison group (CG) it occurred only after 2 years; moreover, intergroup comparison revealed a statistically significant difference after 1 year of follow-up. This finding allows us to conclude that the method of forming a pharyngocolonic anastomosis during bypass esophageal reconstruction developed by the authors demonstrates greater subjective psychological effectiveness compared with the formation of an anastomosis using an oblique-transverse incision of the esophagus.

When performing a comparative analysis of the dynamics of state and trait anxiety using the Spielberger State–Trait Anxiety Inventory (STAI), a statistically significant intergroup difference on the state anxiety subscale was identified only at the 3-year follow-up, indicating comparable psychological responses to their condition in patients of both groups (Table 4).

Table 4. Dynamics of STAI scores in patients with combined post-burn cicatricial strictures of the pharynx, esophagus, and stomach (M ± m)

STAI – State anxiety

Follow-up period	MG (n = 39)	CG (n = 29)	p-value
At admission	58.45 ± 5.59	62.43 ± 5.61	0.616979
At discharge	44.58 ± 3.71*	49.82 ± 4.52	0.373510
After 6 months	32.17 ± 3.47*	34.26 ± 3.51*	0.673367
After 1 year	29.16 ± 2.42*	32.28 ± 2.48*	0.371225
After 2 years	24.14 ± 2.36*	29.31 ± 2.43*	0.131801
After 3 years	21.11 ± 2.31*	27.76 ± 2.35*	0.047716

STAI – Trait anxiety

Follow-up period	MG (n = 39)	CG (n = 29)	p-value
At admission	56.74 ± 4.78	58.69 ± 4.82	0.708402
At discharge	40.22 ± 3.21*	42.67 ± 3.32*	0.597556
After 6 months	33.39 ± 2.89*	35.51 ± 2.98*	0.611295
After 1 year	24.12 ± 2.41*	28.75 ± 2.82*	0.216457
After 2 years	22.03 ± 2.17*	26.44 ± 2.24*	0.162123
After 3 years	22.02 ± 2.21*	25.85 ± 2.22*	0.225870

* Difference compared with the level at admission is statistically significant at **p ≤ 0.05**.

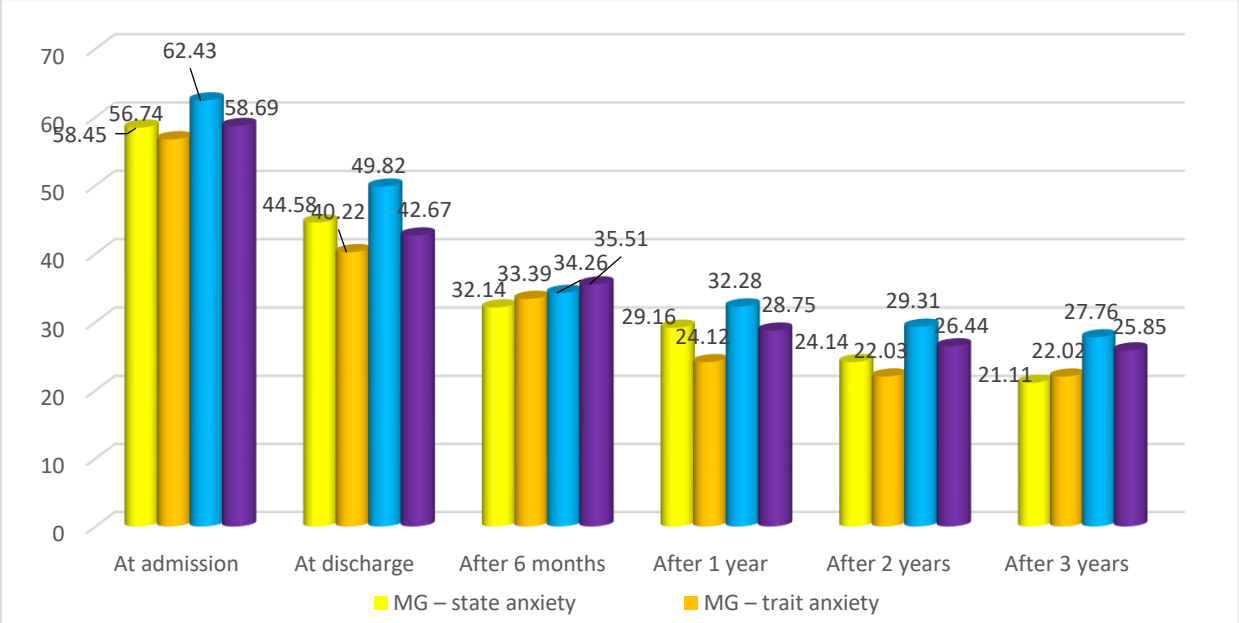


Figure 3. Dynamics of STAI test indicators in patients of both groups.

