УДК 616.2-002.1-053.4/.5-036.3-039.35-02-084 Original research

RISK FACTORS OF RECURRENT RESPIRATORY INFECTIONS IN EARLY SCHOOL-AGE CHILDREN

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Key words: *respiratory infections, children, risk factors, passive smoking, tonsillitis, prevention, pneumonia, prognosis.*

Bukovinian Medical Herald.

2023. V. 27, № 3 (107). P. 25-29.

DOI: *10.24061/2413-0737.27.3.107.2023.5*

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Resume. *Acute respiratory infections (ARIs) annually rank first in the structure of infectious diseases both in Ukraine and worldwide. ARIs are the leading cause of disability and death in preschool children, and with recurrent episodes, they can impact the physical and psychological aspects of children's health, imposing a significant medical burden on families, healthcare systems, and society as a whole. Preventing recurrent respiratory infections (RRIs) can only be achieved through timely intervention in risk factors.*

Aim*: to determine the influence of risk factors on the development of recurrent episodes of acute respiratory infections in children aged 5 to 7 years and to develop preventive measures for their control in primary healthcare settings.*

Materials and Methods*. The authors retrospectively analyzed medical records of 342 children aged 5 to 7 years. The main group included children with RRIs (264), and the control group consisted of children with sporadic illness episodes (78). Results: the incidence of RRIs in children has two peaks at ages 3 and 6, which is likely associated with the commencement of attendance in childcare settings (kindergarten and school). Key prenatal and postnatal, clinical-anamnestic, and social risk factors that increase the likelihood of recurrent respiratory infections in younger school-age children were identified.*

Conclusions*. factors significantly increasing the likelihood of developing RRIs in a child include: ARI episode within the first 6 months of life (OR = 22, 95% CI 11.6 - 41.7), previous pneumonia (OR = 12, 95% CI 3.7 - 40), and the presence of chronic infection foci in the form of tonsillitis (OR = 8.2, 95% CI 4.3 - 15.6), p=0.0001. Primary healthcare practitioners should follow strategies to modify these risk factors and not wait for further depletion of the child's adaptive potential (sanitation of chronic infection foci, promotion of breastfeeding, and tobacco cessation).*

ФАКТОРИ РИЗИКУ РЕКУРЕНТНОГО ПЕРЕБІГУ ГОСТРИХ РЕСПІРАТОРНИХ ІНФЕКЦІЙ У ДІТЕЙ МОЛОДШОГО ШКІЛЬНОГО ВІКУ

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Ключові слова: *респіраторні інфекції, діти, фактори ризику, пасивне тютюнопаління, тонзиліт, профілактика, пневмонія, прогнозування.*

Буковинський медичний вісник. 2023. Т. 27, № 3 (107). С. 25-29.

Резюме. *Гострі респіраторні інфекції (ГРІ) щорічно посідають перше місце в структурі інфекційної захворюваності як в Україні, так і у світі. ГРІ є основною причиною інвалідності та смерті у дітей дошкільного віку, за умови рекурентного перебігу можуть впливати на фізичні та психічні аспекти дитячого здоров'я та становлять значний медичний тягар для сім'ї, системи охорони здоров'я та суспільства в цілому. Запобігти рекурентним респіраторним інфекціям (РРІ) можна лише за рахунок своєчасного впливу на фактори ризику.*

Мета дослідження *– визначити вплив факторів ризику формування рекурентного перебігу гострих респіраторних інфекцій у дітей від 5 до 7 років та розробити превентивні заходи їх контролю на первинній ланці медичної допомоги.*

Матеріал і методи. *Авторами ретроспективно опрацьовано медичну документацію стосовно 342 дітей віком від 5 до 7 років. До основної групи увійшли діти з РРІ (264), до групи контролю – діти, котрі епізодично хворіють(78).*

