

IMPACT OF CHLORIDE AND LEAD ION CONTENT IN OPEN WATER SOURCES IN KYZYLORDA REGION ON POPULATION'S CANCER INCIDENCE

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ABSTRACT

Relevance: In 2004-2013, the cumulative cancer incidence was about 200 cases per 100 thousand in Kazakhstan, while in the disaster area of Aral Sea – about 225 cases per 100 thousand. For comparison, cancer incidence in the prosperous region of Karaganda was 140 cases per 100,000 people. As of 2021, the incidence of colorectal cancer in Kyzylorda was 17.73 compared to 5.81 per 100,000 people in 2015. Factors of the surrounding macro- and microenvironment are trigger factors for tumor initiation. Salt deposits of the dried Aral Sea in the form of solonchaks spread to the territory of the entire Kyzylorda region. Pesticides and process water have been discharged into rivers for many years, which has led to the accumulation of heavy metal salts in water and soil on the banks of the rivers and in the place of the dried-up Aral Sea, which in turn can affect the increase in cancer incidence.

The aim was to study the dependence of cancer incidence on water pollution by ions of chlorine and lead in open water bodies in the Kyzylorda region.

Methods: Analysis of cancer incidence in 2021 by localization: intestines, stomach, sarcomas, lungs, and melanomas in the Kyzylorda region. Determination of the content of chlorine ions by titration with silver nitrate, spectrophotometric determination of lead ions in the open water sources. Comparative correlation analysis of the concentration of chlorine ions and lead with cancer incidence in this region.

Results: The maximum permissible chlorine and lead ions concentrations in all studied open water sources of the Kyzylorda region exceeded the norm by 1.024-20.26 times and 1.4-14.1 times, respectively. The chlorides in the water increased intestine cancer incidence by 17% with an approximation certainty of 0.38. The lead in water increased the incidence of melanomas by 22%, with an approximation certainty of 0.79. The correlation coefficient was $r=0.618$; $p=0.07$ for exceeding chlorides' MPC and bowel cancer incidence.

Conclusion: Heavy metals like lead in water samples in regions with increased cancer incidence indicate a co-dependent relationship between these factors—pollutants such as chlorides and lead increase intestine cancer and melanoma incidence.

Keywords: Kyzylorda, melanoma, lung cancer, intestine cancer, chloride ions, lead ions.

Introduction: New approaches in tumor diagnostics allowed studying the properties of tumor DNA and RNA, including coding and non-coding regions, size, structure, and other properties responsible for mutagenesis and malignancy in the body [1]. More accurate MN diagnostic methods can determine the influence of DNA-altering factors on the tumor initialization, prognosis, and response to treatment. K-ras and B-raf are classic tumor process markers in the mitogen-activated protein kinases' signaling cascade [2]. K-ras activates B-raf, which transmits a signal to MEK and ERK proteins. Then, the mitogen-activated protein kinase cascade triggers cell proliferation and differentiation; an excessive signal leads to malignization.

The surrounding macro- and microenvironment factors can initiate a tumor [3]. They affect the tumor volume and progression. Microenvironment factors include changes in the extracellular matrix's function and adipocytes, which support tumor progression close to

tumor cells. Macroenvironment factors are systematic changes in the body that affect the growth of blood vessels and lymph nodes and changes in endocrine cascades, which can accelerate tumor growth and provoke resistance to therapy [4]. The pollutants, such as chloride and lead ions, originating from the environment, impact both the tumor and the systematic changes in the body, weakened by oncological processes. Mitogen-activated protein kinase cascade is also altered by pollutants since chemical elements such as chlorine and lead are specific ligands of enzyme proteins.

Studies of the environment and cancer development risk factors describe NaCl salt and heavy metals, including lead, as triggers for mutations and malignancy. They weaken the immune barrier, leading to cardiovascular, allergic, and oncological diseases [5-7]. Heavy metals can bind to receptors on the cell surface, activating altered cellular cascades, including proliferation and cell survival [8, 9].

