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ALLERGIC AND NON-ALLERGIC SKIN DISEASES IN CHILDREN OF UKRAINE: A RETROSPECTIVE STUDY OF THE PREVALENCE AND INCIDENCE OVER THE PAST 24 YEARS

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Ключові слова: *діти, алергічні та неалергічні хвороби шкіри в дітей, атопічний дерматит, захворюваність, поширеність, довкілля, полютанти*
Ключевые слова: *дети, аллергические и неаллергические болезни кожи у детей, атопический дерматит, заболеваемость, распространенность, окружающая среда, поллютанты*

Abstract. Allergic and non-allergic skin diseases in children of Ukraine: a retrospective study of the prevalence and incidence over the past 24 years. Volosovets O.P., Bolbot Yu.K., Beketova G.V., Berezenko V.S., Umanets T.R., Rechkina O.O., Mitiuriaeva-Korniyko I.O., Volosovets T.M., Pochinok T.V. *Bacterial, allergic, parasitic and fungal skin lesions are much more common among children than among adult patients. The aim of this study was to analyze data on the prevalence and incidence of diseases of skin and subcutaneous tissue with allergic and non-allergic origin among children of Ukraine in period from 1994 to 2017. Our main purpose was to determine the possible impact of different adverse environmental factors on children`s growth, including radiation, connected with the Chernobyl disaster in 1986. Over the past 24 years Ukraine has witnessed a 10.3% increase in prevalence of diseases of skin and subcutaneous tissue among children and 8.6% raise of incidence rate with a predominance of*

detection of this pathology in children affected by the Chernobyl accident and children from areas of radiological control. We have found a direct influence of moderate strength on the connection between population-weighted effective dose of total human exposure (in millizieverts) in different regions of the country in the period of 1997-2011 and the incidence and prevalence of skin diseases among children aged 0-14 years, including 2011 ($p<0.05$).This fact may indicate the impact of this disaster on the occurrence and pathogenesis of skin diseases and its consequences among children. During the same period, due to the influence of a number of environmental factors, there was a significant transformation in the structure of skin diseases in children. We have witnessed double increasing of the proportion of allergic lesions of the skin and its elements. The prevalence of diseases of the skin and its elements in general has reached 28.7% against the corresponding reduction of skin infections.

Реферат. Аллергические и неаллергические болезни кожи у детей Украины: ретроспективное исследование за последние 24 года. Волосовец А.П., Больбот Ю.К., Бекетова Г.В., Березенко В.С., Уманец Т.Р., Речкина Е.А., Митюряева-Корнейко И.А., Волосовец Т.Н., Починок Т.В. *У детей значительно чаще, чем у взрослых, встречаются бактериальные, аллергические, паразитарные и микотические поражения кожи. Целью этого исследования был анализ данных распространенности и заболеваемости болезней кожи и подкожной клетчатки аллергического и неаллергического генеза у детей Украины с 1994 по 2017 г. для определения степени влияния на их развитие факторов загрязнения окружающей среды, в том числе радиационных, после Чернобыльской катастрофы в 1986 году. За последние 24 года в Украине наблюдается рост на 10,3% распространенности заболеваний кожи и подкожной клетчатки у детей и на 8,6% показателя заболеваемости с преобладанием выявления этой патологии у детей в возрасте 0-17 лет включительно, потерпевших вследствие аварии на Чернобыльской АЕС, и детей из областей, имеющих в своем составе территории радиологического контроля после аварии. Нами установлено прямое влияние умеренной силы на связь между популяционно-взвешенной эффективной дозой в миллизивертах суммарного облучения всего тела человека у жителей разных регионов страны за период 1997-2011 гг. и показателями первичной заболеваемости и распространенности у детей в возрасте 0-14 лет включительно болезней кожи и подкожной клетчатки в 2011 году ($p<0,05$). Это может свидетельствовать об определенном влиянии последствий этой техногенной катастрофы на возникновение и течение болезней кожи и подкожной клетчатки у детей. За этот же промежуток времени вследствие влияния ряда факторов, в частности экологических, произошла существенная трансформация в структуре болезней кожи у детей в виде роста в 2 раза удельного веса выявления аллергических поражений кожи, достигших удельного веса 28,7% от общей заболеваемости детей болезнями кожи и подкожной клетчатки в целом, на фоне соответствующего уменьшения инфекций кожи.*