We observed a statistically significant reduction in state anxiety according to the STAI test in the main group (MG) already at the time of discharge, whereas in the comparison group (CG) this reduction was noted only 6 months after surgical correction. At the same time, trait anxiety according to the STAI test showed statistically significant changes compared with baseline as early

as discharge in both groups; however, no statistically significant intergroup differences for this scale were achieved throughout the entire follow-up period.

In addition, a dynamic comparative analysis of quality of life (QoL) was performed using the general health questionnaire SF-36. Mean scores were calculated and compared between groups, as well as with baseline values, for each individual scale of the questionnaire and for the overall mean score at each time point (Table 5).

Analysis of the SF-36 results in patients with combined post-burn cicatricial strictures of the pharynx, esophagus, and stomach in both subgroups, compared with general population norms, revealed a marked, nearly fourfold reduction in quality of life on the Physical Functioning (PF) scale. This finding is undoubtedly associated with the underlying pathology, which leads to a pronounced limitation of daily physical activity not attributable to general health status, and consequently also affects Role Physical functioning (RP). The decrease in quality of life with respect to the Bodily Pain (BP) parameter reflects the predominance of subjective pain sensations in patients of the comparison group, although without a statistically significant difference from the main group in terms of limitations of daily activities.

The subjective assessment of general health (GH) at admission was also reduced by nearly fourfold compared with population norms in both study groups, with a slightly worse trend observed in the main group. Quality of life according to the Vitality (VT) scale was found to be almost twofold lower than population norms, which is quite logical given the presence of developing alimentary disorders that inevitably affect vitality, energy, and vigor in patients of both groups.

Table 5. Dynamics of SF-36 questionnaire scores in patients of the study groups (M ± m)

Indicator	Before treatment	At discharge	After 6 months	After 1 year	After 2 years	After 3 years
	MG (n = 39)					
PF	16,44±4,68	35,79±5,53#	47,41±6,81#	51,85±7,39#	56,12±7,51#	58,41±7,43#
RP	15,32±4,69	34,81±5,32#	47,22±6,88#	51,36±7,37#	56,18±7,27#	59,14±7,39#
BP	14,41±3,47	28,34±6,47#	45,23±6,66#	52,25±6,82#	54,18±7,23#	57,86±7,57#
GH	16,37±2,59	32,44±6,62#	46,92±6,75#	52,16±7,28#	55,46±7,27#	58,59±7,18#
VT	23,19±4,87	37,19±6,29#	45,68±6,17#	54,25±7,01#	57,14±7,07#	61,65±7,29#
SF	12,46±3,19	27,55±6,45	46,27±6,09#	53,23±6,26#	58,89±6,42#	62,17±6,35#
RE	14,28±3,65	32,47±5,44#	48,99±5,92#	55,11±6,29#	59,42±6,19#	62,24±6,41#
MH	19,56±3,81	30,12±6,52#	46,61±5,46#	54,18±6,69#	58,17±6,52#	61,91±6,59#
Mean score	16,50±3,12	34,46±6,04#	46,04±6,33#	53,17±7,14#	56,20±7,09#	58,56±7,18#
Mean increase$	-	17,96±3,04	29,54±3,07	36,67±3,86*	39,72±3,94*	42,06±3,79*
CG (n = 29)						
	Before treatment	At discharge	After 6 months	After 1 year	After 2 years	After 3 years
PF	15,26±5,44	33,24±5,72#	40,91±8,69#	43,22±7,27#	45,32±7,19#	48,21±7,15#
RP	15,03±5,10	33,89±5,36#	41,12±7,94#	44,41±7,12#	47,11±7,10#	49,81±7,16#
BP	16,39±3,07	26,78±5,99#	41,63±7,78#	46,21±7,14#	49,41±6,98#	52,22±7,04#
GH	15,97±3,09	30,87±6,58#	41,38±7,74#	46,27±7,10#	49,21±7,09#	52,24±7,11#
VT	23,41±4,88	36,29±6,44#	40,21±6,94#	43,21±7,16#	45,32±7,21#	48,81±7,21#
SF	12,28±4,04	20,09±5,94#	41,21±6,96#	45,24±7,11#	47,46±7,08#	50,04±7,09#
RE	13,98±3,31	30,86±5,69#	39,21±6,06#	43,27±7,14#	45,67±7,04#	49,14±7,17#
MH	19,39±3,92	30,03±6,68#	37,41±6,61#	42,23±7,17#	45,03±7,03#	48,29±7,08#
Mean score	16,46±4,97	30,26±6,12#	40,39±7,14#	44,26±7,19#	46,82±7,09#	49,85±7,08#
Mean increase$	-	13,79±1,16	23,92±2,15	27,79±2,18	30,35±2,11	33,38±2,09

