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ASSESSMENT OF THE CONCENTRATION OF NITRIC OXIDE IN EXHALED AIR (FENO) IN PRIMARY SCHOOL CHILDREN IN KRAKOW AND RUZOMBERK IN RELATION TO AIR POLLUTION IN THESE CITIES

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Ключевые слова: *оксид азота, FeNO, смог, твердые частицы, дети, воспаление дыхательных путей, астма*

Abstract. Assessment of the concentration of nitric oxide in exhaled air (FeNO) in primary school children in Krakow and Ruzomberk in relation to air pollution in these cities. Czubaj-Kowal M., Friediger T., Połcik-Jastrząb M., Sokołowski M., Hudakova Z.*The measurement of the exhaled nitric oxide (FeNO) is a recognized biomarker in the detection and monitoring of airway inflammatory infections, this including asthma. Due to its simplicity, and noninvasiveness, it is more and more widely used in diagnostics of children. Few studies indicate the relationship between FeNO and atmospheric air pollution. The goal of the following study was the measuring of FeNO for 8-9 year old children in Krakow and Ruzomberok and relating the results of these measurements to the level of air pollution in the PM10 and PM2,5 range. 250 children aged 8-9 (125 in Krakow and 125 in Ruzomberok) attending third grades of primary schools, have constituted the research group. The measurement has been taken in accordance with the applicable standards with the application of a MediSOFT Belgium analyzer with a disposable head with an antibacterial filter. The results of the measurements have been referred to the PM10 and PM2,5 concentration of particulate matter in the air. Within the group of 125 children participating in the study in Krakow, the FeNO levels were normal for 104 (83.2%) children and increased for 21 (16.8%) children. During the period of the study, the average PM10 concentration was 55,7 µg/m^3 and PM2,5 was 37.0 µg/m^3. As far as the group of 125 children examined in Ruzomberok, the FeNO levels were correct (5-20 ppb) for 114 (91,2%) children and increased (21-55) for 11 children (8.8%). During the period of the study, the average PM10 concentration was 24.1 µg/m^3 and PM2,5 was 15.4 µg/m^3. As one can see from the comparison, 1.9 times more increased FeNO levels have been recorded in Krakow than in Ruzomberok (18.6 vs 8.8%), and, within the range of the heavily increased values (>50 ppb), this difference was as much as 4 times greater (3.2% vs 0.8%). These results correlate with the PM10 and PM2,5 levels in Krakow, which are respectively 2.3 and 2.4 times higher than those in Ruzomberok.*

Реферат. Оцінка концентрації оксиду азоту в повітрі, що видихається (FeNO), у дітей молодшого шкільного віку в Кракові і Ружомбероці у зв'язку із забрудненням повітря в цих містах. Чубай-Коваль М. , Фрідігер Т., Полчік-Ястшоб М., Соколовський М., Худакова З. *Вимірювання оксиду азоту (FeNO), що видихається, є визнаним біомаркером у виявленні та моніторингу запальних інфекцій дихальних шляхів, у тому числі астми. Завдяки своїй простоті і неінвазивності він все ширше застосовується в діагностиці дітей. Нечисленні дослідження вказують на зв'язок між FeNO і забрудненням атмосферного повітря. Мета цього дослідження – вимірювання FeNO у дітей 8-9 років у містах Краків та Ружомберок і зіставлення результатів цих вимірювань з рівнем забруднення повітря в діапазоні PM10 і PM2,5. Досліджувану групу склали 250 дітей у віці 8-9 років (125 у Кракові і 125 у Ружомбероці), учнів третіх класів початкової школи. Вимірювання були проведені відповідно до існуючих стандартів із застосуванням аналізатора MediSOFT, Бельгія з одноразовою насадкою з антибактеріальним фільтром. Результати вимірювань стосувалися концентрацій твердих частинок у повітрі PM10 і PM2,5. У групі з 125 дітей, що беруть участь у дослідженні в Кракові, рівні FeNO були нормальними в 104 (83,2%) дітей і підвищеними в 21 (16,8%) дитини. Протягом періоду дослідження середня концентрація PM10 становила 55,7 мкг/м^3, а PM2,5 - 37,0 мкг/м^3. У групи 125 дітей, обстежених у Ружомбероці, рівні FeNO були в нормі (5-20 год/млрд) у 114 (91,2%) дітей і* *підвищеними (21-55) в 11 дітей (8,8%). Протягом періоду дослідження середня концентрація PM10 становила 24,1 мкг/м^3, а PM2,5 – 15,4 мкг/м^3. Як видно з порівняння, у Кракові зареєстровано підвищення рівнів FeNO в 1,9 раза більше, ніж у Ружомбероці (18,6 проти 8,8%), і в межах сильно збільшених значень (> 50 частин на мільярд) ця різниця була в 4 рази більше (3,2% проти 0,8%). Ці результати корелюють з рівнями PM10 і PM2,5 в Кракові, які відповідно в 2,3 і 2,4 раза вище, ніж у Ружомбероці.*