Diseases of the skin and subcutaneous tissue (hereinafter – SD) in children is one of the most common pathological conditions in childhood, where their course is determined by the anatomical and physiological features of the skin of the child, heredity, the level of hygiene, social development of the region of residence, ecology and a number of congenital anomalies [2, 5, 8, 15]. Bacterial, allergic, parasitic and fungal skin lesions are much more common in children than in adults, which is often associated with environmental influences [1, 7, 9, 12, 13]. Uncommon foci of chronic infections (tonsillitis, caries, etc.) also have an unconditional influence on the occurrence and course of skin diseases [5, 9].

Recently, the tendency to severe SD in children has been attracting attention, which may be the reason for the onset of allergic march with the subsequent development of bronchial asthma [7, 14]. Thus, today in Ukraine there are more than 500 thousand patients with atopic dermatitis, including more than 40 thousand children, which affects the quality of life of children and is difficult to treat [2, 5, 7, 15]. The state of the environment and the state of health of the child population of Ukraine were negatively affected by the consequences of the Chernobyl accident [1, 6, 10, 11].

The aim of this study was to analyze data on the incidence and prevalence of allergic and non-allergic SD in children of Ukraine from 1994 to 2017 to determine the impact of environmental pollutants on their course, including radiation.

MATERIALS AND METHODS OF RESEARCH

We analyzed the dynamics of the incidence and prevalence of SD in children of Ukraine, in particular from regions with territories of radiological control (hereinafter – TRC) after the Chernobyl accident. A separate group of observations were children born to participants of the liquidation of the Chernobyl accident.

Methods of statistical and epidemiological analysis of the data of the Center for Medical Statistics of the Ministry of Health of Ukraine (hereinafter - the Center of the MH of Ukraine) on the prevalence and incidence of SD in children from 1994 to 2017 were used [2, 3]. We used the U-criterion of signed-ranks (Wilcoxon-Mann-Whitney test) to compare the incidence of SD in children from the same areas

in 1994 and 2017 [3, 4] and statistical analysis of data from the Center of the MH of Ukraine for the last 24 years. The k-means method was used to conduct a cluster analysis of regions depending on the incidence of SD in children to the level of the indicator in Ukraine and the presence of TRC in the region [4].

According to the State Statistics Service of Ukraine, the volumes of pollutant emissions into the atmosphere in 2015 were determined in the regions [11]. The population-weighted effective dose in millisieverts (mSv) of the total irradiation of the whole body of residents from different regions of the country was determined according to Vasylenko V.V. and Chepurny M.I. (2011), presented in section 3.1.3 of the National Report of Ukraine: "25 years of the Chernobyl disaster. Safety of the future" [1]. We used Spearman's correlation coefficient to determine the degree of correlation and correlation between pollutant emissions into the atmosphere from all sources of pollution, population-weighted effective dose of total radiation of the whole human body in different regions and levels of SD in children [4]. Excel-2010 and STATISTICA 6.1 software (StatSoftInc., Serial № AGAR909E415822FA) were used for statistical processing of results.

RESULTS AND DISCUSSION

Among pediatric diseases, newly detected skin lesions of allergic and non-allergic origin occupy the second place (5.1% of the total number of newly detected diseases in children) after respiratory diseases, and the fourth one (4.4%) in prevalence, second only to respiratory pathology, digestive tract diseases and eye diseases. This only emphasizes the socio-medical significance of this complex series of pathological conditions that significantly affect the quality of life of patients. In 1994, SD also ranked 2nd among 17 common pathologies of childhood.