Note: PF – Physical Functioning, RP – Role Physical Functioning, BP – Bodily Pain, GH – General Health, VT – Vitality, SF – Social Functioning, RE – Role Emotional Functioning, MH – Mental Health.

* Difference is statistically significant compared with the corresponding indicator of the parallel group at $p \leq 0.05$.

$ Compared with the baseline level.

Difference is statistically significant compared with the pre-treatment value within the same group at $p \leq 0.05$.

Social Functioning (SF) reflects the degree of socialization of the patients; a decrease in this subscale was observed to be 4.5-fold in the main group and fivefold in the comparison group relative to population norms, indicating a reduction in the frequency and quality of relationships with friends, relatives, colleagues, and surrounding individuals. Low scores on the Role Emotional (RE) scale indicate a significant impact of depressed emotional status on daily life activities; in both groups, the mean score on this scale was approximately fourfold lower than population norms.

The subjective assessment of Mental Health (MH), which reflects mood, happiness, calmness, and emotional well-being, showed that at admission patients in the main group demonstrated a 2.9-fold reduction compared with population norms, whereas in the comparison group the reduction was 3.1-fold. It should be noted, however, that no statistically significant differences between the groups were observed on the SF-36 scales at admission ($p \geq 0.05$), although the greatest difference was recorded for the Vitality (VT) parameter, with smaller differences observed for Bodily Pain (BP) and Mental Health (MH).

We found no statistically significant differences from baseline across all SF-36 questionnaire scales in either group from the time of hospital discharge through the end of the follow-up period. It should also be noted that no statistically significant intergroup differences were observed for any of the SF-36 indicators at any time point during dynamic follow-up. Based on the obtained quality-of-life (QoL) results, it can be concluded that the emotional and physical components of patients' functioning are subjectively similar for both surgical techniques; that is, when surgical intervention is performed adequately and competently, the specific method used has little impact on patients' long-term outcomes.

However, comparative intergroup analysis of the increase in the mean SF-36 score relative to baseline revealed a statistically significant difference in favor of the main group (MG) at 1 year after surgical correction ($p = 0.049336$). A similar pattern was observed at 2 years after surgery ($p = 0.039937$) and at 3 years of follow-up ($p = 0.049075$). Nevertheless, a clear and persistent trend was identified: over time, the MG demonstrated higher QoL scores across all SF-36 scales, indicating greater subjective clinical, social, and mental functioning in patients who underwent surgical correction using the authors' developed method of pharyngocolonic anastomosis during bypass esophageal reconstruction.

Thus, although a certain degree of subjective similarity was observed between the two management strategies, the dynamics of overall condition and dysphagia according to the Visual Rating Scale (VRS), anxiety and depression according to the HADS, and state and trait anxiety according to the STAI suggest that, when choosing a technique for pharyngocolonic anastomosis during bypass esophageal reconstruction, preference should be given to the method developed by the authors. This preference is based primarily on its greater economic efficiency, assuming comparable physical capacities of the patients. The use of this technique may reduce the physical, psychological, and social consequences of combined post-burn cicatricial strictures of the pharynx, esophagus, and stomach, accelerate the recovery of physical and mental health, and facilitate patients' social reintegration.

