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***Brief Communication***

# Determination of the Product of DNA Oxidation in the Blood of Women Living in the Sub-Aral Area

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**Keywords:** Aral Sea region; Oxidative stress; 8-OH-deoxyguanosine; Reproductive health

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**Abstract**

To assess the impact of climatic and anthropogenic factors of the Aral Sea region on reproductive health, we examined 300 women living in the Kyzylorda region of Kazakhstan, which borders the Aral Sea region. The survey was based on comprehensive clinical-functional and laboratory studies accounting on regional environmental and ecological factors. The survey subject was the area of 2 settlements in Kyzylorda region. In both areas, it was revealed that the examined women of the age group 30-39 years old had increased values of oxidative stress indices comparison with Atasu village of Karaganda region.

## Introduction

The Aral Sea, located on the border between Kazakhstan and Uzbekistan, was once the fourth largest inland sea in the world. Since the 1960s, the volume of water has decreased fourteen times [1], [2]. The inflow of water to the Aral Sea came from the rivers the Amu Darya from Tajikistan and the Syr Darya-from Kyrgyzstan. In the early 20th century, the demand for river water to supply local agriculture, primarily the cotton industry, led to the construction of irrigation systems [3]. As a result, a very inefficient water distribution system has emerged, accompanied by excessive use of resources. The subsequent failure to maintain the infrastructure, combined with large emissions of pollutants, had serious consequences for the people living in the areas around the Aral Sea. The literature describes numerous evidence of deterioration in the health of the local population [4]. Respiratory diseases, including tuberculosis (most of which are drug-resistant) and cancer, digestive disorders, anaemia and infectious diseases are common diseases in the region. Problems with the liver, kidneys and eyes can also be associated with toxic dust storms characteristic of the area [5].

All this has led to an unusually high mortality rate among vulnerable groups of the population: the infant mortality rate is 75 for every 1,000 newborns, and the maternal mortality rate is 12 for every 1,000 females [6]. Life in the Aral Sea area has detrimental effects on fertility, both for people who grew up in this area and for adult immigrants [7], [8].

As part of the scientific and technical program "Integrated approaches to managing the health of the population of the Aral Sea region", carried out by staff

of the Karaganda State Medical University in 2014-2016, the influence of environmental factors on the reproductive function at the molecular-cellular level of women living in the populated areas of the Republic of Kazakhstan adjacent to the Aral sea region was studied.

Oxidative stress is the result of excessive formation of reactive oxygen species regarding the degree of antioxidant protection. Physiological oxidative stress exists a priori in the body of both women and men, but with an excess of radical compounds, it can become pathological.

Oxidative stress contributes to the ageing and development of several diseases that affect the fertility of women and men. Endothelial dysfunction, secondary to oxidative stress, contributes to the development of obstetric complications, such as early and repeated pregnancy loss, pre-eclampsia, intrauterine growth retardation and premature birth [9].

Based on the preceding, the purpose of our study was to determine the quantitative content of 8-hydroxy-2-deoxyguanosine, a product of DNA oxidation, in the blood of women living in the Aral Sea Region.

## Material and Methods

Women aged 18 to 49 years living in Aralsk and Aiteke-Bi, Kyzylorda region, were surveyed and divided into 3 groups: 18-29 years old, 30-39 years old, and 40-49 years old. Atasu of the Karaganda region was chosen as the region of comparison, as it is characterised by a favourable environmental situation.

The study used the method of reversed-phase variant HPLC with some modifications [13, 14]. Chromatographic methods allow to obtain the most accurate quantitative result, as well as simultaneously and quantitatively determine all available modified bases.

## Results

According to the results of the analysis, the concentration of 8-OHdG fluctuated within 18.96–51.93 ng/ml in the studied samples. An elevated level of 8-OHdG was determined in women of the age group of 30-39 years old, living in the town of Aralsk (51.93 ng/ml) and the village Ayteke-Bi (48.69 ng/ml), compared with 8 OHdG 33.51 ng/ml in women living in the village Atasu of the Karaganda region.

**Table 1: The content of 8-hydroxy-2'-deoxyguanosine (8-OHdG, ng/ml) in the blood of women living in the settlements of Kyzylorda and Karaganda regions (M ± m)**

| Region | Age, number surveyed | 8-OHdG (ng/ml) M ± m |
|---|---|---|
| Kyzylorda region | | |
| Aralsk. n = 150 | 18-29 years old. n = 50 | 18.96 ± 0.86 |
| | 30-39 years old. n = 50 | 51.93 ± 0.89* |
| | 40-49 years old. n = 50 | 32.62 ± 1.25 |
| Ayteke-Bi. n = 150 | 18-29 years old. n = 50 | 22.21 ± 0.98 |
| | 30-39 years old. n = 50 | 48.69 ± 0.92* |
| | 40-49 years old. n = 50 | 32.54 ± 1.12 |
| Karaganda region | | |
| Atasu. n = 225 | 18-29 years old. n = 75 | 19.05 ± 0.78 |
| | 30-39 years old. n = 75 | 33.51 ± 0.98 |
| | 40-49 years old. n = 75 | 30.06 ± 0.89 |

Note the statistical significance of differences between the studied region and the comparison region: $p < 0.05$ *. Comparison of groups was carried out according to the criterion of Kruskal-Wallis

## Discussion

8-OH-deoxyguanosine (8-OHdG) is a modified nucleoside produced in a DNA molecule as a result of the action of reactive oxygen species and other damaging factors. Since its discovery in 1983 [10], this compound is determined in various tissues and body fluids: in blood, urine, brain, liver, etc., as a biomarker of oxidative stress [11]. It has been established that in women with the presence of more than 30% of damaged oocytes, the level of intrafollicular 8-oxodeoxyguanosine is significantly increased, which indicates DNA damage due to oxidative stress [9].

Currently, the European Committee is organized, with which research groups from Italy, France, Slovakia, Belgium, Germany, Denmark, Sweden, Poland, Switzerland, and Spain (more than 25 laboratories) collaborate, in which work is underway to standardize DNA disorders, in particular, the level of 8-hydroxy-2'-deoxyguanosine in cellular DNA is normalized at the level of 0.5-5 damage per 106 guanosine bases [12].

As a result of the analysis, increased values of oxidative stress indices were found among women of the age group 30-39 years old living in the town of Aralsk and Ayteke-bi of the Kzylorda region in comparison with Atasu village of Karaganda region.

It should be noted that these settlements are most closely located in the Aral Sea region. This may mean that the residents of these cities are exposed to adverse environmental factors caused by the drying up of the Aral Sea. The presence in the blood of the examined quantities of markers of lipid peroxidation and DNA damage above the norm can be considered as a prognostically unfavourable sign that indicates the development of pathological processes.

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