Interestingly, in 2017, SD in children accounted for 30.6% of the number of SD cases detected for the first time among the population of Ukraine (192,1012 registered cases or 45.9 per 1 000 population), which directly indicates the early onset of these diseases and continuation of their course in adulthood.

Thus, in 2017, according to the Ministry of Health of Ukraine, the incidence of SD in children aged 0-17 years was 497,307 of new cases or 65.3 per 1,000 children (of which 24407 first detected cases of SD in children aged 0-17 years). The prevalence of SD in children was 589,651 or 77.4 per 1,000 children.

For the first time, 29,334 cases of SD were diagnosed in children affected by the Chernobyl accident, or 75.4 per 1,000 children, which is by 15.8% more than the average incidence of SD in children in Ukraine. The prevalence of SD in these children was 35,297 or 91.0 cases per 1,000 children, being by 17.5% higher than the national prevalence of SD.

In the general structure of the incidence of the pediatric population, SD made up 5.1% in 2017 against 5.75% in 1994. Similar dynamics was also observed in the moderate decrease in the proportion of SD in the structure of the overall prevalence of childhood diseases from 6.6% to 4.4% of the prevalence. In 1994, there were 79,116 cases of SD detected for the first time, or 60.1 per 1,000 children. The prevalence of SD was 914,118 or 70.2 per 1,000 children aged 0 to 17 years.

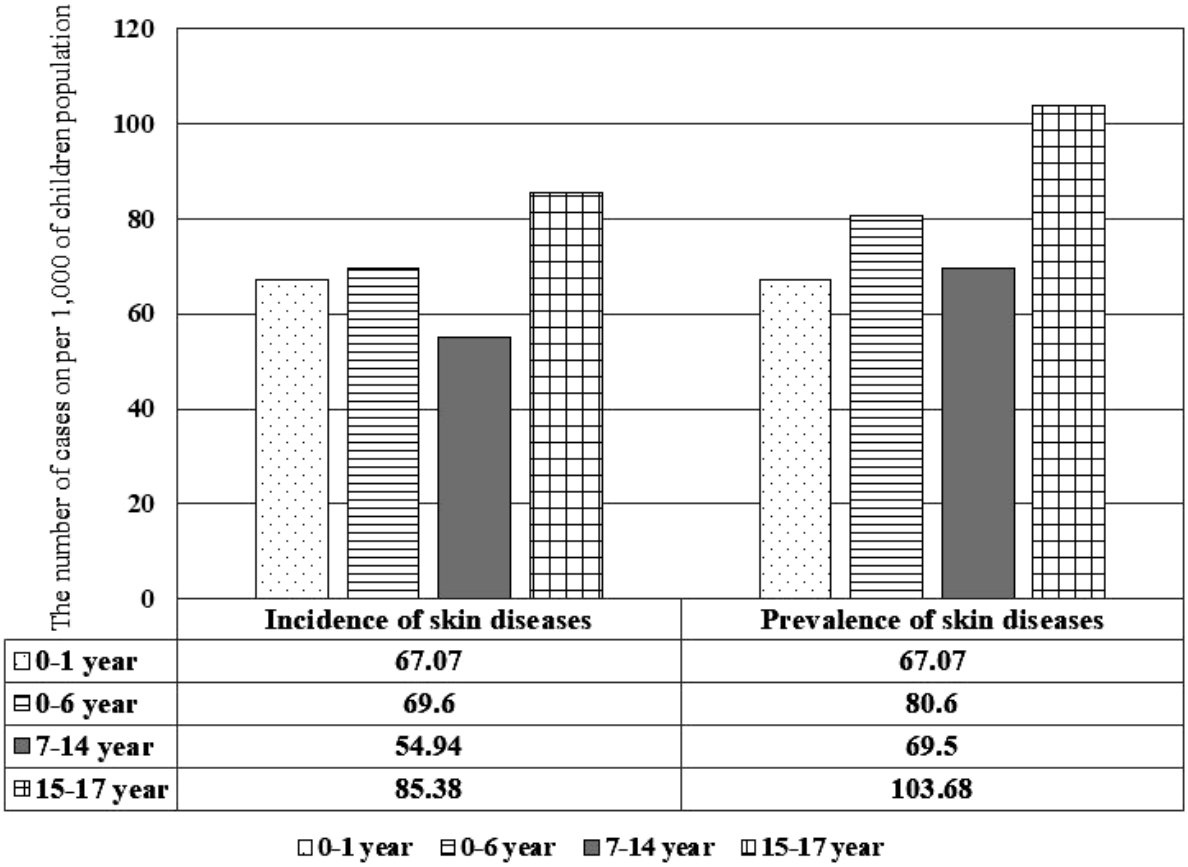
Most cases of SD are now detected at the age of 0 to 6 years including – 44.2% (in 1994 – 41.9%), which, apparently, indicates a negative change in the health of preschool children and increase in time of influence of aggressive environmental factors on the child's body. Thus, in 2017, 24,007 cases of SD or 67.02 per 1,000 children were diagnosed in infants, primarily due to skin infections and contact dermatitis. As can be seen in Figure 1, the lowest number of newly diagnosed cases of SD was observed in adolescence – 18.0% (in 1994 – 14.3%), but the incidence and prevalence of SD in this age cohort reached the highest values (85.3 and 103.6 per 1,000 children, respectively). Accordingly, the index of accumulation of chronic pathology increased from 1.16 in children aged 0-6 years including to 1.21 in children aged 15-17 years including.

