PharmacologyOnLine

Archives • 2021 • vol.2 • 796-805

ZINC SUPPLY OF THE POPULATION OF UKRAINE: CONSEQUENCES FOR HEALTH AND REPRODUCTION

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Abstract

Zinc (Zn) is one of the most biologically significant essential metals, performing signal, adaptive, metabolic, structural, protective, restorative and other physiological functions in the human and animal. Zn homeostasis and functional activity are maintained with the participation of a wide range of epigenetic factors (natural and anthropogenic geobiospheric, alimentary, industrial, social and economic), which are formed in specific regional conditions of the population's life. Despite the long-term study of this problem and a large number of publications, many of its aspects remain insufficiently studied, especially in critical epidemiological situations. Therefore, the purpose of this work was to compare the epidemiological indicators of zinc content in biosubstrates of the inhabitants of Ukraine in the period 2008-2019. (before the COVID-19 pandemic) and in the period 2020-2021 (during the pandemic) for use in therapeutic and prophylactic purposes in the future. The zinc content in blood, hair and urine of 1819 people aged 17-67 years (average age 37 years, men 673, women 1146) was determined using the EMAS-200 CCD atomic emission spectrometer in the period from 2008 to 2021. The results were statistically processed by nonparametric methods. The obtained results showed a generally satisfactory supply of Zn for the population of Ukraine at the regional level with a tendency to limit the size of the cohort of the surveyed with significant deviations. At the same time, attention is drawn to the indicators that indicate a decrease in the general physiological level of the body supply of the examined persons with Zn. They can be deformed due to the uncontrolled intake of zinc preparations by a part of the population during the COVID-19 pandemic. Therefore, further research is needed to study the mechanisms of the observed changes and to develop measures to optimize regional norms of Zn.

All human studies were conducted in compliance with the rules of the Helsinki Declaration of the World Medical Association "Ethical principles of medical research with human participation as an object of study". Informed consent was obtained from all participants.

Keywords: *zinc, blood, urine, hair, Ukraine*

Introduction

The outbreak caused by the SARS-CoV-2 coronavirus, which affected the population of about 200 countries (180 million cases and 3.8 million deaths), was declared a pandemic by the World Health Organization (WHO) on March 11, 2020 [1].

In the treatment and prevention of infectious diseases of various etiologies, biologically active additives, including vitamins and microelements, play an important role. Since the beginning of the pandemic, more than 50 thousand scientific articles have been published on the possible mechanisms of action of drugs on the course of COVID-19. Naturally, zinc, with its central position in the metabolism of RNA and DNA, the functioning of the T-cell link of immunity, in the metabolism of lipids and proteins, as well as participation in the structure and maintenance of activity of more than 300 metalloenzymes, immediately attracted the attention of researchers [2]. The hormones (insulin, corticotropin, somatotropin, gonadotropins) depend on the body's supply of zinc. It is no coincidence that one of the main risk factors for the severe course of COVID-19 and its life-threatening complications is diabetes mellitus, which, with hormone therapy, shown in the treatment of pneumonia caused by COVID-19, leads to a sharp and uncontrolled increase in blood glucose. [3].

In addition, Zn, which is delivered to cells with the metallothionein, is able to regulate adaptation mechanisms in hypoxic conditions due to its antioxidant effect, reduce the nonspecific permeability of cell membranes (exert a membrane-protective effect) and participate in the prevention of fibrosis, which is also one of the typical complications of viral pneumonia [3].

In addition, zinc is especially important for male reproductive health [4]. This is especially important in the context of a declining population in Ukraine.

It has been shown that Zn has the ability to increase innate and adaptive immunity in various viral infections [**Errore. Il segnalibro non è definito.**]. The inclusion of Zn in a therapeutic complex can enhance the effectiveness of its other components. [5]. Conversely, the efficiency of Zn can be increased by using, for example, chloroquine as an ionophore. Zinc inside the infected cell can inhibit the process of viral replication [6].

