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The Biological Significance of Zinc and Selenium Levels in Women of Reproductive Age Infected with Chronic Hepatitis B Virus Residing in Island Coastal Areas

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Abstract This article focuses on a comparative evaluation of how particular micronutrients (such as zinc and selenium) affect the clinical course of the disease, its outcomes, and the incidence of complications in women of reproductive age with chronic viral hepatitis B residing in various regions of the island, particularly in the city of Urganch. The levels of selenium and zinc in the blood serum of practically healthy women of reproductive age in Urganch, an area known for its ecological challenges, fall below the standard range.

Keywords Aral Sea, Zinc, Selenium, Chronic viral hepatitis B

1. Introduction

The disruption of ecological balance in the external environment adversely impacts liver function. Approximately two-thirds of exogenous substances with hepatotoxic effects are metabolized and neutralized within the liver. Unfavorable environmental factors diminish the functional efficacy of nonspecific resistance systems, notably including antioxidant defense mechanisms, thereby primarily compromising the body's detoxification capacities [2].

Presently, within the Aral Sea region, a desert has emerged, characterized by recurring dust and salt storms, resulting in the dispersal of 40 to 160 million tons of particulate matter. Predominantly comprised of sulfate and chloride salts, these airborne particles have significant implications for human health. Through a comprehensive review of literature, it has been observed that the levels of substances such as phenol, pesticides, and arsenic in the soil of the Aral region have doubled, thereby disrupting the balance of essential micronutrients within the human body. Prolonged chronic exposure to 'low concentration' metals (Hg, Pb, Cd, As, Mn, Fe) further exacerbates the depletion of selenium levels [1].

Clinical and experimental findings have demonstrated the intricate balance of trace element composition within body tissues, wherein alterations in the concentration of one element can precipitate changes in others. Microelements such as Zinc (Zn) and Selenium (Se) modulate intracellular systems, enhancing the production or efficacy of numerous cellular cytokines that bolster immune responses. Moreover, several trace elements serve as integral components of the body's antioxidant defense mechanism, contributing to the functionality of diverse enzyme systems and upholding the stability and activity of protein molecules. Investigating their roles in the onset and progression of specific pathological processes remains a pertinent area of research [3,4,5].

Zinc stands as a pivotal trace element within the human body, with approximately 2 grams distributed across various organs and tissues of an adult. It serves as a catalyst for around 300 metalloenzymes, playing a crucial role in nucleic acid synthesis and degradation, protein metabolism, and nitrogen metabolism. Additionally, zinc exhibits notable antioxidant properties. [4]. Accordingly, it is relevant to study the effect of certain micronutrients on the clinical-laboratory course of chronic viral hepatitis B in women of reproductive age living in environmentally unfavorable conditions.

2. Purpose of the Research

The purpose of this study is to conduct a comparative investigation into the impact of specific microelements (zinc, selenium) on the clinical trajectory of the disease, its ramifications, and the extent of complication development among women of reproductive age afflicted with chronic

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viral hepatitis B residing in the city of Urganch.

3. Materials and Methods

To achieve the objectives outlined, we conducted a prospective case-control study involving 92 patients diagnosed with chronic hepatitis B who underwent treatment. The study comprised three distinct groups. The primary group consisted of 52 women of reproductive age who received treatment for chronic viral hepatitis B between 2019 and 2023 at the Infectious Diseases Hospital in the Urganch district of the Khorezm region. The comparative group comprised 40 women of reproductive age who received treatment for chronic viral hepatitis B during the same period at the Republican Specialized Epidemiology, Microbiology, and Infectious Diseases Center under the Ministry of Health of the Republic of Uzbekistan. The control groups were delineated as follows: Control Group I included 10 healthy women of reproductive age residing in the Urganch district of the Khorezm region, while Control Group II comprised 15 healthy women of reproductive age residing in Tashkent city. Several criteria were deemed significant for patient inclusion in the study, including an age range of 18 to 49 years, female gender, voluntary consent to participate, and confirmation of chronic viral hepatitis B diagnosis through serological methods. Patients with a medical history of oncological, hematological, hepatic, renal, or cardiac chronic conditions, as well as pregnant or lactating women, individuals who declined participation in the study, those whose disease was not confirmed through serological examination, and individuals below 18 years or above 49 years of age were excluded from the study. Patients who presented at the hospital and satisfied the aforementioned criteria were enrolled in the study group via random sampling, resulting in a total of 92 individuals. The mean age of the patients was recorded as 42.5±0.7 years.