Conclusion. Formation of a pharyngeal anastomosis is inherently more technically demanding than the creation of an esophageal anastomosis. This is largely due to the anatomical characteristics of this region as well as the severity of cicatricial changes in the pharynx. Most surgeons involved in esophageal surgery, particularly in the management of post-burn cicatricial

strictures, employ the same technique for pharyngeal anastomosis as for esophageal anastomosis. Although published results in the available literature demonstrate a tendency toward improvement, they remain far from optimal. The proposed variant of pharyngeal anastomosis is not a panacea for complications such as anastomotic leakage or the development of cicatricial strictures in the long-term period; however, it allowed a substantial reduction in their incidence.

Comparative intergroup analysis of the results of surgical correction of combined post-burn cicatricial strictures of the pharynx, esophagus, and stomach according to the Visual Rating Scale (VRS) demonstrated greater subjective effectiveness of the method of forming a pharyngocolonic anastomosis during bypass esophageal reconstruction developed by the authors compared with the standard surgical technique. According to the HADS depression subscale, normalization of patients' condition in the main group (MG) occurred after 6 months, whereas in the comparison group (CG) it was observed only after 2 years. Moreover, intergroup comparison revealed a statistically significant difference after 1 year of follow-up, indicating greater subjective psychological effectiveness of the authors' developed method of pharyngocolonic anastomosis during bypass esophageal reconstruction compared with the formation of an anastomosis using an oblique-transverse incision of the esophagus.

We observed a statistically significant reduction in state anxiety according to the STAI test in the main group already at discharge, whereas in the comparison group this reduction was noted only 6 months after surgical correction. At the same time, trait anxiety according to the STAI test showed statistically significant changes compared with baseline as early as discharge in both groups; however, no statistically significant intergroup differences for this scale were detected throughout the entire follow-up period. Comparative intergroup analysis of the increase in the mean SF-36 score relative to baseline demonstrated a statistically significant difference in favor of the main group at 1 year after surgical correction ($p = 0.049336$). An identical pattern was observed at 2 years after surgery ($p = 0.039937$) and at 3 years of follow-up ($p = 0.049075$).

Nevertheless, a clear and persistent trend was identified: over time, the main group demonstrated higher quality-of-life scores across all SF-36 scales, indicating greater subjective clinical, social, and mental functioning in patients who underwent surgical correction using the authors' developed method of pharyngocolonic anastomosis during bypass esophageal reconstruction. Based on the obtained quality-of-life results, it can be concluded that, although a certain degree of subjective similarity exists between the two management strategies, the dynamics of overall condition and dysphagia according to the Visual Rating Scale, anxiety and depression according to the HADS, and state and trait anxiety according to the STAI support the preference for the authors' developed method when selecting a technique for pharyngocolonic anastomosis during bypass esophageal reconstruction. This preference is largely justified by its greater economic efficiency, assuming comparable physical capacities of patients, and may contribute to reducing the physical, psychological, and social consequences of combined post-burn cicatricial strictures, accelerating recovery of physical and mental health, and enhancing patients' social reintegration.

Conclusion statement. The method of forming a pharyngocolonic anastomosis during bypass coloplasty implemented in clinical practice improved the effectiveness of surgical correction in patients with combined post-burn cicatricial strictures of the pharynx, esophagus, and stomach, reduced the recurrence rate of dysphagia, enhanced quality of life, and promoted patients' social rehabilitation.

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EVALUATION OF THE EFFECTIVENESS OF SURGICAL INTERVENTION IN INTRAOCULAR LENS SUBLUXATION IN THE PEDIATRIC POPULATION

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Abstract. *This article presents an analysis of two clinical cases of late postoperative complications following congenital cataract extraction in children, accompanied by intraocular lens (IOL) subluxation and iris capture. It is shown that displacement of the IOL leads to pupil deformation and a decrease in visual functions. Based on clinical observations, the effectiveness of a combined surgical approach involving iridoplasty is demonstrated. The study concludes that preventive iridoplasty is advisable when iris capture is detected in order to form a functional pupil and prevent recurrence of complications. The aim of the study was to analyze clinical cases of IOL subluxation after cataract extraction with intraocular lens implantation and to identify the features of the applied surgical treatment strategy.*

Keywords: *congenital cataract, intraocular lens subluxation, iridoplasty, postoperative complications.*

Introduction

Surgical treatment of congenital cataract in children remains one of the major complex problems in ophthalmic practice. Despite advances in minimally invasive technologies, a high incidence of late complications after cataract extraction persists in pediatric patients, among which intraocular lens (IOL) subluxation occupies a leading position. According to the literature, the incidence of IOL displacement in childhood ranges from 5% to 20%, which is significantly higher than in adult patients [1,2,3,9]. The increased risk is associated with anatomical and physiological features of the pediatric eye, including a prolonged period of eyeball growth, increased elasticity of the capsular–zonular apparatus, pronounced postoperative inflammatory response, as well as a tendency toward synechiae formation and capsular contraction [4,5,14,15].