Air pollution is one of the most serious threats of the modern world on a global scale. This regards mainly the countries with a low and medium level of development, especially large metropolitan areas.

According to UNICEF data from 2016, 300 million children all around the world live in areas where air quality standards are exceeded sixfold [1, 2, 3].

Scientific reports indicate the specific impact of PM2,5 and PM10 on the respiratory and cardiovascular systems through making changes in the lung efficiency, respiratory infections and allergic reactions [4]. They cause lung oxidative stress and inflammation, which is related to the development of asthma and COPD. With prolonged exposure, respiratory tract remodeling and chronic inflammation occur, as well as irreversible structural changes [5].

Due to the developmental period, children are most exposed to the penetration and concentration of pollutions in the respiratory tract and to the toxic effects of their activity. The risk of developing asthma increases 3 times for children living in large cities with a significant degree of air pollution [6, 7, 8, 9, 10].

Nitric oxide (NO) is a molecule with a high biological activity, playing an important part both in human physiology and pathology. Its effect on the body depends on the concentration. In low concentrations, it regulates homeostasis of the circulatory, respiratory, and immune systems and conduction of the nervous system. In high concentrations, it acts proinflammatory and in a cytotoxic manner directly or through the active metabolites.

The measurement of FeNO is a relatively new diagnostic method and its beginning is dated back to the end of the 20th century. The presence of nitric oxide in exhaled air was indicated for the first time by Gustafsson in 1991, and the first guidelines for its measuring were published in 1999 by the American Thoracic Society (ATS) [11].

The measurement of the concentration of nitric oxide in exhaled air (FeNO) is currently a recognized biomarker and quantitative determinant in the detection and monitoring of respiratory track inflammations, especially eosinophilic inflammation and asthma. In the recent years, the FeNO measurement is becoming more and more widely applied in respiratory system disease diagnosis of children. It is a modern, simple, noninvasive examination and can be performed many times for every cooperating child [12, 13]. Until now, few studies show a relationship between FeNO and atmospheric air pollution [14,15,16].

The aim of the study was to measure FeNO for 8-9 year old children, both healthy and with respiratory tract diseases in Krakow and in Ruzomberok. FeNO measurements were related to the level of atmospheric air pollution in these cities.

MATERIALS AND METHODS OF RESEARCH

The measurement of nitric oxide concentration in exhaled air comprised 250 children aged 8-9 years old, attending third grades of primary schools in Krakow and Ruzomberok. The research group consisted of 125 pupils of the third grades of primary schools in Krakow on the 15th, 18th and 22nd of January 2018 and 125 pupils from 4 primary schools in Ruzomberok on the 4th and 5th of February 2019.

The study group included both healthy children and those with respiratory diseases, including asthma.

The FeNO levels were related to the concentration of PM 10 and PM 2,5 in the atmospheric air.

The analysis comprised the pupils whose parents had previously given their written consent to conduct the study. The parents of all the children had previously received an information leaflet regarding the purpose and methodology of the planned measurement and the manner in which the children should be prepared for the study.

The study has been conducted in accordance with the standards applicable for FeNO measurements with the application of the MediSoft Belgium company analyzer. The children did not eat, drink or exercise two hours prior to the measurement. Prior to the examination itself, the children have been instructed about the manner it is performed in and were subject to an initial test so as to check the correctness of the sample. The test was about calmly inhaling and exhaling through a disposable head with an antibacterial filter [21].