Active agricultural activities such as cotton cultivation, a decrease in the water level in the Syrdarya and Amudarya rivers, and a gradual drying of the Aral Sea have increased the content of pollutants in the environment [10]. Salt deposits of the dried Aral Sea in the form of solonchaks spread all over the Kyzylorda region [11]. Many years of discharge of pesticides and process waters into rivers resulted in the accumulation of heavy metal salts in water and soil on the banks of the rivers and the place of the dried-up Aral Sea.

From 2004 to 2013, the cumulative cancer incidence in Kazakhstan was about 200 cases per 100,000 people, while in the disaster area of the Aral Sea, it reached 225 cases per 100,000 [12]. As a comparison, in the prosperous region of Karaganda, cancer incidence was 140 per 100,000. The colorectal cancer incidence in Kyzylorda was 17.73 in 2021 compared to 5.81 in 2015. This study was necessitated by an insufficient knowledge of chemical pollutants' effect on the Kyzylorda region population's health.

The aim was to study the dependence of cancer incidence on water pollution by ions of chlorine and lead in open water bodies in the Kyzylorda region.

The study tasks included an ecological analysis of chlorine and lead ions content in open water source samples in the Kyzylorda region and a comparative correlation analysis of chlorine and lead ions concentration with cancer incidence in this region.

Materials and methods: The water samples were taken from open sources (the Syrdarya River and its tributaries) in Zhanakorgan, Shieli, Kyzylorda, Terenozek, Baikonur, Kamysty Bas, and Aral localities to assess the ecological state of the Kyzylorda region (March 2021). The samples were examined for the content of chlorine and lead ions in the Republican Scientific Research Center "KAZEKOLOGIIYA."

We determined water chlorides using the Mohr method and the International Organization for Standardization (ISO) standard. Chlorides were determined by titration with silver nitrate with potassium chro-

mate indicator. We used 25 ml burettes, conical flasks, and graduated pipettes to conduct the reaction. If the initial pH of the water sample was higher than 5, nitric acid was used to titrate the probe to pH 4.4. If the sample pH was less than 5, calcium carbonate was used.

Lead was determined according to the ISO standard by flame absorption spectrometric method. The method involves aspirating the sample into the flame of an AAnalyst 400 atomic absorption spectrophotometer (Perkin Elmer, MA, USA). Hydrochloric and nitric acids were used to prepare the probe. Graduated pipettes, measuring flasks, and burettes were used to conduct the reaction. We used standard samples of lead ions dissolved in nitric acid to construct the calibration curve, which was measured and plotted as a standard. The reference peak for lead is 283.3 nm.

Based on the statistical department of the Regional Cancer Center of the city of Kyzylorda, incidence data were obtained in 2021 by localization: intestines, stomach, soft tissues, lungs, and melanomas.

The study was carried out as part of the dissertation work "Studying the influence of environmental factors on the occurrence of cancer in the Aral region" by F.K. Rakhimbekova, a candidate at Satpayev University.

We determined the indicators of maximum permissible concentrations (MPC) and compared them with the incidence in this region. Due to their relatively close location and similar environmental conditions, we united the Zhalagash, Terenozek, Kazaly, and Karmakshi districts. International sources recommend that the content of chlorides and lead should be low and not exceed 100 mg/l for chlorides and 0.005 mg/l for information in water [13-14]. Based on this comparison, we constructed graphs and analyzed the linear trend equations and the values of the accuracy of the R2 approximation. Further, the correlation coefficient between exceeding MPCs and cancer incidence was studied.

Results: All the studied water samples from open sources of the Kyzylorda region exceeded the MPCs (Table 1).

Table 1 – Chloride and lead ion content in open water sources in Kyzylorda region (March 2021)

Locality	Chloride and lead ion content in open water sources in Kyzylorda region (March 2021)					
	Chlorides (Cl ⁻), mg/l	Norm (Cl ⁻), mg/l	Multiplicity of MPC Cl ⁻	Pb ²⁺ , mg/l	Norm Pb ²⁺ , mg/l	Multiplicity of MPC Pb ²⁺
Zhanakorgan	175.2	100	1.752	0.022	0.005	4.4
Shieli	259.75	100	2.6	0.034	0.005	6.8
Kyzylorda	4355.5	100	43.555	0.0425	0.005	8.5
Terenozek	102.415	100	1.024	0.0206	0.005	4.12
Baikonur	256.6	100	2.566	0.007	0.005	1.4
Kamysty Bas	258.8	100	2.588	0.02	0.005	4
Aral	2025.97	100	20.26	0.0705	0.005	14.1