In recent years there has been a relative decrease in the percentage of detection of SD in children aged 7-14 years including (from 42.9% to 37.3% of the number of newly registered cases in children aged 0-17 years including) against the background of an increase in primary incidence in adolescents (from 14.3% to 18.5% of the number of reported cases of SD in general).

The number of newly diagnosed cases of atopic dermatitis (AD) in children aged 0-17 years in 2017 was 27,803 new cases or 3.7 per 1,000 children, and the prevalence was 66,389 or 8.7 per 1,000 children. For comparison: in 1997, 33,592 primary cases of AD were diagnosed, or 3.4 per 1,000 children. The prevalence of AD was 60372 or 6.1 per 1,000 children aged 0 to 17 years including.

The incidence of contact dermatitis (CD) in children aged 0-17 in 2017 was 97,603 new cases or 12.8 per 1,000 children, and the prevalence was 103,228 or 13.6 per 1,000 children. For comparison: in 1994, the first detected cases of CD were 46,440 cases or 3.9 per 1,000 children. The prevalence of

CD was 51,173 or 4.5 per 1,000 children aged 0 to 17 years including. That is, in recent decades, the incidence and prevalence of contact dermatitis in children has increased more actively compared to atopic dermatitis. Contact dermatitis among allergic skin lesions has become most frequent dermatosis in all age groups, which is actively manifested in young children and requires appropriate therapeutic and management measures.



	Incidence of skin diseases	Prevalence of skin diseases
0-1 year	67.07	67.07
0-6 year	69.6	80.6
7-14 year	54.94	69.5
15-17 year	85.38	103.68

Fig. 1. Changes in prevalence and incidence of skin and subcutaneous tissue diseases depending on the age of children (per 1,000 of children population) in 2017

An alarming fact is that we have found an increase in the structure of the incidence and prevalence of SD in the proportion of allergic skin lesions in children in general. Thus, the total incidence of atopic dermatitis and contact dermatitis in 1994 was 10.6% of the total incidence of SD in children, and the prevalence – 14.1%. As of 2017 (the last year when medical statistics on the population over 1 year of age was published), the proportion of children with allergic skin lesions increased to 25.2% and the prevalence – to 28.7%. That is, during 24 years of observations there was a significant transformation in the structure of the prevalence of SD in children due to a 1.9-fold increase in the proportion of allergic skin lesions against a decrease in the proportion of non-allergic lesions, including infectious lesions of skin and subcutaneous fatty tissue (from 31.0% in 1994 to 23.3% in 2017) and parasitic skin lesions, etc. (Fig. 2).