The content of zinc in the body under physiological conditions depends on environmental and epigenetic factors (natural clarkes of trace elements, features of the typical diet of the population, the state of the essential microbiome and virioma, the presence of systemic, infectious and other types of diseases) [7].

Undoubtedly, the role of zinc in the immune response to viral infection is important. Zn activates a number of immune response pathways such as the NF-κB signaling pathway. NF-κB affects the expression of pro-inflammatory cytokines, namely IL-1b, IL-6, IL-8, TNF-α and MCP-1, chemokines, acute phase proteins (CRP and fibrinogen), matrix metalloproteinases, adhesion molecules, growth factors and other factors involved in the inflammatory response such as COX-2 and iNOS [8, 9]. Adequate zinc levels stabilize CD4 + and CD8 + T cell counts and are critical for antiviral immunity [10, 11].

Thus, based on scientific and practical data, at the beginning of 2020, the media began to actively promote the use of zinc in high doses for the prevention of COVID-19 [12, 13].

However, despite the absolute need for zinc for the normal functioning of the body, its toxic effect is well known when the daily intake is exceeded with food and in the composition of biological additives [14, 15]. One of the most well-known consequences of excess zinc intake is its effect on copper metabolism. [16-18]. Excessive zinc intake leads to malabsorption and copper deficiency [20, 21], as a result, to microcytic anemia and neutropenia [22]. With the intake of zinc and copper in the recommended physiological doses, their antagonism is not observed, however, when any of these microelements are exceeded, the absorption of the second decreases [23. 24]. Another aspect of zinc toxicity is associated with the pancreas as a target organ with an excess of Zn in the body [25]. With excessive oral intake of zinc, symptoms such as: tachycardia, nausea, vomiting, diarrhea, vascular shock develop, signs of damage to the parenchyma of the pancreas and liver [26].

To increase the effectiveness of therapeutic measures in the COVID-19 pandemic and prevent its complications, it is important to have information on regional indicators of zinc supply to the population.

ISSN: 1827-8620

Therefore, the **purpose** of our work was to compare the epidemiological indicators of the zinc content in biosubstrates of the inhabitants of Ukraine in the period 2008-2019. (before the COVID-19 pandemic) and in the period 2020-2021 (during the pandemic) for therapeutic and prophylactic purposes.

Methods

The content of zinc in blood, hair and urine of 1819 people aged 17-67 years (average age 37 years, men 673 people, women 1146 people) was studied for a long period of time from 2008 to May 2021. The zinc content was also measured in 108 semen samples from patients with excretory toxic male infertility. Measurement of Zn content in samples carried out on an EMAS-200 CCD atomic emission spectrometer. The instrument was calibrated using a FLUKA multi-element standard solution. For analysis, the hair was cut from the occipital region of the head, not more than 3 cm from the skin surface, in order to obtain a picture for the last 2 months. The research results were processed by the methods of variational and correlation analysis using the Microsoft® Office Excel 2003 software application (license No. 74017-640-0000106-57490) according to the recommendations set forth in the manuals of S.N. Lapach et al. [27] and M.Yu. Antomonov [28].

Results

A significant amount of information has been accumulated in the literature on the required intake of zinc. [29]. At the same time, the optimal and maximum allowable level of zinc intake differs by two or more times, which makes it possible to change the diet without the danger of developing toxicosis. Based on the results of our own sample studies of the components of the food ration and finished food products, as well as a survey of the surveyed persons, it can be argued that the population of the surveyed regions of Ukraine is insufficiently supplied with zinc in the population plan. In addition, this indicator is significantly influenced by a number of dynamic epigenetic and epidemiological factors, which almost randomly reduce the intake of zinc into the body and its bioavailability.

At the first stage of information analysis, it was necessary to understand how the surveyed individuals in the general population are distributed according to the zinc content in biosubstrates, whether there are pronounced gender differences and whether there is a need for a separate analysis of the population zinc content in men and women. In fig. 1 shows a diagram showing that the mean quartile values for men and women are practically the same, despite the significantly different sample sizes, so all the obtained values can be analyzed without taking into account gender differences for the population as a whole.