Результати та обговорення*. Захворюваність дітей з РРІ має два сплески захворюваності – три та шість років, що ймовірно пов'язано з початком відвідування дитячих колективів (дитячий садок та школа). Виділено основні пери- та постнатальні, клініко-анамнестичні та соціальні фактори ризику, що підвищують шанси на реалізацію феномену рекурентних респіраторних інфекцій у дітей молодшого шкільного віку.*

Висновки*. Фактори, що суттєво підвищують шанси на формування рекурентних респіраторних інфекцій у дитини: епізод гострого*

респіраторного захворювання в перші шість місяців життя (ВШ=22 95% ДІ 11,6 - 41,7), перенесена пневмонія (ВШ=12 95% ДІ 3,7 - 40) та наявність хронічного вогнища інфекції у вигляді тонзиліту (ВШ=8,2 95% ДІ 4,3 - 15,6) p=0,0001. Лікарям первинної ланки медичної допомоги слід керуватися стратегіями впливу на модифіковані фактори ризику та не очікувати подальшого прогресування вичерпання адаптаційного потенціалу організму дитини (санація хронічних вогнищ інфекції, пропагування грудного вигодовування та відмови від тютюнопаління).

Respiratory pathology continues to dominate the structure of infectious diseases, especially in children aged 1 to 7 years [1]. Up to 70% of visits to primary healthcare physicians involve issues related to the recurrent illnesses of children with recurrent respiratory infections (RRIs) [2]. The problem of RRIs remains unresolved due to the lack of internationally agreed-upon recommendations regarding clear classifications of this phenomenon and its clinical management, increased healthcare budget expenditures, the emergence of antibiotic resistance (due to irrational treatment of acute respiratory infection episodes (ARIs)), and the negative impact of frequent ARIs on the physical, mental, and social aspects of children's health, leading to the eventual depletion of a child's adaptive potential [3,4]. Children with RRIs often become patients subjected to excessive and unjustified administration of immune boosters, vitamin complexes, probiotics, and other pharmacological agents with low levels of evidence [5]. Currently, numerous conflicting research findings concerning modern modified predictors of RRI development, along with the clarification of their impact strength, hinder the formation of an evidence-based preventive system. The paper aims to determine the influence of risk factors on the development of recurrent episodes of acute respiratory infections in children aged 5 to 7 years and to develop preventive measures for their control in primary healthcare settings.

Materials and Methods. A retrospective analysis of medical documentation (hospital medical records - Form No. 003/o) and outpatient data, along with clinical examination of children and results of specialist consultations, was conducted at the Specialized Medical and Rehabilitation Center for Children and Adolescents (SMRCCA) from 2018 to 2020.

Inclusion criteria for the main group were as follows (in accordance with the consensus of the Immunological Research Group of the Italian Society of Pediatrics regarding recurrent respiratory infections) [6]: children aged 5 to 7 years with any of the following factors: six or more episodes of acute respiratory infections (ARIs) per year, one or more episodes of upper respiratory tract infections per month from September to April, or three or more episodes of lower respiratory tract infections per year. The control group consisted of children aged 5 to 7 years who were matched by age and gender with the main group but did not have a history of recurrent ARIs. Exclusion criteria included children under 5 or over 7 years of age and children with severe hereditary diseases (cystic fibrosis, immunodeficiencies, etc.). The control group comprised children with infrequent ARIs (4 or fewer episodes per year), matched by age and gender. All information was collected according to research protocols without disclosing confidential data.

Study Design: a retrospective non-randomized study aimed at determining the odds ratio of the studied factors' influence.

The actual study was conducted in accordance with the principles of the Helsinki Declaration on Human Rights (64th World Medical Association General Assembly, Fortaleza, Brazil, October 2013) and the Universal Declaration on Human Rights and Bioethics (UNESCO session, Paris, France, October 19, 2005).

Statistical data analysis was performed using the MS Excel package and the "Statistica v.6.1" software (№AGAR909E415822FA, Statsoft inc. USA).