The FeNO result has been given in ppb values (*parts per billion*, number of parts per billion, 10^{-9}), i.e. in a zero-dimensional notation of the ratio of two values. As in most scientific studies, the limit value that has been applied, was the norm set for children on the level of 20 ppb [27]. The values of concentration above the accepted norm have been divided into 3 groups:

Group I NO 21-50 ppb, group II NO 51-99 ppb, group III NO >99 ppb.

The degree of air pollution has been obtained from the Voivodeship Inspectorate for Environmental Protection in Krakow *http://monitoring.krakow.pios.gov.pl* and from the OZ Ochrana ovzdusia dolny Liptov *https://www.ovzdusie.sk.*

The FeNO measurement results and the correlation with the PM 10 and PM 2,5 levels has been analyzed separately in both of the cities and subsequently the analyses have been compared to one another.

RESULTS AND DISCUSSION

125 children participated in the study in Krakow. The FeNO concentration range was from 5-125 ppb (16 ppb on average). For 104 children, which constituted 83,2% of the examined population, the FeNo values were correct and amounted to 5 – 20 ppb. In 21 children, which constituted 16.8% of the studied population, FeNO values exceeded the accepted norm and amounted to 21-125 ppb. Among the increased results in group I (21-50 ppb), 17 measurements were obtained, which constituted 13,6% of the general population, in the second group (51-99 ppb) 3 measurements (2,4%) and in the third group >99ppb, 1 measurement was obtained (0,8%).

All of the FeNO measurement results are shown in figure 1.

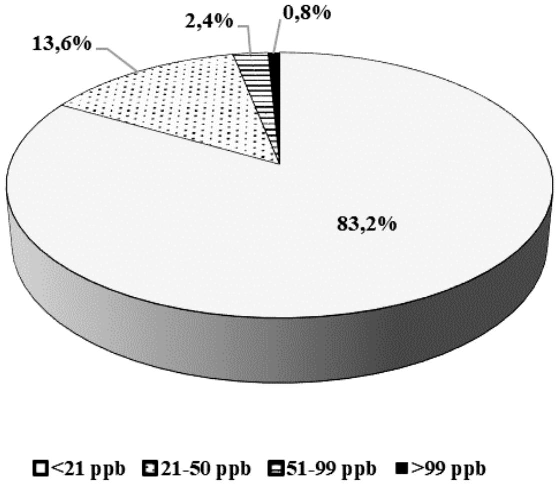

Fig. 1. The percentage distribution of the values of all FeNO measurements in Krakow

A separate percentage analysis of the increased FeNO results themselves is as follows: group I (21-50 ppb) – 80,95%; group II (51-99 ppb) - 14,3%; group III (>99ppb) – 4,75%. The results of the percentage distribution of the incorrect FeNo values are shown in figure 2.

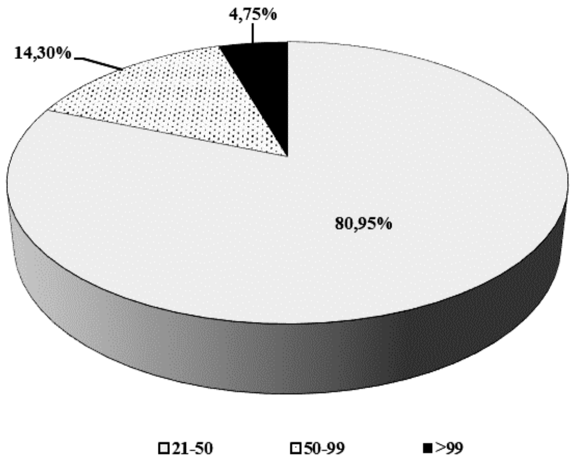

Fig. 2. Percentage distribution of incorrect FeNO values in Krakow

The air pollution level in Krakow when the survey has been conducted, i.e. the 15th, 18th and 18th of January 2018 was on average 55,7 [μg/m^3] for PM10 and 37,0 [μg/m^3] for PM2,5. The concentrations of the suspended particulates on the examination date in the PM10 fraction were: 15.01.2018 – 75[μg/m^3]; 18.01.2018 – 38[μg/m^3]; 22.01.2018 – 54[μg/m^3], an in the PM2,5 fraction, these were: 15.01.2018 – 50[μg/m^3]; 18.01.2018 – 18[μg/m^3]; 22.01.2018 – 43[μg/m^3].