One of the important aspects in the study of the provision of the population with zinc is the question of how its content in the population changes over several years (over the years). To answer this question, we statistically processed the data on the content of zinc in the blood (Fig. 1), urine (Fig. 2) and hair (Fig. 3). The time intervals 2008-2014, 2014-2019 and 2020-2021 were considered.

In fig. 2 presents the mean quartile values of zinc concentrations in the blood of the examined. At the same time, it follows from the data obtained that there is a pronounced tendency to a decrease in the level of zinc in the blood for all quartiles, except for the first. This is consistent with the protracted socio-economic crisis in the country. Only the number of people with critically low levels of zinc in their blood decreased insignificantly, i.e. We are talking, most likely, about the predominantly alimentary origin of the identified dynamics of this indicator.

The data obtained with a high degree of probability testify in favor of admission by the surveyed in 2020-2021. Zinc preparations due to the threat of infection with the SARS-CoV-2 virus. This can be clearly seen from the diagram of the distribution of zinc concentrations in the blood of the surveyed in different years (Fig. 3). From the data in Fig. 3 shows that the content of zinc in the blood was within the conditional norm (1.2-9 mg/l (ppm)) in 2008-2014 in 82% of the surveyed, in 2015-2019. - in 86.6%, and during the COVID-19 epidemic (2020-2021) - in 95.6% of the surveyed population. It is especially important that in 2020-2021. There were no cases of critical zinc deficiency.

If we evaluate the data obtained by the optimal physiological values (5-9 ppm), then the distribution of the examined according to the zinc content in the range of the conditional norm differs significantly. The number of the population with a physiologically optimal zinc content tends to decrease from 58.5% in 2008-2014 to 27.3% in 2020-2021. At the same time, the number of people with a zinc concentration of 2-5 ppm increased significantly from 31.7% in 2008-2014 to 63% in 2020-2021 (Fig. 3 B).

Increased excretion of zinc in urine in 2020-2021 was higher than the recommended norm (0.2-0.4 ppm), as can be seen in Fig. 4, which is especially clearly seen in the upper quartile (0.75). The median urinary zinc content also exceeded the physiologically accepted upper limit of the norm (0.4 ppm). The distribution patterns for quartiles 0.25 and 0.5 were almost identical, while for quartile 0.75, practically no changes were observed in the period up to 2020. And only during the COVID-19 pandemic there is an increase in this indicator by 20%.

We observe a population decrease in the concentration of zinc in the blood and an increase in its excretion in the urine, which is clearly seen from the change in the median concentrations of zinc in the blood and urine in different years (fig. 5)

Perhaps this picture is observed due to a decrease in the natural content of bioavailable zinc in food (which we wrote about earlier [30]) and the intake of various vitamin complexes and dietary supplements with forms of zinc less bioavailable for intestinal absorption to compensate for the intake of zinc, the excess of which is excreted in urine and feces. In addition, for normal interorgan transport of absorbed zinc, complete protein nutrition is necessary, since zinc is transported exclusively in the form of protein complexes [21].

During the observation period the population concentration of zinc in the blood decreased by 33%, while the excretion of zinc in the urine increased 1.6 times (Fig. 6).

Quartile mean values of zinc concentration in hair significantly differ in 2015-2021 and 2008-2014. The general trend is consistent with an increase in all quartiles. Since 2015, the concentration of zinc in hair has stabilized and slightly differ in the periods 2015-2019 and 2020-2021. (fig. 7). This can be explained by a change in the nature of the population's diet in the last decade (greater availability and variety of imported food products and finished products), as well as the use of biologically active additives (including trace elements) and the use of the latter as therapeutic agents. Therefore, over the past seven years, the values of the calculated quartiles have remained practically unchanged.

The semen of patients with excretory-toxic male infertility in Ukraine contains significantly less zinc than the semen of fertile men in this region. The general decrease in the consumption of bioavailable zinc in the population leads to an increase in the number of infertile married couples (fig. 8).