In the analysis, the following methods were employed: calculation of intensive and extensive indicators, mean values, standard deviations, data comparison using Pearson's $\chi 2$ test, and determination of odds ratios with a 95% confidence interval. The critical level of statistical significance was set at $p<0.05$.

Data analysis regarding the main characteristics of the respondents (Table 1) indicated that, in terms of age and gender, patients in the studied main group and control group were comparable, allowing for a comparison of their examination results based on other parameters.

Table 1

Characteristics of Children in the Main and Control Groups

Indicator	Main group N=264	Control group N=78	p value
Average age	6 років (SD=0,37)	6 років (SD=0,41)	p = 0,274
Male gender	154 (58%)	44 (56%)	p = 0,863654
Female gender	110 (42%)	34 (44%)	

Results and Discussion. We conducted a retrospective study of 264 medical histories of children aged 5-7 years who met the criteria for recurrent respiratory infections (RRI) (the main group) and 78 children with infrequent illnesses (the control group). In the initial assessment of the obtained results, we analyzed the annual number of acute respiratory infection episodes among participants in both grou ps (Figure 1).

According to our data (Fig. 1), the incidence of ARI episodes in children with RRIs shows two peaks at ages 3 and 6, which is likely associated with the start of attending childcare settings (kindergarten and school) and is consistent with the literature [7]. It's also worth noting that

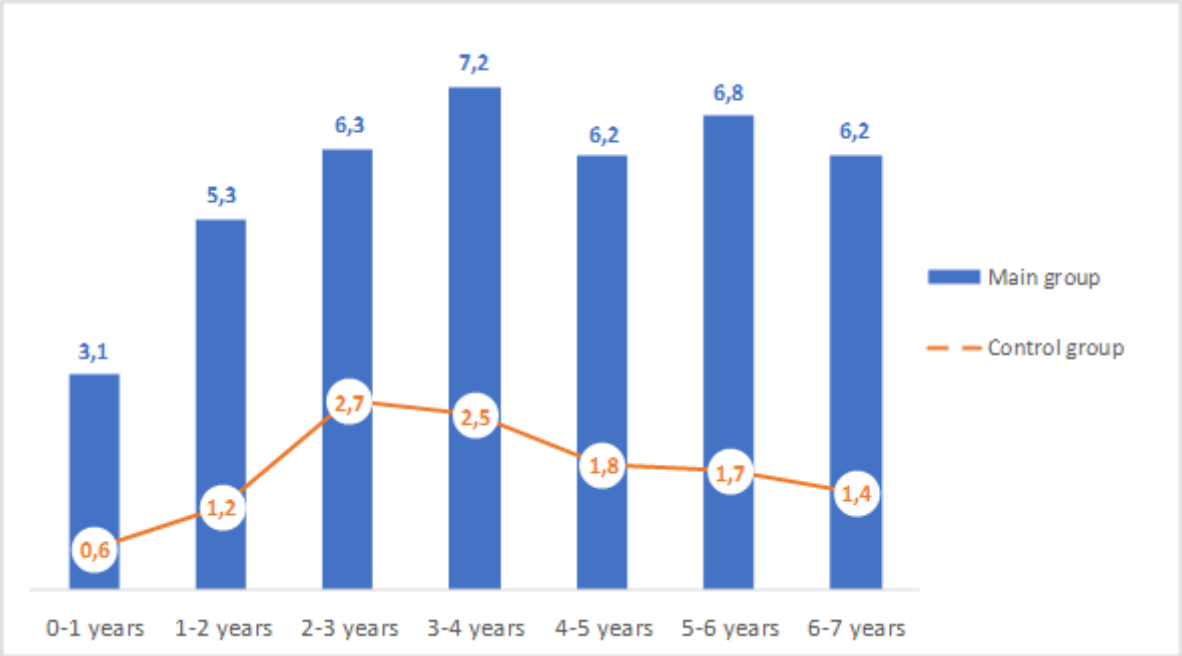

Fig.1. The Number of ARI Episodes According to Age in Children in the Main and Control Groups