The PM10 and PM2,5 concentration levels are shown in figure 3 and in table 1.

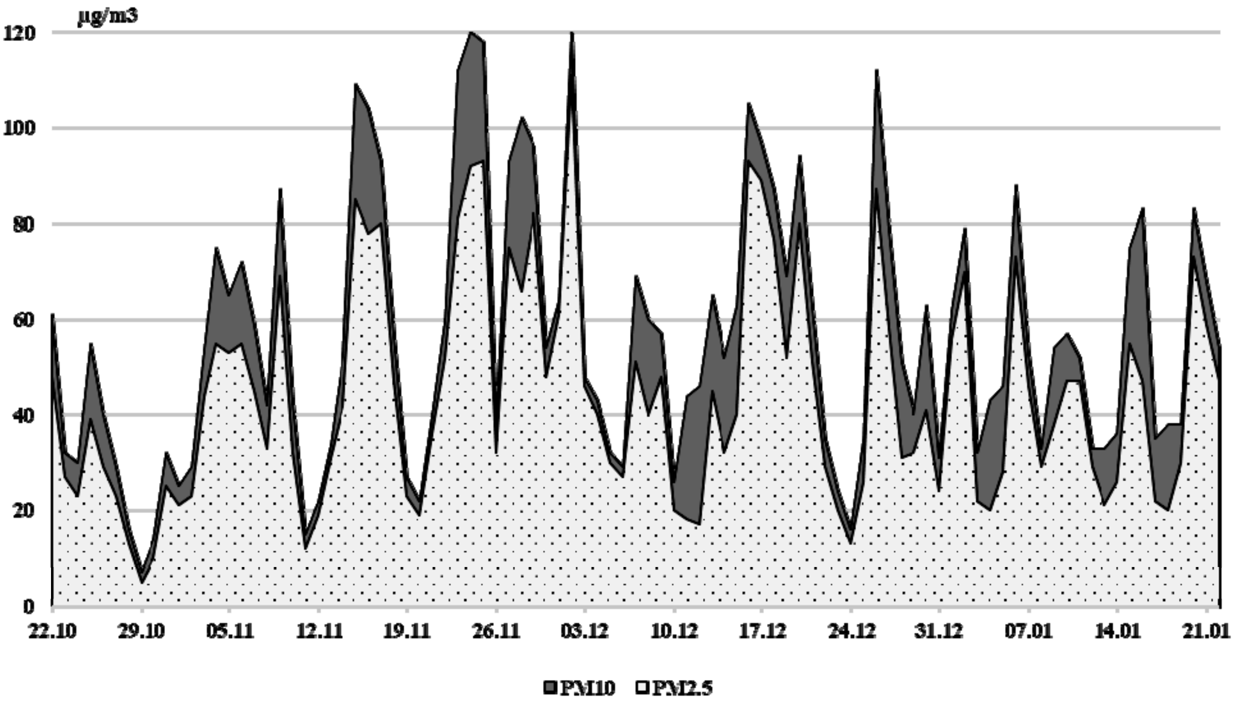

Fig. 3. PM10 and PM2,5 concentration levels in Krakow

125 participated in the study in Ruzomberok. The FeNO concentration range was from 4-55 ppb (11,9 ppb on average).

For 114 children, which constituted 91,2% of the examined population, the FeNO values were correct and amounted to 5-20 ppb. For 11 children, which constituted 8,8% of the analyzed population, the FeNO values have exceeded the accepted norm and amounted to 21-55 ppb. Amongst the increased results in group I (21-50 ppb), 10 measurements have been obtained, which constituted 8% of the general population, 1 measurement has been obtained in group II (51-99 ppb), which constituted 0,8% of the general population, and no measurement has been obtained in group III (>99 ppb) (Fig. 4).