For the determination of the etiological factor of chronic viral hepatitis, serological markers including HBsAg and polymerase chain reaction (PCR) were employed to detect viral DNA. According to the findings of the investigation, all 92 observed patients tested positive for HBsAg.

The assessment of the chronic infectious process activity was established through an analysis of the nature and severity of primary symptoms, including intoxication, levels of bilirubin and liver-specific enzymes, hepatosplenomegaly, presence of acute or chronic liver failure manifestations, and other pertinent indicators.

The analysis of selenium and zinc microelement levels in patients' blood serum was conducted at the clinical laboratory of the Republican Center for Scientific Research of Specialized Epidemiology, Microbiology, Infectious, and Parasitic Diseases using the "endpoint chemical analyzer" method.

The digital data obtained from the research underwent statistical analysis utilizing the method of variational statistics, employing the software "Microsoft Excel" 2003 (HP). Parameters such as arithmetic mean (M), standard deviation, standard error of the mean (m), and relative values (expressed as levels or percentages) of the investigated variables were calculated using variational parametric and non-parametric statistical techniques. Additionally, the probability of error (R) was determined through error probability calculations. Quantitative changes with a confidence level ($r<0.05$) were considered statistically significant.

Correlation-regression analysis, specifically utilizing Pearson's coefficient, was executed employing a medical statistical calculator available at https://medstatistic.ru/calculators to ascertain the correlation between the groups under examination.

The odds ratio (OR) was calculated to assess statistically significant differences in quality markers between groups, with a 95% confidence interval (CI) determined for this measure. Statistical significance was assessed differently based on the magnitude of the odds ratio: for cases where the odds ratio was up to 5, analysis of four-way tables using Fisher's exact test was employed; when the odds ratio ranged from 5 to 10, the $\chi 2$ test with Yates correction was utilized; and for odds ratios exceeding 10, the $\chi 2$ test was applied.

4. Results

The average age of the patients of the main group of the study was 32.9±0.44, and that of the comparative group was 38.7±0.5 years (p=0.000000), that is, the patients of Urganch city were reliably younger than the patients of Tashkent city.

In the comparative group, 30.0% (12) of the women exhibited a chronic infectious process characterized by minimal activity, while 65.0% (26) demonstrated moderate activity, and 5.0% (2) displayed high activity. The average duration of hospitalization (bed-days) for this group of patients was recorded as 18.25±0.32.

In the main group, 9.6% (5) of patients exhibited a chronic infectious process with minimal activity ($\chi 2=6.237$, P=0.013), 55.8% (29) displayed moderate activity ($\chi 2=0.801$, P=0.371), and 34.6% (18) demonstrated maximum activity ($\chi 2=11.655$, P<0.001). The average duration of hospitalization (bed-days) for this group of patients was recorded as 22.3± 0.28 days (P=9.52).

Upon examining the selenium and zinc levels in the blood serum of patients within the study group, it was discovered that in Control Group I, comprising healthy women from Urganch city, the average selenium level was 51.3±0.23 μg/dl, whereas in healthy women from Tashkent city, it averaged at 87.7±3.4 μg/dL. A significant disparity between the groups was evident (p=0.000000), indicating that the selenium levels in the blood serum of women from Tashkent city aligned with the reference value, whereas the value of this trace element in healthy women from Urganch city was 1.1 times lower than the reference value level. The mean serum selenium concentration among women diagnosed with chronic viral hepatitis B in Urganch within the main group was determined to be 48.7±0.98 μg/dl, which represents a reduction of 1.0 times compared to healthy women in Urganch (p=0.012297) and a decrease of 1.2 times relative to the reference value (p=0.000000). Conversely, among women

infected with chronic viral hepatitis B in Tashkent city, the mean serum selenium concentration was measured at 56.6±1.2 μg/dl, showing no statistically significant deviation from the reference value (p=0.257674). However, the serum selenium value of women infected with chronic viral hepatitis B living in Urganch city was significantly lower than the value of women infected with chronic viral hepatitis B living in Tashkent city by 1.2 times (p=0.000002).