Apparently, this phenomenon is based on many factors: heredity, changes in the lifestyle of Ukrainian families, the nature of children's nutrition and consumption of beverages saturated with dyes and other impurities, polypragmatism in pharmacotherapy, increasing exposure to household chemicals and other allergens and unconditional increase of impact of pollution.

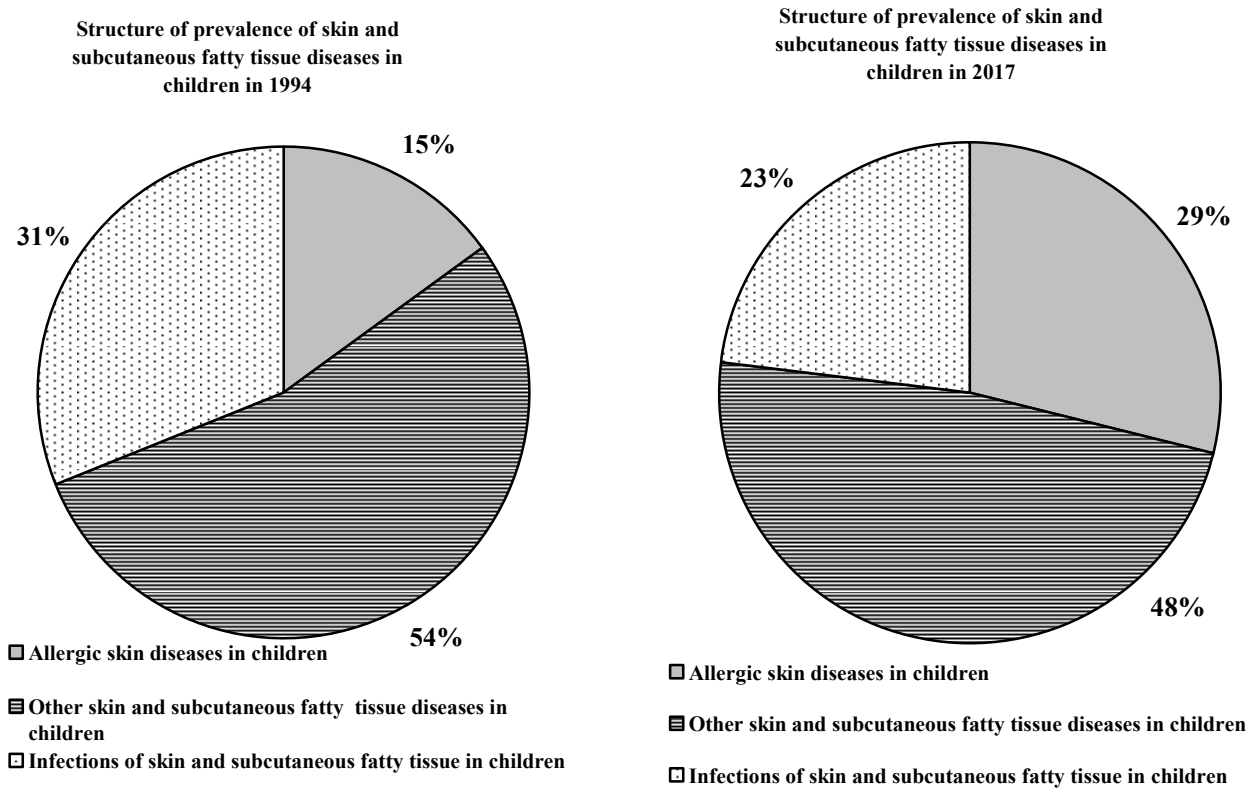


Fig. 2. Dynamics of increase in percentage of allergic lesions of the skin among other skin and subcutaneous fatty tissue diseases in children of Ukraine over the last 24 years