Thus, the results of determining the zinc content in biosubstrates of the population at the regional level give a comprehensive picture of the homeostasis of this bioelement and trace the tendencies of its changes, which is important for planning therapeutic and prophylactic measures.

Conclusions

1. The studies carried out give a detailed picture of the population dynamics of the zinc content in the inhabitants of Ukraine, which is important for building a system for the diagnosis, treatment and prevention of viral infections.
2. Traced the relationship of quantitative indicators of changes in the concentration of zinc in the blood, urine and hair of the examined.
3. It has been established that a fairly large contingent of the population of Ukraine (15% in 2008-2014, 20% in 2015-2019 and 9.3% in 2020-2021) has a pronounced zinc deficiency (blood content less than 2 ppm).
4. The cohort of those surveyed with a critically exceeded zinc content in biosubstrates is progressively decreasing (from 11% in 2008-2014 to 4.4% in 2020-2021). Despite the decrease in the number of people with critically low zinc content in 2020-2021, the average population indicators of the level of zinc in biological media among residents of Ukraine tend to decrease.

The problem of providing the human with zinc in the individual and population aspects remains relevant and requires continuation of comprehensive research, taking into account the complexity, multidimensional mechanisms of zinc participation in physiological and pathological processes, as well as the need to assess the relationship with other bioelements in biosystems.

ISSN: 1827-8620

Acknowledgments

The authors declare that there are no conflicts of interest.

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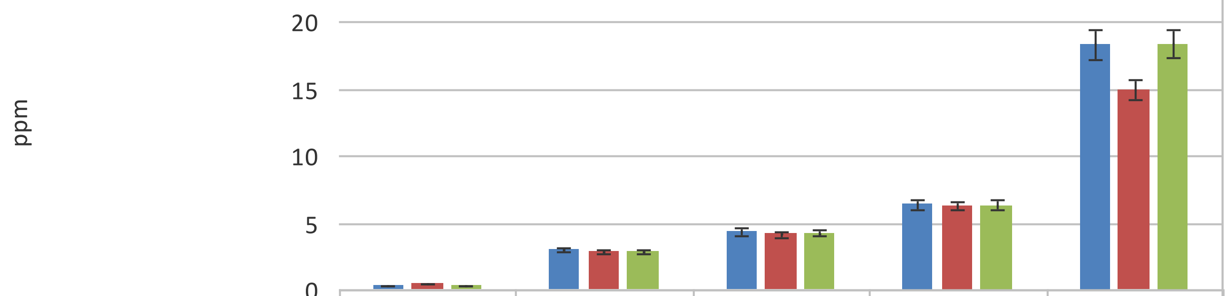


	Min	0,25	0,5	0,75	Max
Women	0,34	2,95	4,29	6,38	18,30
Men	0,40	2,85	4,14	6,30	14,91
All examined	0,34	2,85	4,24	6,32	18,30