Decentration or subluxation of the IOL leads to reduced visual quality, abnormal pupil shape, higher-order aberrations, and an increased risk of amblyopia. In the absence of timely correction, this complication may result in persistent visual impairment or childhood disability [6,7,8,12]. The choice of optimal surgical tactics for late IOL displacement in children remains debatable. Repositioning, stabilization, IOL exchange, or combined surgical interventions should be selected individually, taking into account the anatomical and functional condition of the eye and the severity of the complication [8,10,11,13]. The presented clinical cases demonstrate an approach to selecting surgical treatment tactics for late IOL subluxation in a child after congenital cataract removal.

The aim of the study was to analyze clinical cases of IOL subluxation after cataract extraction and implantation of an intraocular lens, and to identify the characteristics of the applied surgical treatment strategy.

Materials and Methods. We analyzed clinical observation cases of patients N.M. and Kh.A. treated at the ophthalmology department of the clinic of Tashkent State Medical University. Patient N.M., born on May 27, 2014 (10 years old), from Namangan region, Namangan city.

Complaints: according to the mother, a change in pupil shape and decreased visual acuity of the left eye.

Patient Kh.A., born on September 20, 2013 (9 years old), from Andijan region.

Complaints: according to the mother, change in pupil shape of the right eye, decreased visual acuity, and discomfort in bright light.

The patients underwent comprehensive ophthalmological examinations, clinical and laboratory investigations, as well as consultations with related specialists (otolaryngologist, pediatrician, neurosurgeon, neurologist).

Results. Patient Kh.A. Anamnesis morbi: According to the mother, the disease was first noticed at the age of three years, when the parents observed a change in the color of the pupil of the right eye. The patient consulted an ophthalmologist at the local place of residence and was diagnosed with congenital cataract of the right eye (OD) and referred to the clinic of TashPMI, where planned surgical treatment was recommended. On 07.10.2022, the patient underwent surgery: OD – total cataract extraction with intraocular lens implantation (+19.0 D). The early postoperative period was uneventful. One year after surgery, the parents noticed a change in the shape of the pupil of the right eye and sought medical care at the TashPMI clinic. Examination revealed IOL subluxation with partial iris capture. The diagnosis of OD – IOL subluxation was established, and surgical treatment was recommended. On 19.10.2023, the patient underwent OD – IOL reposition and synechiotomy. The postoperative course was stable, with improvement in visual acuity. However, at a follow-up examination six months later, the parents again reported decreased visual acuity and pupil deformation. Status oculorum: OD – Calm, no pathological discharge. The cornea is transparent. The anterior chamber is of moderate depth, aqueous humor is clear. The pupil is black, oval, deformed, and displaced upward. The optical part of the IOL is displaced upward by 1 mm. Iris capture of the IOL haptic element is noted from 11 to 1 o'clock. Fundus reflex is uneven pink. Extraocular movements are full. OS – Calm, no pathological discharge. The cornea is transparent, the anterior chamber is of moderate depth, aqueous humor is clear. Iris structure and relief are preserved. The pupil is round, black, with preserved reaction. The lens is transparent. Fundus reflex is pink. Extraocular movements are full.

Fundus examination: OU – The optic disc is round with clear margins, pale pink in color, vascular caliber preserved. Visual acuity: Visus OD/OS = 0.2 (uncorrected) / 1.0. B-scan ultrasonography: Retina attached, vitreous body without echopathology. A-scan: 22.85 mm / 22.90 mm. Laboratory findings: Complete blood count, urinalysis, stool analysis, and blood biochemistry were within normal limits. ECG showed sinus rhythm. Blood tests for HIV, hepatitis B and C were negative.

Specialist consultations:

Pediatrician – no acute somatic pathology.

Otolaryngologist – ENT organs without pathology.

Neurologist – no abnormalities detected.

Based on the clinical findings, the diagnosis of OD – IOL subluxation was confirmed. Repeat surgical treatment was performed: OD – synechiotomy, IOL reposition, partial anterior vitrectomy, and iridoplasty.