Table 1

PM10 and PM2,5 concentration levels in Krakow during the days of the study

	15.01.18	18.01.18	22.01.18	average
PM10 [μg/m^3]	75	38	54	55,7
PM2,5 [μg/m^3]	50	18	43	37,0

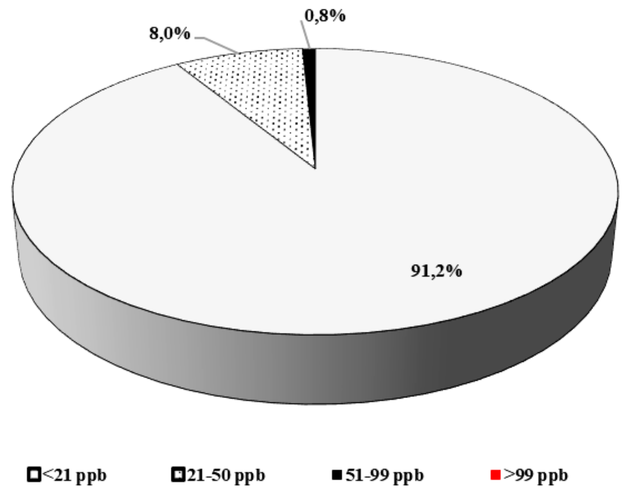

Fig. 4. The percentage distribution of the FeNO measurement values in Ruzomberok

A separate percentage analysis of the elevated FeNo values themselves is as follows:

group I (21-50 ppb) – 90,9%, group II (51-99 ppb) – 9,1%, group III (>99 ppb) – no measurement has been obtained. Figure 5 presents the results of the percentage distribution of incorrect FeNO values.

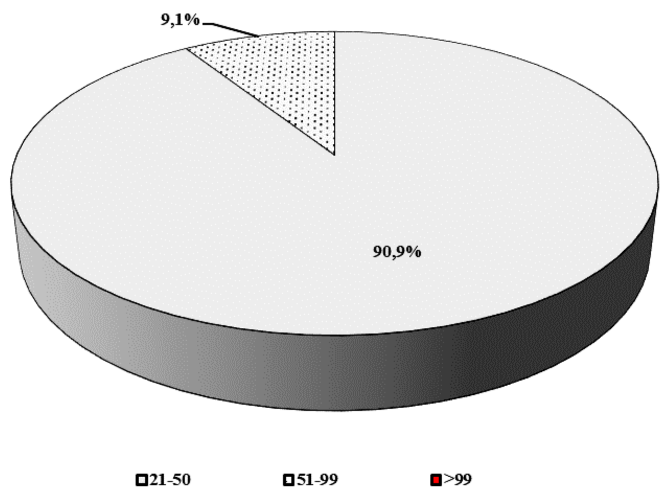

Fig. 5. Percentage distribution of incorrect FeNO values in Rużomberk

The level of air pollution in Ruzomberok during the study, i.e. the 4th and 5th of February 2019 was, on average – 24,1 [µg/m^3] for PM10, for PM2,5 – 15,4 [µg/m^3]. For the individual days of the testing of the suspended particulates within the PM10 fraction, these were as follows: 04.02.2019 – 12,5 [µg/m^3]; 05.02.2019 – 35,6 [µg/m^3]; and as far as the PM2,5 fraction is concerned, these were as follows: 04.02.2019 – 5,7 [µg/m^3]; 05.02.2019 – 25,0 [µg/m^3].

The PM 10 and PM 2,5 concentration levels are shown in figure 6 and in table 2.

In the studied population of children in Krakow, 83.2% of pupils had normal FeNO values, while in 16.8% of children FeNO values were raised above 20 ppb. The FeNO results greatly exceeding the norm, i.e. >50 ppb have been obtained for 3,2% of the examined children, which constituted 19% of the group of children with incorrect results. During the research period, the average air pollution values in Krakow within the PM10 and PM2,5 fractions were respectively: 55,7 µg/m^3 and 37,0 µg/m^3.