Our retrospective analysis of the incidence and prevalence of SD in children over the past 24 years has revealed that in Ukraine there is a moderate increase in the detection of SD. As can be seen in Figure 3, over the past 24 years, the incidence of SD in children aged 0-17 years including increased by 8.6% ($p>0.05$), the prevalence of SD in children aged 0-17 years including – by 10.1% ($p<0.05$). Among children living in regions without TRC, this indicator decreased by 2.9%. In the meantime the incidence of SD in children aged 0-17 years, including those affected by the Chernobyl accident, increased by 20.4% during this period. At the same time the incidence of SD in children from regions with TRC increased by 18.02%, which indicates a possible prolonged impact of the consequences of the Chernobyl accident on the development of SD in children.

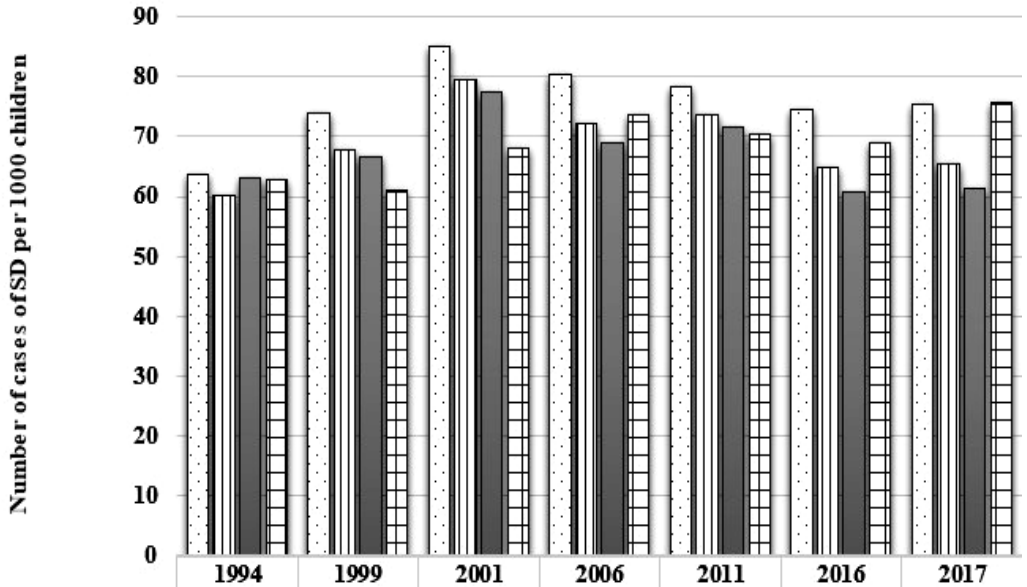
These data correspond to the global trend of increasing incidence of SD, primarily of allergic origin, in most countries, especially among those with a high index of socio-economic development [15]. The first wave of increase in SD incidence by 32.4% was in 1994-2003, then SD revealing decreased to 65.5 per 1,000 children in 2017, but this reduction did not significantly affect the overall trend of increasing incidence and prevalence of SD in children, which was emphasized above.

One of the factors of the relative reduction in the prevalence of SD in children in the last decade is a reduction of pollutant emissions into the air by 20.2% in this period due to reduced industrial capacities, which, however, reached 105.5 kg per person in 2015 [11].

It is appropriate, the first wave of increase in the incidence of AD in children was also observed in the late 90s of the twentieth century. Subsequently, the detection of AD began to decrease to 2.44 per 1,000 children in 2003. From 2004 to 2017, there was a moderate increase (+ 8.3%) of this indicator to 3.65 per 1,000 children, which corresponded to the general trend of increasing incidence of SD in children in the country. Similar dynamics of changes over time was characteristic of the incidence in CD

in children but this indicator increased more intensively – more than three times, compared with 1994 – 13.55 per 1,000 children in 2017 against 4.6 per 1,000 children.