The highest cancer incidence (per 100,000 people) was observed in intestine cancer – 17.13 in

Kyzylorda vs. 8.6 in the Republic of Kazakhstan (RK); stomach cancer – 8,685 in Terenozek and

Zhalagash vs. 13.5 in the RK; breast cancer – 7.3 to 7.8 in Shieli, Zhanakorgan, and Kyzylorda vs. 26.3 in the RK; lung cancer – around 13 in Terenozek and Zhalagash vs. 18.9 in the RK.

Table 2 – Kyzylorda region population’s cancer incidence, 2021

Sampling areas	Incidence (per 100,000 people)					
	Colorectal cancer	Stomach cancer	Sarcomas	Breast cancer	Lung cancer	Melanoma
Zhanakorgan	5.26	1.32	2.63	7.89	9.21	0
Shieli	5.1	6.36	3.82	7.64	11.46	2.56
Kyzylorda	17.13	3.26	4.1	7.35	14.7	2.45
Terenozek – Zhalagash	10.18	8.685	1.395	1.395	12.975	0
Baikonur	10.14	5.1	5.1	2.5	5.07	0
Karmakshy–Kazaly	8.66	3.25	1.3	7.15	8.435	1.52
Aral	4.11	1.3	2.5	1.3	5.48	0

The linear dependence of exceeding the MPCs of pollutants and the increase in cancer incidence showed a positive trend for chlorine ions, colorectal cancer, lead ions, and melanomas (Figures 1, 2). The

chlorides in the water increased intestine cancer incidence by 17% with an approximation certainty of 0.38. The lead in water increased the incidence of melanomas by 22%, with an approximation certainty of 0.79.

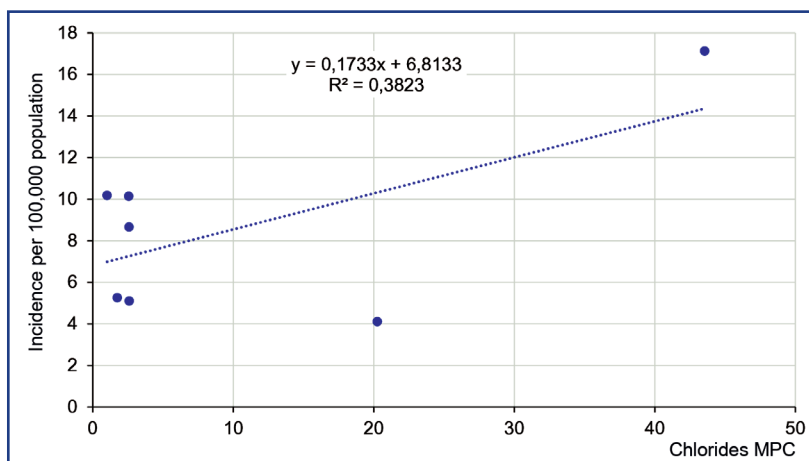


Figure 1 – Dependence of intestinal cancer incidence on exceeding the chlorides MPC in the Kyzylorda region water

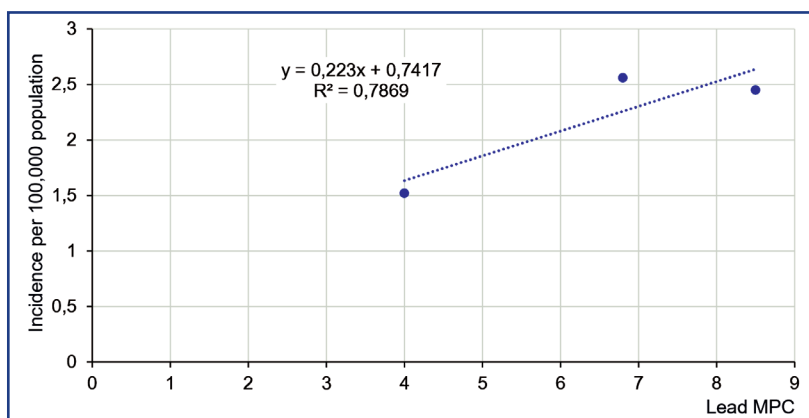


Figure 2 – Dependence of melanoma incidence on exceeding the lead MPC in the Kyzylorda region water

The correlation coefficient was $r=0.618$; $p=0.07$ for exceeding chlorides’ MPC and bowel cancer incidence.