Surgical procedure:

The operative field was treated with betadine. A blepharostat was applied. Paracentesis was performed at the 8 o'clock position. Viscoelastic was injected into the anterior chamber. Iris revision revealed flat synechiae from 11 to 1 o'clock with IOL capture, which were dissected using a microspatula and Vannas scissors. The IOL was repositioned into the posterior chamber. Partial anterior vitrectomy was performed. A 3.0 mm central opening was created in the posterior capsule. Iridoplasty was carried out using a modified McCannel technique with 10-0 suture material, achieving restoration of a central, round pupil. The anterior chamber was irrigated with saline solution followed by 0.1% dexamethasone solution. Paracentesis hydration was performed, sterile air was injected, and subconjunctival injections of dexamethasone and ceftriaxone (0.3 ml each) were administered. An aseptic monocular dressing was applied. Postoperative treatment included topical dexamethasone 0.1% eye drops administered hourly and moxifloxacin 0.5% eye drops six times daily. On the first postoperative day, the surgical wound was clean, sutures were intact, the cornea was transparent, the anterior chamber was of moderate depth, and the aqueous humor was clear. The pupil was round and centrally located. The IOL position was central, and intraocular pressure was within normal limits. At discharge, the patient's general condition was satisfactory. Ophthalmological examination revealed a clear cornea, central and round pupil with coloboma at 12 o'clock, central IOL position, pink fundus reflex, and normal intraocular pressure. Visual acuity was OD – 0.5 and OS – 1.0. During a 1.5-year follow-up period, the operated eye remained stable with no signs of recurrent iris capture or IOL dislocation. Visual acuity was preserved, indicating a positive outcome of the surgical intervention. Patient N.M. Anamnesis morbi: According to the mother, the disease was noticed at the age of two years when a gray coloration of the pupils of both eyes was observed. The patient was referred to the clinic of Tashkent State Medical University, where the diagnosis of OU – congenital cataract was established. On 05.04.2022, OD – total cataract extraction with IOL implantation (+20.0 D) under capsular tension ring support was performed. On 08.06.2022, OS – total cataract extraction with IOL implantation (+19.0 D) and basal iridectomy was carried out. The patient was discharged in satisfactory condition. At a six-month follow-up examination, both eyes were calm with transparent corneas and clear aqueous humor. In the right eye, the pupil was oval, the IOL was centrally positioned, and uneven posterior capsule opacification was noted. In the left eye, superior IOL displacement from 10 to 12 o'clock with iris capture was detected. The optical part of the IOL remained central, while the haptics were not visualized. The pupil was deformed due to traction of the iris margin. Extraocular movements were full in both eyes.

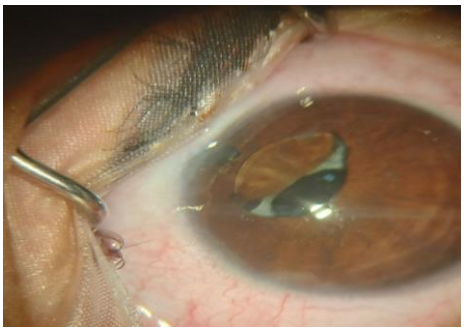


Figure 1. Patient: iris capture of the pupil by the haptic element of the intraocular lens in the left eye before surgery.

Visual acuity: Visus OD/OS = 0.6 (uncorrected) / 0.1 (eccentric fixation). B-scan ultrasonography: OU – vitreous body without echopathology, retina attached.

A-scan: 23.10 mm / 22.72 mm.

Laboratory findings: Complete blood count, urinalysis, stool analysis, and blood biochemistry were within normal limits. ECG revealed sinus rhythm. Blood tests for HIV, hepatitis B and C were negative.

Specialist consultations: Pediatric examination – no acute somatic pathology detected.

Otolaryngological examination – ENT organs without pathology.

Neurological examination – asthenoneurotic syndrome.