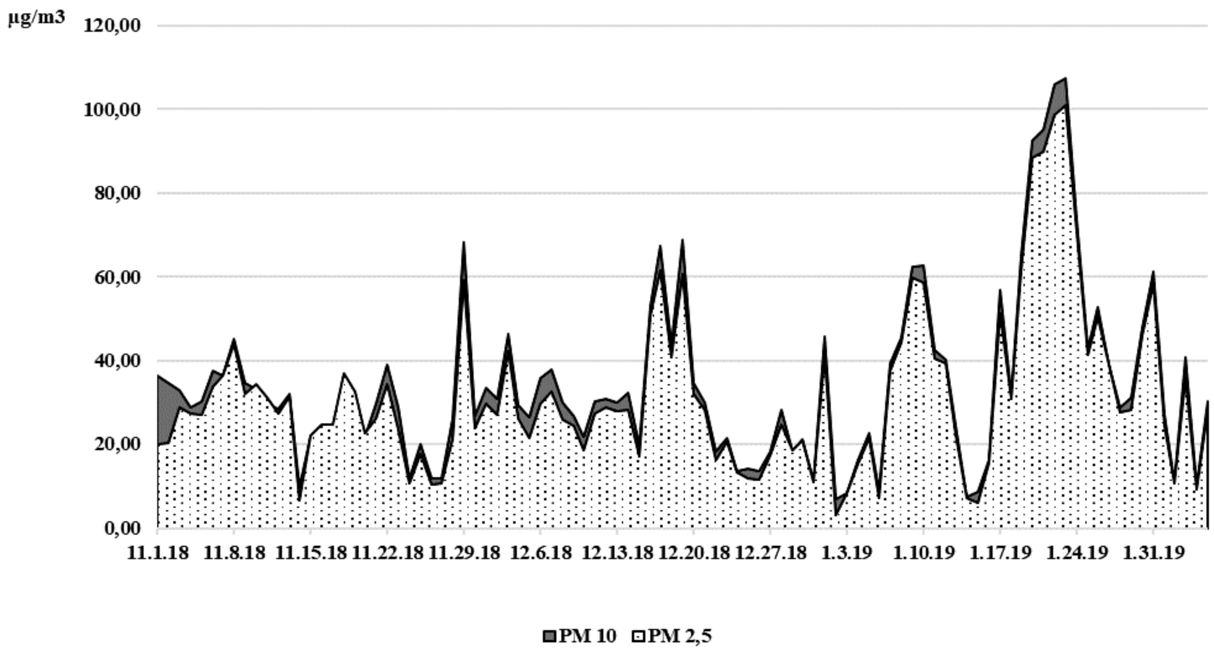

Fig. 6. the PM10 and PM2,5 concentration levels in Ruzomberok

Within the children population examined in Ruzomberok, the FeNo values were correct for 91,2% of the pupils, and for 8,8% of the children, the FeNO values were increased above 20 ppb. The FeNO results greatly exceeding the norm, i.e. >50 ppb have been obtained for 0,8% of the examined children, which constituted 9,1% amongst the group of children with the incorrect results. During the research period, the average air pollution values in Ruzomberok in the PM10 and PM2,5 fractions were respectively: 24,1 µg/m^3 and 15,4 µg/m^3.

Figure 7 presents a comparison of the FeNO measurement results for Krakow vs Ruzomberok.

Table 2

The PM10 and PM2,5 concentration levels during the study

	04.02.2019	05.02.2019	Average
PM10 [µg/m^3]	**12,5**	**35,6**	**24,1**
PM2,5 [µg/m^3]	**5,7**	**25,0**	**15,4**

A comparison of the FeNO studies in both of the cities shows that 1,9 times more of increased FeNo values>20 ppb have been recorded in Krakow than in Ruzomberok (18,6% vs 8,8%). This difference is even more visible when we take into consideration the greatly increased FeNO >50 ppb results, where 4 times more children have been recorded in Krakow than in Ruzomberok (3,2% vs 0,8%). When measuring, higher concentrations of suspended particulates in the atmospheric air both in PM10 as well as in PM2,5 have been recorded in Krakow than in Ruzomberok. For PM10, these values were 2,3 times bigger (55,7 vs 24,1 µg/m^3), and 2,4 times bigger for PM2,5 (37,0 vs 15,4 µg/m^3). All of the children with increased FeNO values have been instructed to visit specialist pulmonology or allergy clinic so as to further diagnose for respiratory tract diseases, this including asthma. For the children who have already been diagnosed with asthma, for whom increased FeNO values have been observed, control was recommended so as to modify the treatment.