Discussion: Exceeding the chlorine and lead MPCs indicates significant environmental pollution in the

Kyzylorda region (Table 1). As described by Morris et al., exceeding the pollutants’ MPCs in water is a risk factor for developing many diseases, including cancer [15]. According to Li et al. [16], the pathogenic factor

of pollutants significantly reduces the polluted local population's quality of life and health [16].

Not all linear graphs of the correlation of exceeding MPCs and cancer incidence showed a significant increase in incidence, proving a multifactorial etiology of cancer [17]. Figures 1 and 2 show that pollutants increase intestine cancer and melanoma incidence by 17-22%. El-Tawil and Clapp et al. describe the pathogenic role of chlorides and lead in cancer development [18, 19].

When entering the body with water and food, chlorides mix with hydrogen protons, forming hydrochloric acid in the stomach (1). Its excess can enter the upper (esophagus) and lower (intestines) parts of the gastrointestinal tract [20].



A reliable correlation between exceeding the MPCs of chlorides and intestinal cancer incidence increase indicates the role of increased Cl-content as a factor contributing to malignancy and subsequent cancer development [21].

Conclusion: Heavy metals like lead in water samples in increased cancer incidence regions indicate a co-dependent relationship between these factors: pollutants such as chlorides and lead increase intestine cancer and melanoma incidence.

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АҢДАТПА

ҚЫЗЫЛОРДА ОБЛЫСЫНДАҒЫ АШЫҚ СУ КӨЗДЕРІНДЕГІ ХЛОРИД ПЕН ҚОРҒАСЫН ИОНЫНЫҢ ХАЛЫҚТЫҢ ҚАТЕРЛІ ІСІК АУРУЫНА ӘСЕРІ

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Өзектілігі: 2004-2013 жылдар аралығында Қазақстанда онкологиялық аурулардың жиынтық көрсеткіші 100 мың адамға шаққанда 200 жағдайды құраса, Арал теңізінің апатты аймағында шамамен 100 мыңға шаққанда 225 жағдайды құрады. Салыстырмалы түрде айтсақ, өркендеген Қарағанды өңірінде қатерлі ісік ауруы 100 мың тұрғынға шаққанда 140 жағдайды құрады. 2021 жылы Қызылорда қаласында тоқ ішек қатерлі ісігімен сырқаттанушылық 2015 жылғы 100 000 тұрғынға шаққанда 5,81 көрсеткішпен салыстырғанда 17,73 құрады.

Айналадағы макро- және микроорта факторлары ісік инициациясының триггер факторлары болып табылады. Кейін қалған Арал теңізінің сортаң түріндегі тұзды шөгінділері бүкіл Қызылорда облысының аумағына тарады. Көптеген жылдар бойы пестицидтер

мен технологиялық сулар өзендерге төгілуде, бұл өзендердің жағалауларында және кеуіп қалған Арал теңізінің орнында су мен топырақта ауыр металл тұздарының жиналуына әкеліп соқтырды, бұл өз кезегінде әсер етуі мүмкін. қатерлі ісік ауруының артуы.

Зерттеудің мақсаты – Қызылорда облысындағы ашық су айдындарындағы хлор және қорғасын иондарымен судың ластануына қатерлі ісік ауруларының тәуелділігін зерттеу.

Әдістері: Қызылорда облысы бойынша 2021 жылы локализация бойынша онкологиялық ауруларды талдау: ішек, асқазан, саркомалар, өкпе және меланома. Күміс нитратымен титрлеу арқылы хлор иондарының құрамын анықтау, ашық су көздеріндегі қорғасын иондарын спектрофотометриялық анықтау. Хлор мен қорғасын иондарының концентрациясының осы аймақтағы ісік ауруымен салыстырмалы корреляциялық талдауы.