During the examination of zinc levels in the blood serum of patients within the research group, it was observed that the average zinc concentration in the blood serum of women from control group 1 was 3704.3±74.3 μg/l, whereas in women from control group 2, it measured 5048.7±110.1 μg/l, with the reference lower limit being 4000 μg/l. The zinc levels in healthy women residing in Urganch were found to be statistically significantly lower compared to those in women from Tashkent (p=0.000000) and below the lower limit of the reference range (p=0.037162). The average zinc concentration in the blood serum of patients in the primary group was 3344.2±83.3 μg/l, which was 1.1 times lower than that of healthy women in Urganch (p=0.001987). Conversely, patients in the comparative group exhibited an average zinc value of 4307.7±17.7 μg/l, indicating levels within the reference range. A statistically significant difference was observed between patients in the primary and comparative groups (p=0.000000).

When examining the levels of trace elements relative to the activity level of chronic infectious processes in patients belonging to both the main and comparative groups, it was discovered that among the five patients in the main group with minimally active chronic infections, the average selenium concentration in blood serum was 52.2±1.1 μg/dl. In contrast, the comparative group exhibited a value of 62.9± 2.3 μg/dl, which aligned with the reference range, indicating a significant difference between the groups (p=0.000489). Moreover, patients in the main group with moderately active chronic infections had a notably lower selenium level in blood serum (47.7±0.87 μg/dl) compared to their counterparts in the comparative group (55.5±1.6 μg/dl) (p= 0.007239).

Table 1. The fluctuation in the concentration of certain trace elements in the blood serum of patients within the research group, contingent upon the activity of the chronic infectious process

Chronic process activity	Microelement	
	Selenium (μg/dL)	Zinc (μg/l)
Main group (n=52)		
minimal activity (n=5)	52,2±1,1	3827,6±71,2
moderate activity (n=29)	47,7±0,87	3140,2±68,7
high activity (n=18)	44,3±0,73	3054,8±54,3
Comparative group (n=40)		
minimal activity (n=12)	62,9±2,3	4764,7±56,7
moderate activity (n=26)	55,5±1,6	4204,9±43,7
high activity (n=2)	49,9±1,1	3997,5±44,6
	p^1=0.000489 p^2=0.007239 p^3=0.000550	p^1=0.000000 p^2=0.000000 p^3=0.000000

Patients with a high activity level of chronic infectious processes exhibited a similar trend, wherein the serum selenium levels in the main group were notably lower compared to those in the comparative group (r=0.000550) (refer to table 1). Furthermore, when examining the correlation between selenium levels and the activity of chronic infectious processes, a strong positive correlation was observed both in the main group of patients (r=1.0) and in the comparative group (r=0.97). This indicates that as the level of selenium in blood serum decreased, the activity of the chronic process intensified.

5. Discussion

Based on the analysis of our results, the patients under observation in our study are women of reproductive age diagnosed with chronic viral hepatitis B. Notably, women residing in Urganch city were found to be on average 6 years younger than those in Tashkent city (p<0.001). Despite the predominance of moderate to high activity levels of chronic infectious processes among women in Urganch city and longer duration of illness compared to Tashkent city, the disparity between these variables did not reach statistical significance (p>0.05).

Although the selenium and zinc levels in the blood serum of practically healthy women of reproductive age in Tashkent were within the reference range, these trace elements exhibited lower values in patients with chronic viral hepatitis B. Notably, as the levels of these elements decreased, the chronic infectious process intensified. The levels of selenium and zinc in the blood serum of women of reproductive age residing in Urganch, an area known for its ecological challenges, were significantly lower than the reference range. Moreover, in women diagnosed with chronic viral hepatitis B, these trace elements exhibited further declines, contributing to the exacerbation of the chronic infectious process. Sheybak V. M. and colleagues (2013) emphasized the importance of zinc trace elements in protein and nitrogen metabolism in the human body, along with their antioxidant properties. A decline in their levels results in reduced protein synthesis, elevated ammonia levels in the bloodstream, and deterioration of the patient's health. Troshina E.A. (2018) suggests that trace elements Zn and Se exert their influence on regulatory intracellular systems, enhancing the production or function of various cellular cytokines that promote immune mechanisms. Insufficiency of these micronutrients in the body leads to weakened immune responses, disruption in the balance of Th1/Th2 cytokines, and the development of an inadequate immune response.

6. Conclusions

The levels of selenium and zinc in the blood serum of practically healthy women of reproductive age in Urganch, an area known for its ecological challenges, fall below the standard range. Similarly, women diagnosed with chronic

viral hepatitis B exhibit deficiencies in serum selenium and zinc, regardless of their geographical location. Furthermore, there exists a strong, positive correlation between the decline in selenium and zinc levels and the activity of the chronic infectious process.

Conflict of interest. The authors declare no conflict of interest.

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