Figure 1. Gender characteristics of the zinc content in the blood

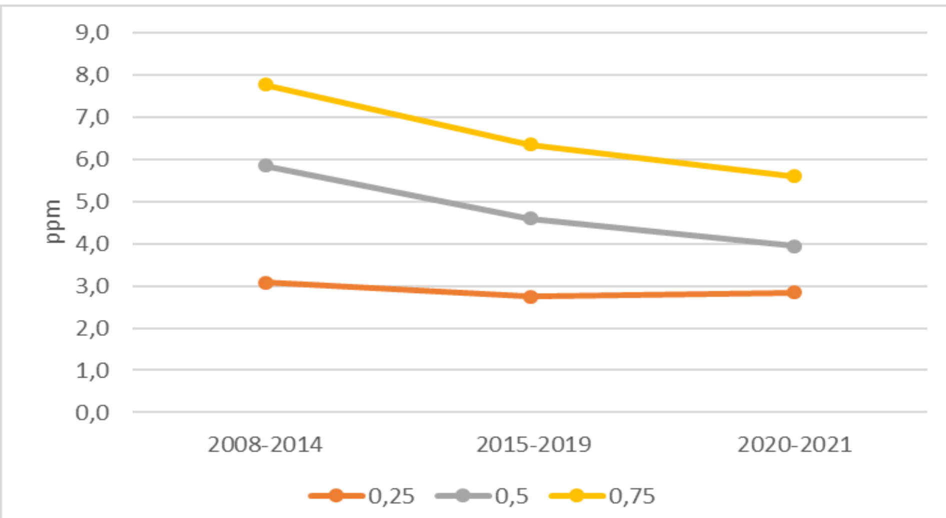
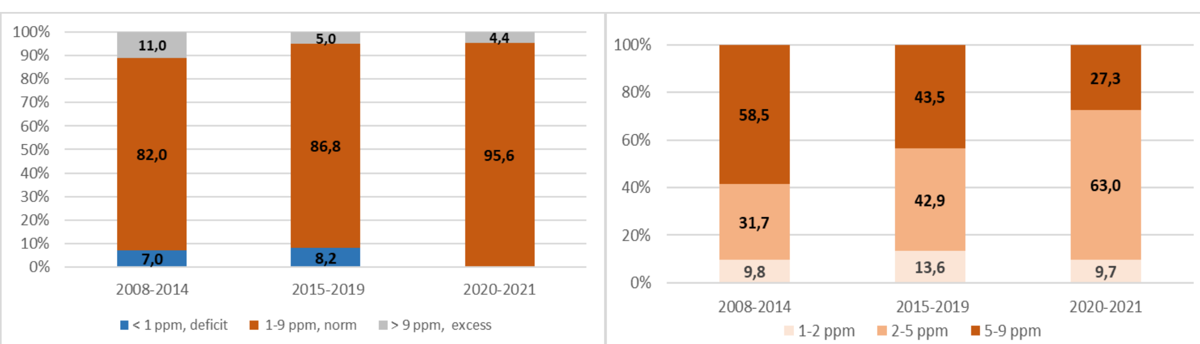


Figure 2. Changes in the content of mean quartile values of zinc concentration in the blood of people examined in different years



ISSN: 1827-8620

Figure 3. Distribution of the examined by the content of zinc in the blood,% (A) and by its content in the range of the conditional norm,% (B), depending on the period of the survey

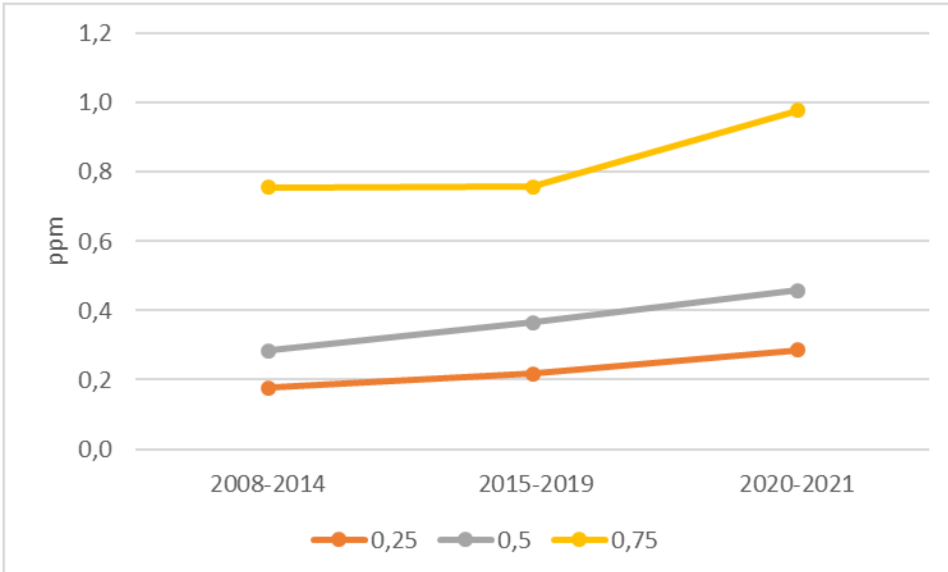


Figure 4. Changes in the content of mean quartile values of zinc concentration in urine of people examined in different years