Нәтижелері: Қызылорда облысының барлық зерттелген ашық су көздерінде хлор мен қорғасын иондарының шекті рұқсат етілген концентрациясы нормадан 1,024-20,26 есеге жоғары болды; тиісініне 1,4-14,1 есе. Суда хлоридтердің болуы 0,38 жуық сенімділікпен ішек қатерлі ісігінің ауруын 17%-ға арттырды. Суда қорғасынның болуы 0,79 жуық сенімділікпен меланома ауруын 22%-ға арттырды. Корреляция коэффициенті $r=0,618$; $p=0,07$ хлоридтердің ШРК асып кетуі және ішек ісігінің жиілігі.

Қорытынды: Қатерлі ісік ауруы жоғары аймақтардағы су үлгілерінде қорғасын сияқты ауыр металдардың болуы осы факторлардың өзара тәуелді байланысын көрсетеді. Хлоридтер мен қорғасын сияқты ластаушы заттар ішек ісігі мен меланома ауруын арттырады.

Түйінді сөздер: Қызылорда, меланома, өкпе рагы, ішек ісігі, хлор иондары, қорғасын иондары.

АННОТАЦИЯ

ВЛИЯНИЕ СОДЕРЖАНИЯ ИОНОВ ХЛОРА И СВИНЦА В ОТКРЫТЫХ ИСТОЧНИКАХ ВОДЫ В КЫЗЫЛОРДИНСКОЙ ОБЛАСТИ НА ОНКОЗАБОЛЕВАЕМОСТЬ НАСЕЛЕНИЯ

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Актуальность: В 2004-2013 годах суммарная онкозаболеваемость составила около 200 случаев на 100 тысяч населения по Казахстану, в то время как в зоне бедствия Аральского моря – около 225 случаев на 100 тысяч населения. Для сравнения, онкозаболеваемость в благополучном регионе Караганды составила 140 случаев на 100 тысяч населения. На 2021 год, заболеваемость колоректальным раком в Кызылорде составила 17,73 по сравнению с 5,81 на 100 тысяч населения в 2015 году.

Факторы окружающей макро- и микросреды являются триггерными факторами инициации опухоли. Отложения соли высохшего Аральского моря в виде солончаков распространились на территорию всей Кызылординской области. Пестициды, применяемые в сельском хозяйстве, и техническая вода сбрасывались на протяжении многих лет в реки, что привело к накоплению солей тяжелых металлов в воде и почве на берегах рек и на месте высохшего Аральского моря, что, в свою очередь, может влиять на повышение онкозаболеваемости.

Цель исследования – изучить зависимость онкозаболеваемости от загрязнений воды ионами хлора и свинца открытых водоемов в Кызылординской области.

Методы: Проведен анализ онкозаболеваемости в 2021 году в Кызылординской области по локализациям: кишечник, желудок, саркомы, легкие и меланомы. Определено методом титрования нитратом серебра содержание ионов хлора, спектрофотометрическое определение ионов свинца в воде открытых водоемов. Выполнен сравнительный корреляционный анализ концентрации ионов хлора и свинца с онкозаболеваемостью данного региона.

Результаты: Предельно допустимые концентрации (ПДК) ионов хлора и свинца во всех исследуемых открытых водоемах Кызылординской области превышали норму в 1,024-20,26 раз и 1,4-14,1 раз, соответственно. Присутствие хлоридов в воде повысило заболеваемость колоректальным раком на 17%, при достоверности аппроксимации 0,38. Наличие свинца в воде повысило заболеваемость меланомами на 22%, при достоверности аппроксимации 0,79. Коэффициент корреляции превышения ПДК хлоридов и увеличения заболеваемости колоректальным раком составил $r=0,618$; $p=0,07$.

Заключение: Наличие тяжелых металлов, в данном случае свинца, в пробах воды в регионах с повышенной онкозаболеваемостью указывает на созависимую связь этих факторов. Такие загрязнители, как хлориды и свинец, способствуют повышению заболеваемости раком кишечника и меланомой.

Ключевые слова: Кызылорда, меланома, рак легких, рак кишечника, ионы хлора, ионы свинца.

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