children who entered the main observation group from birth to 7 years of age have significantly higher ARI incidence rates compared to practically healthy same-age peers (the control group): 3.1 versus 0.6 in the first year of life; 5.3 versus 1.2 in the second year; 5.8 versus 2.7 in the third year; 7.2 versus 2.5 in the fourth year; 6.2 versus 1.8 in the fifth year; 6.8 versus 1.7 in the sixth year; 6.2 versus 1.4 in the seventh year. Thus, children with RRIs already demonstrate increased susceptibility to ARI from their first year of life compared to episodically ill peers, a trend that persists throughout the first seven years of life.

We conducted a comparison of primary prenatal and postnatal risk factors for the development of RRIs (Table 2).

Table 2

Prenatal and Postnatal Risk Factors in Children with RRIs and Episodically Ill Children

Indicator	Main group (n=264)	Control group (n=78)	p value
Premature birth	45 (17%)	8 (10%)	p = 0.201363
Cesarean section	42 (16%)	12 (15%)	p = 0.948091
Toxicosis during pregnancy	130 (49%)	24 (31%)	p = 0.00593*
Anemia during pregnancy	63 (24%)	10 (13%)	p = 0.053108
High blood pressure during pregnancy	58 (22%)	6 (8%)	p = 0.007466*
Intrauterine hypoxia	68 (26%)	12 (15%)	p = 0.080263
The presence of ARI in the first 6 months of life	227 (86%)	17 (22%)	p = 0.00001*
Breastfeeding up to 6 months	95 (36%)	52 (67%)	p = 0.00001*

* statistically significant differences

According to our data, children experiencing recurrent ARI episodes differed from practically healthy peers in terms of the following prenatal risk factors from the mother's side: maternal toxemia and elevated blood pressure during pregnancy.

Considering the potential impact of frequent ARI episodes leading to the depletion of physical adaptive potential, we compared the basic anthropometric data of children in both groups, including height, birth weight, chest circumference/head circumference ratio, height, weight, and chest circumference at admission to the hospital. As a result, it was found that participants in the main group did not have significant differences at birth. However, children in the RRI group had significantly lower weight and chest circumference measurements at admission, with no changes in height, independent of gender.

As it is known [8], breastfeeding can support a child's immune system until the transition to solid food. This fact may explain that 64% of children with RRIs did not receive breastfeeding during the first 6 months of life, while statistically, they experienced more ARI episodes during

the same period compared to control group peers ($p < 0.001$).

Clinical, anamnestic, and social characteristics of the main and control groups are presented in Table 3.

According to our results, dental caries is equally prevalent among the examined children, while adenoid vegetations and chronic tonsillitis were more prevalent in children with RRIs ($p < 0.001$). Children in the main group had significantly higher incidence rates of atopic dermatitis ($p = 0.00971$), which, according to literature [9], is an early manifestation of sensitization in the body. In the social profile of children with RRIs, significant predictors included the influence of passive smoking on frequent respiratory illnesses in children ($p < 0.001$). Our study emphasized its relevance in the context of increasing numbers of parents who smoke. Children with RRIs were usually second-born in the family ($p < 0.001$), which can be explained as an additional source of infection transmission from an older sibling. Complicated ARI episodes (pneumonia, otitis) were statistically more common in the main group of children ($p < 0.001$), while bronchitis with obstructive syndrome occurred at similar frequencies in both groups ($p = 0.51$).

In accordance with the objective of this study, we identified risk factors for RRIs and calculated odds ratios for statistically significant clinical, anamnestic, social, prenatal, and postnatal indicators, as presented in Table 4.