In 2017, the largest number of children aged 0-17 years, including the first detected SD was found in Ternopil region (91.6 cases per 1,000 children), Rivne (88.32), Dnipropetrovsk (87.19), Ivano-Frankivsk (86.67), Kyiv (85.0), Cherkasy (82.56), Mykolaiv (81.99), Zhytomyr (78.15). Of the 8 mentioned regions, five (Rivne, Zhytomyr, Kyiv, Cherkasy, Ivano-Frankivsk) are the northern regions, which are located closest to Chornobyl with the still existing TRC. Other regions with a high incidence of SD have a strong potential for industrial and agricultural production with a significant load of pollutants on the environment.



	1994	1999	2001	2006	2011	2016	2017
Children from regions with TRC	63.8	74.02	85	80.38	78.36	74.42	75.3
Ukraine	60.08	67.9	79.6	72.16	73.74	64.76	65.3
Children from regions without TRC	63	66.5	77.5	69.1	71.6	60.84	61.2
Children affected by Chernobyl accident	62.8	60.97	68.04	73.67	70.38	68.92	75.64

Fig. 3. Dynamics of incidence of skin and subcutaneous tissue diseases of children of Ukraine, children affected by Chernobyl accident, children from regions with TRC, children from regions without TRC from 1994 to 2017

In general, in 7 out of 9 regions with TRC, the incidence of SD was higher than the national average.

Low levels of SD incidence in children aged 0-17 years including were observed in Vinnytsia (49.81 per 1,000 children), Zakarpattia (53.5), Kherson (54.69), Donetsk (55.87), Zaporizhzhia (57.01) and Lviv (57.41) regions.

In 1994, the following regions were the leaders in the incidence of SD in children aged 0-17 years: Sevastopol (87.2 cases per 1,000 children), Cherkasy

(83.1), Crimea (82.2), Kirovohrad (77.8) and Dnipropetrovsk (74.7) regions.

The lowest incidence rates of SD in children were observed in Lviv (39.3 cases per 1,000 children), Chernivtsi (47.0), Sumy (48.0), Odessa (56.5), Transcarpathia (57.1), Volyn (55.8) and Zhytomyr (53.1) regions.

At that time, only in 2 out of 9 regions with TRC the incidence of SD was higher than the national average. That is, 24 years ago numerically fewer regions with TRC were among the leading ones regarding incidence rates. In general, the incidence of SD in children from regions with TRC in 1994 exceeded that in the country and the incidence of SD in children from other regions of the country without TRC (Fig. 3).

During 24 years of observation in Ternopil, Rivne, Zhytomyr, Ivano-Frankivsk and Lviv regions, there was noted the progression of the incidence of SD in children by 46.1%-48.3% as compared to the incidence of SD in 1994. While in Donetsk, Zaporizhzhia, Kirovohrad, Kharkiv and Kherson regions the increase in incidence was negative, which correlated with the decrease in industrial emissions into the atmosphere in these regions.

The incidence rates of SD in children living in areas with TRC were higher than the national indicators by 15.3% ($p>0.05$) and the incidence of SD in children from other regions – by 23.03% ($p>0.05$). The incidence of SD in children aged 0-17 years, including those affected by the Chernobyl accident, did not differ from the incidence of SD in children from regions with TRC and was higher by 15.8% ($p>0.05$) than the incidence of this pathology in the country and by 23.6% ($p>0.05$) than the incidence in children from areas without TRC (Fig. 3). In other words, the children who suffered as a result of the Chernobyl accident are now as close as possible to the incidence of SD in children living in areas with TRC. Indirectly, this may indicate the continuing effects of this man-made disaster on the occurrence and course of SD in these children. It should be noted that this trend has appeared only in the last 5 years. At the same time, the incidence of SD in children living in areas with TRC during all 24 years has always been higher than the national indicators and those of children living in relatively "clean" regions and victims of the Chernobyl accident.