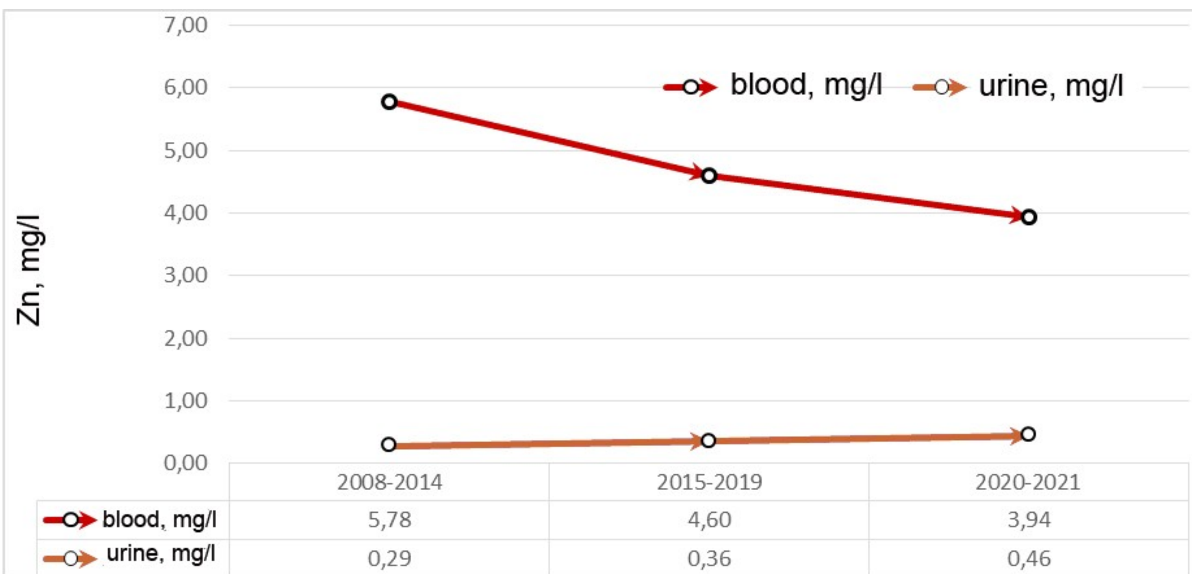


Figure 5. Dynamics of changes in the median content of zinc in blood and urine in the cohort of the surveyed in different years

ISSN: 1827-8620

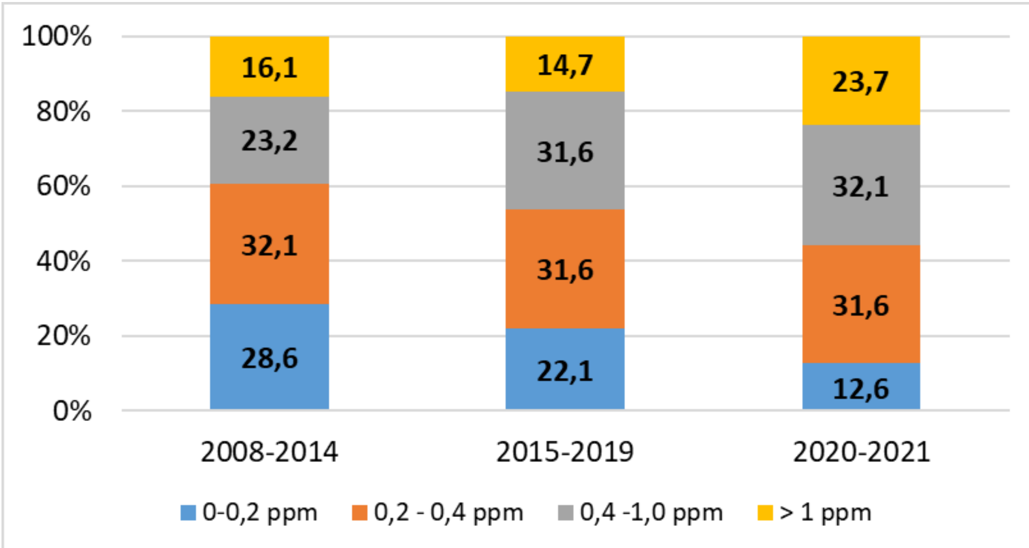


Figure 6. Distribution of the surveyed in cohorts in different years by the content of zinc in urine, %