Analysis of the results in Table 4 showed that the most significant predictive factors for future Recurrent Respiratory Infections (RRI) in younger school-age children were: an episode of Acute Respiratory Infection (ARI) within the first 6 months of life (OR=22), a history of pneumonia (OR=12), and the presence of chronic infection foci in the form of tonsillitis (OR=8.2). These findings emphasize additional points of intervention for healthcare providers managing this group of children (modified risk factors): timely management of chronic infection foci (adenoid vegetation, tonsillitis), increased

Table 3

Clinical, Anamnestic, and Social Characteristics of the Main and Control Study Groups

Indicator	Main group N=264	Control group N=78	p value
Foci of chronic infection:			
adenoid vegetations	108 (41%)	12 (15%)	p = 0.000059*
chronic tonsillitis	164 (62%)	13 (17%)	p = 0.00001*
caries	100 (38%)	27 (43%)	p = 0.695994
Allergic anamnesis:			
eczema	21 (8%)	5 (7%)	p = 0.834447
atopic dermatitis	61 (23%)	7 (9%)	p = 0.00971*
food allergy	68 (26%)	14 (18%)	p = 0.204686
Social factors			
incomplete family	42 (16%)	7 (9%)	p = 0.176385
first child in the family	74 (28%)	61 (78%)	p = 0.00001*
second child in the family	167 (64%)	15 (19%)	p = 0.00001*
smoker in the family	108 (41%)	13 (17%)	p = 0.000145*
Complicated course of ARI:			
pneumonia	87 (33%)	3 (4%)	p = 0.00001*
otitis	140 (53%)	24 (31%)	p = 0.000873*
carditis	16 (6%)	2 (2,5%)	p = 0.354206
bronchitis with BOS	55 (21%)	13 (10%)	p = 0.516584

* statistically significant differences

Table 4

Odds Ratios for RRI in Children Based on Anamnestic Data

Category of risk factors	Indicator	Odds Ratios (95% CI)	p value
Unmodified	Toxicosis during pregnancy	2,1828 (1,2746 - 3,7382)	0,0045
Unmodified	Otitis media as a complication of ARI	2,5403 (1,4831 - 4,3512)	0,0007
Unmodified	Atopic dermatitis	3,0479 (1,3323 - 6,9725)	0,0083
Unmodified	High blood pressure during pregnancy	3,3786 (1,39810 - 8,1646)	0,0068
Modified	Smoker in the family	3,4615 (1,8179 - 6,5914)	0,0002
Modified	Adenoid vegetations	3,8077 (1,9636 - 7,3835)	0,0001
Modified	Lack of breastfeeding for the first 6 months	4,2048 (2,406 - 7,3485)	0,0001
Unmodified	The second child in the family	7,2309 (3,9047 - 13,3907)	0,0001
Modified	Chronic tonsillitis	8,2 (4,3008 - 15,6342)	0,0001
Unmodified	Pneumonia	12,2881 (3,7676 - 40,0786)	0,0001
Unmodified	ARI in the first 6 months of life	22,0143 (11,607 - 41,7531)	0,0001

motivation for breastfeeding for at least the first 6 months of a child's life, and avoiding smoking in the family.

Conclusions

1. Factors significantly increasing the chances of developing RRI in children include: an episode of ARI within the first 6 months of life (OR=22, 95% CI 11.6 - 41.7), a history of pneumonia (OR=12, 95% CI 3.7 - 40), and the presence of chronic infection foci in the form of tonsillitis (OR=8.2, 95% CI 4.3 - 15.6) p=0.0001.

2. Primary healthcare providers should follow strategies to address modified risk factors and not anticipate further depletion of the child's adaptive potential (management of chronic infection foci, promotion of breastfeeding for at least the first 6 months of a child's life, and discouraging smoking in the family).

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

This research is part of the scientific work of the Department of Family Medicine of the Faculty of Postgraduate Education and Propaedeutics of Internal Medicine, Dnipro State Medical University and is funded by the state budget of the Ministry of Health of Ukraine.

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Надійшла до редакції 15.09.23

Рецензент – проф. Л.П. Сидорчук