We found a direct effect of moderate strength on the relationship between population-weighted effective dose of total human exposure in mSv in residents of different regions of the country in the period 1997-2011 and the prevalence and incidence of SD in children aged 0-14 years including in 2011 ($\rho=0.437$, $\rho=0.377$, respectively). The determined critical value of the Spearman correlation coefficient with the number of degrees of freedom (f) – 21 indicates that the dependence of the traits was statistically significant ($p<0.05$) on the relationship between radiation and the prevalence of SD in children. But at the same time, we did not establish statistical significance of the relationship between the incidence of SD in children and the population-weighted effective dose of total radiation of the whole body ($p>0.05$). The population-weighted effective dose of total radiation of the whole human body in the population of Ukraine for the period from 1997 to 2011 was 0.32 mSv and was twice as significant as 0.69 mSv in the period from 1987 to 1996 [1].

We did not find a direct effect ($\rho=0.029$) on the relationship between the volume of pollutant emissions into the air per capita and the incidence and prevalence of SD in children. The determined critical value of the Spearman correlation coefficient with the number of degrees of freedom (f) – 21 indicated that the dependence of the studied traits was statistically insignificant ($p>0.05$). Similar results were obtained by us in assessing the correlation between pollutant emissions and the incidence and prevalence of atopic and contact dermatitis in children.

The clustering of regions of Ukraine depending on the levels of SD incidence and the presence of TRC in the regions is presented in the Table. Apparently, due to the unsatisfactory state of the environment and changes in health, there was an increase in the incidence of skin diseases in the leading regions: Rivne, Ivano-Frankivsk and Kyiv from among the regions with TRC and Ternopil and Dnipropetrovsk regions – without TRC.

All these areas are characterized by a significant ecotoxic load on the body of children due to the most developed industrial and agro-industrial complexes of these areas. The relatively low incidence of SD in children from Vinnytsia, Zakarpattia and Kherson regions (one of the least polluted one in the country) can also be explained by the state of ecology and, possibly, low detection of skin pathology in children; this requires appropriate management decisions. and improvement of training of qualified medical personnel.

Clustering of regions of Ukraine according to incidence of skin and subcutaneous tissue diseases depending on presence of TRC in the regions

Level of incidence of SD in children	Regions with TRC	Regions without TRC
Regions with incidence of SD in children higher than national	Rivne Ivano-Frankivsk Kyiv	Ternopil Dnipropetrovsk Mykolaiv
Regions with incidence of SD in children within national indicator	Cherkasy Zhytomyr Chernihiv Volyn Sumy	Kirovohrad Chmelnytsk Poltava city of Kyiv Charkiv Chernivtsi Luhansk Odessa Lviv Zaporizhzhia Donetsk
Regions with incidence of SD in children lower than nationai	Vinnytsia	Cherson Zakarpattia

CONCLUSIONS

1. Over the past 24 years in Ukraine there has been a 10.3% increase in the prevalence of skin and subcutaneous tissue diseases in children and a 8.6% increase in incidence of this pathology with a predominance of its detection in children aged 0-17 years, including, those affected by Chernobyl accident, and children from regions with TRC after the Chernobyl accident. There was established a direct effect of moderate strength on the relationship between population-weighted effective dose in millisieverts of total human exposure in different regions of the country for the period 1997-2011 and the prevalence of SD in children aged 0-14 years including in 2011 ($p < 0.05$). This indicates a certain impact of the consequences of the greatest man-made disaster in human history on the occurrence and course of skin and subcutaneous tissue diseases in children.

2. During the same period caused by a number of factors, including environmental, there was a significant transformation in the structure of skin diseases in children due to a 2-fold increase in the proportion of allergic lesions of the skin and subcutaneous tissue, reaching 28.7% of the proportion prevalence of skin diseases and subcutaneous tissue in general against the background of a corresponding reduction in non-allergic lesions.

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

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