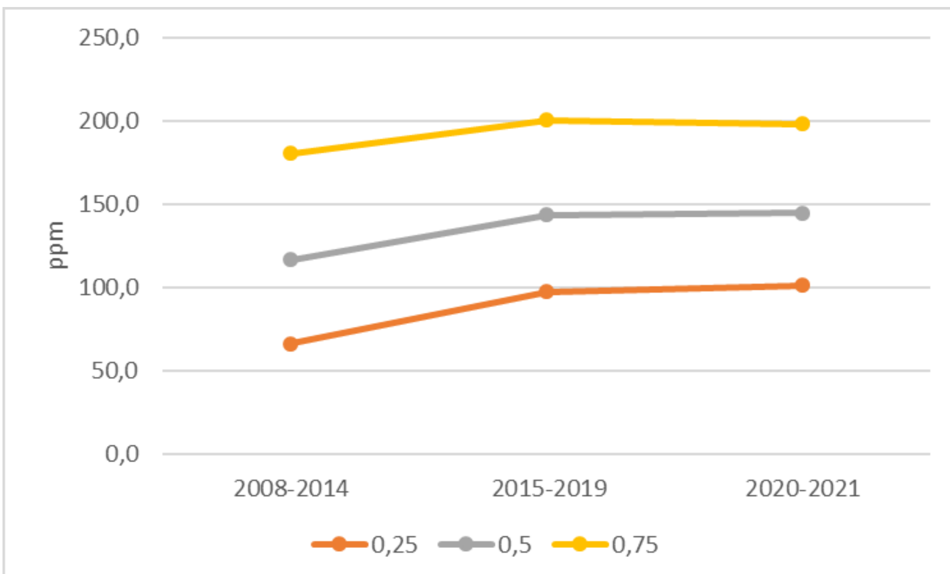


Figure 7. Change in the content of mean-quartile values of the concentration of zinc in hair

ISSN: 1827-8620

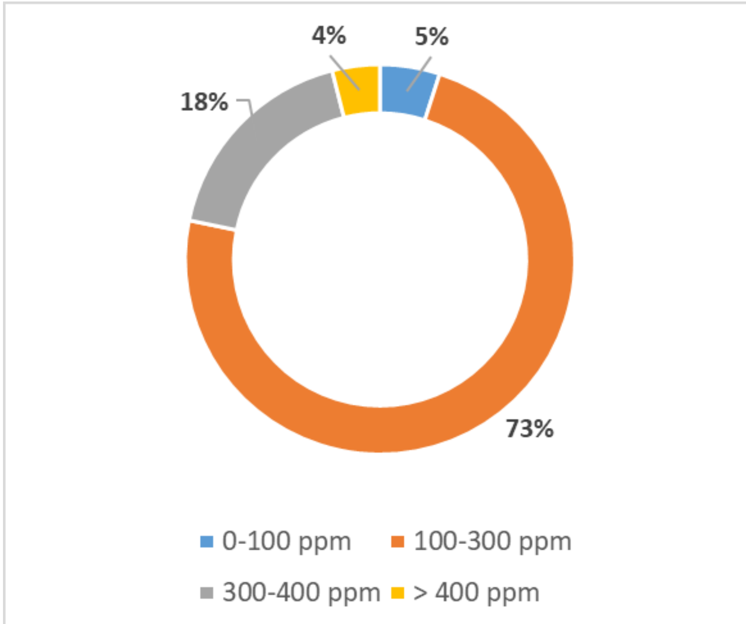


Figure 8. Distribution of patients with excretory-toxic male infertility depending on the zinc content in semen

ISSN: 1827-8620