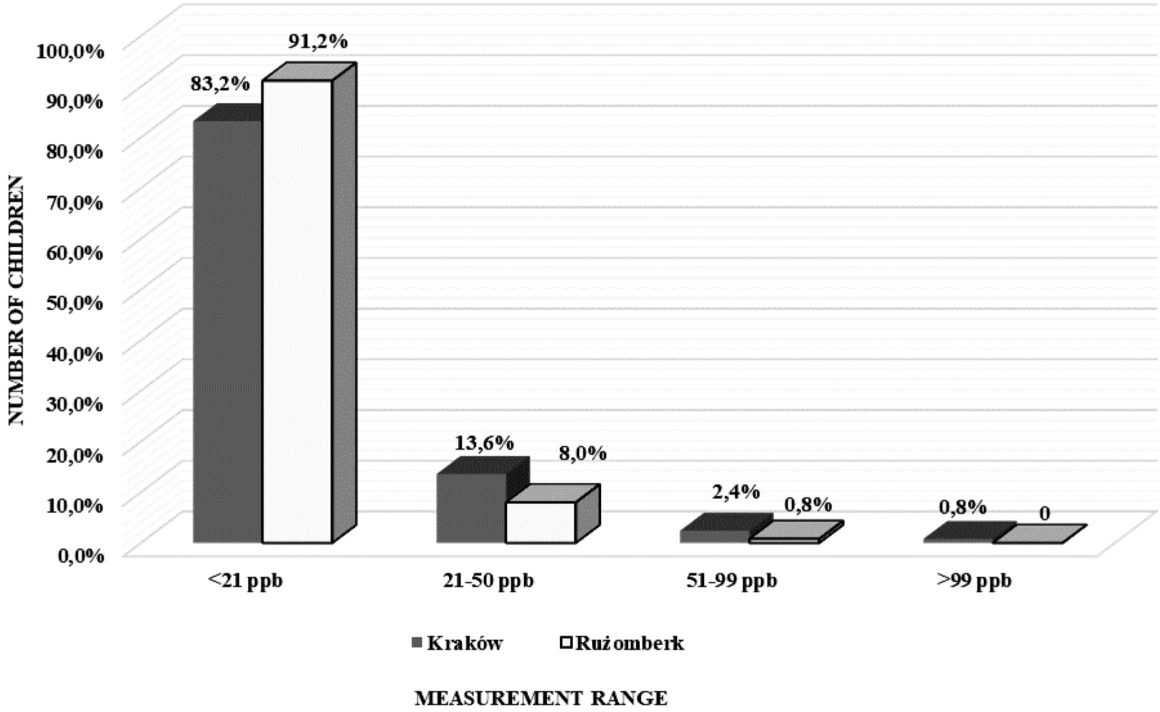

Fig. 7. A comparison of the FeNO measurement results for Krakow vs Ruzomberok

CONCLUSIONS

1. Within the conducted research, 1,9 times bigger FeNo values have been recorded for the Krakow area children than for those from Ruzomberok (18,6 vs 8,8%), which correlated to a 2,3 times bigger concentration of suspended particulates PM10 and a 2,5 times bigger PM2,5 concentration in Krakow during the research period.
2. The study shows that there is a positive correlation between nitric oxide concentration in the exhaled air and the PM10 and PM2,5 suspended particulates concentration in atmospheric air.
3. The children from the area with a bigger degree of air pollution had a bigger nitric oxide concentration in the exhaled air.
4. Due to its simplicity and noninvasiveness, FeNO measurement should be more and more widely applied in respiratory tract disease diagnostics for children, especially for those living in areas with a significant degree of atmospheric air pollution.
5. The FeNO study allowed to identify the children with the increased values indicating respiratory tract inflammations, and then to include them in further diagnostics for respiratory tract diseases, this including asthma.

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