Based on the above findings, the clinical diagnosis of OS – intraocular lens subluxation was established. Therefore, surgical treatment was performed: OS – synechiotomy, IOL reposition, partial anterior vitrectomy, and iridoplasty. Surgical procedure: The operative field was treated with betadine. A blepharostat was applied to the left eye. Paracentesis was performed at the 8 o'clock position. Viscoelastic was injected into the anterior chamber. Iris revision using a spatula revealed flat synechiae from 11 to 2 o'clock with IOL capture. The synechiae were dissected using a microspatula and Vannas scissors. The IOL was repositioned into the posterior chamber. Partial anterior vitrectomy was performed. Fibrosis of the posterior capsule was noted, with a central opening measuring 3.0 mm. Iridoplasty was performed using a modified McCannel technique with 10-0 suture material. Approximation of the iris edges was achieved, restoring a central and round pupil. A full-thickness corneal entry into the anterior chamber was made. Under visual control, the peripheral iris edge in the defect area was sequentially grasped and sutured. A second pass was performed to fix the opposite iris segment, after which the suture was externalized through the cornea. Knot formation was performed using a Zinskey instrument, resulting in a single secure suture and adequate approximation of the iris edges with restoration of the central pupil position. The pupil became round. The anterior chamber was irrigated with saline solution followed by 0.1% dexamethasone solution. Hydration of the paracentesis site was performed, and sterile air was injected into the anterior chamber. Subconjunctival injections of dexamethasone and ceftriaxone (0.3 ml each) were administered. Antiseptic eye drops were instilled, and an aseptic monocular dressing was applied. Postoperative topical treatment included dexamethasone 0.1% eye drops (2 drops hourly), moxifloxacin 0.5% eye drops (2 drops six times daily), and Kupen Forte 0.5% eye drops (2 drops three times daily).

First postoperative day: OS – surgical wound clean, sutures intact, cornea transparent, anterior chamber of moderate depth, aqueous humor clear. The pupil was centrally located and round. An air bubble was present in the pupillary area. The IOL position was central. Intraocular pressure was within normal limits. At discharge: The patient's general condition was satisfactory. Body temperature was 36.6°C. Vesicular breathing was noted in the lungs. Heart sounds were rhythmic. The abdomen was soft and painless, with regular bowel movements and diuresis.

OS – calm, no pathological discharge. The surgical wound was clean, sutures intact. The cornea was transparent, the anterior chamber was of moderate depth, and the aqueous humor was clear. The pupil was centrally located and round (Figure 2), with coloboma at the 12 o'clock position. The IOL position was central. Fundus reflex was pink. Intraocular pressure was within normal limits. Visual acuity at discharge: Visus OD – 0.6; OS – 0.8. The combined surgical intervention made it possible to eliminate the mechanical iris capture and restore the anatomy of the anterior segment. In the postoperative period, the patient was followed up dynamically by an ophthalmologist with regular examinations. During the two-year follow-up after surgery, a stable ophthalmological condition was observed, with no signs of recurrent iris capture or dislocation of the optical elements of the intraocular lens. Functional outcomes, including visual acuity, remained

at high levels, indicating a sustained positive anatomical and functional result of the performed intervention.

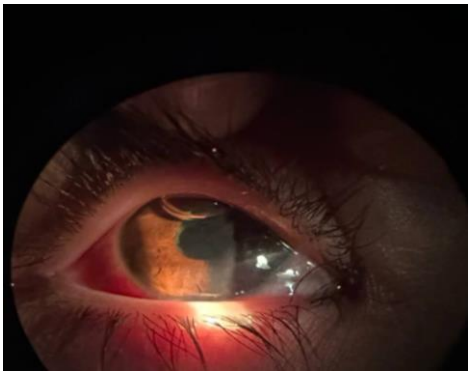


Figure 2. Patient: centrally located, round pupil after surgical treatment.

Conclusion. Clinical observation demonstrated the characteristic manifestations of a mechanical IOL-related complication, namely iris capture of the lens and pupil deformation. Analysis of the therapeutic measures showed that the combination of synechiotomy, IOL reposition, vitrectomy, and iridoplasty is an effective method for eliminating this complication. The obtained data indicate that iridolenticular capture of the intraocular lens in pediatric patients leads to persistent dysfunction of the iris sphincter, accompanied by pupil deformation and insufficiency. Under conditions of ongoing traction, there is a high risk of recurrent pupil capture and secondary subluxation of the optical part of the IOL. Therefore, when iris capture is detected, performing iridoplasty using a modified McCannel technique with 10-0 suture material is advisable. This approach allows restoration of the central position and round shape of the pupil, enabling the formation of a functional pupil with a diameter of approximately 3 mm and preventing recurrent involvement of the iris in the IOL area.

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