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ORIGINAL ARTICLE

ORAL HEALTH STATUS OF PRESCHOOL CHILDREN WITH RECURRENT UPPER RESPIRATORY TRACT INFECTIONS

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ABSTRACT

Background: The adverse social, educational, and economic consequences of recurrent respiratory tract infections have led to increased attention from healthcare professionals to this problem. The aim of this study was to assess the level of oral health and the factors of local nonspecific defense in children with recurrent upper respiratory tract infections.

Materials and Methods: The oral health status of 52 preschool children with recurrent upper respiratory tract infections (RRIs) and 35 healthy peers was evaluated. Caries indices (dmf, dmfs, DMF, DMFS), oral hygiene indices (Stallard, Silness–Löe), periodontal indices (PMA%, bleeding index, Schiller–Pisarev test), the confidence interval of oral fluid pH fluctuations, and its biochemical parameters (catalase activity, malondialdehyde, lysozyme, urease, and elastase) were determined.

Results: In children with RRIs, a decrease in the level of oral health to 66.7% was observed, attributable to the high prevalence of dental caries and gingivitis. A weakening of the nonspecific defense factors of oral fluid was also identified, characterized by an unstable pH state, decreased catalase activity ($p < 0.001$) and lysozyme activity ($p < 0.001$), and increased concentrations of malondialdehyde ($p < 0.001$), urease ($p < 0.001$), and elastase.

Conclusion: High caries prevalence, unfavorable oral hygiene and periodontal indices, and weakened local nonspecific defense mechanisms in children with RRIs necessitate the development of targeted therapeutic and preventive measures.

Keywords: dental health, nonspecific resistance, recurrent respiratory tract infections, children

INTRODUCTION

Recurrent respiratory tract infections (RRIs) represent repeated cases of acute respiratory infections with a high frequency of episodes (eight or more per year). The adverse social, educational, and economic consequences of RRIs determine the increased attention of medical professionals to this problem[1–3]. The proportion of RRIs of the upper respiratory tract in various age groups ranges from 4.0–18.0% to 27.0–40.0%, with the most consistently high level observed in the preschool child population[4]. The predisposition of preschool children to RRIs is a result of the physiological immaturity of both systemic and local immunity[5–6].

In children with frequent year-round episodes of acute infections of the upper respiratory tract, significant alterations in the microbiome of the oral cavity and upper airways have been identified[7–8]. There is evidence that children with RRIs exhibit a low level of oral hygiene and an increased progression of dental caries affecting both primary and permanent dentitions[9–11]. The 20-year prospective Espoo Cohort Study established that frequent acute upper respiratory tract infections in early childhood were predictors of a higher prevalence of dental caries in permanent teeth during adulthood[12]. Also, from a public health perspective, research demonstrating the impact of early childhood caries on the increased frequency of acute respiratory infection episodes in children is highly significant[13–15]. Furthermore, it was established that in young adults aged 20–27 years, the risk of lower respiratory tract diseases increased in proportion to the number of filled teeth, reaching its peak in individuals with ten or more filled teeth[16].

However, a literature analysis has revealed that over the past 10 years, only a small number of publications have been dedicated to the dental problems of children with RRIs.

The oral cavity serves as the entry point for microbial agents into the human body, and the protective mechanisms of saliva constitute one of the first barriers encountered by respiratory pathogens[17]. Therefore, studying the state of the nonspecific protective factors of the oral cavity in children with RRIs is of significant interest. Research in this direction may assist in the development of therapeutic and preventive measures aimed at improving the quality of both oral and respiratory health in children.

The study was aimed at assessing the level of dental health and the factors of local nonspecific defense in children with RRIs of the upper respiratory tract.

MATERIALS AND METHODS

An analytical comparative cross-sectional study was conducted involving 52 children with recurrent respiratory tract infections (RRIs) (the main group), including 29 (55.8%) boys and 23 (44.2%) girls, and 35 apparently healthy children (the control group), including 19 (54.3%) boys and 16 (45.7%) girls. No formal sample size calculation was performed; the sample size was determined by the number of eligible participants available during the study period.

To be included in the study, a child had to meet the following criteria: age 6–7 years, absence of hereditary or systemic chronic diseases, no acute respiratory infections within the previous month, no use of antibiotics or nonsteroidal anti-inflammatory drugs within the previous month, no regular medication intake, and willingness to cooperate.

The children included in the study were from families with a moderate socioeconomic status, assessed according to indicators such as household income and parental educational level.

A mandatory requirement for participation was obtaining voluntary written informed consent from parents or legal guardians. The study was carried out in accordance with ethical principles, including the World Medical Association Declaration of Helsinki.

The clinical examination was performed in the dental office of the Municipal Budgetary Educational Institution “Secondary General Education School – Combined Kindergarten No. 6” in Simferopol. Information regarding episodes of RRIs was obtained from medical records and additionally through questionnaires completed by parents.

The Infectious Index (II) was calculated as the ratio of the total number of acute respiratory infection episodes over one year to the child’s age. The Resistance Index (RI) was calculated as the ratio of the number of acute respiratory infection episodes to the number of months of observation.

During the dental examination, the following parameters were assessed: dental caries indices (dmf, dmfs, DMF, DMFS), oral hygiene status using the Silness–Löe and K. Stallard indices, and periodontal condition using the PMA%, bleeding index, and Schiller–Pisarev test. Based on these findings, the Dental Health Level (DHL) was calculated as a percentage. The assessment was based on numerical health indicators defined for nine groups of dental diseases [18]. The DHL value depends on the severity of the pathology, the degree of impairment of masticatory function, and the extent of required therapeutic interventions.

To assess the acid–base status of oral fluid, pH measurements were performed on three samples using a portable pH meter/millivoltmeter pH-410.

The arithmetic mean of the values was calculated, after which the confidence interval of deviation (ΔpH) from the mean value was determined using the following formula:

$$\Delta pH = t_{3;0.95}\sqrt{\sum_{i=1}^{3}(\Delta pHi)^{2}/3(3-1)}, \text{ where}$$

$t_{3;0.95}$ was Student's coefficient with a 0.95 confidence probability for three measurements;

ΔpHi was the deviation of the pHi values from the arithmetic mean.

This calculation was performed after a preliminary graphical analysis to evaluate whether the data could be approximated by a normal distribution. A biochemical analysis of mixed saliva was performed in 31 children with RRIs (study group) and 21 healthy children (control group). Oral fluid was collected in the morning into sterile tubes using the spitting method. The children had not eaten breakfast and had not performed morning oral hygiene. The samples were stored at −20 °C. After thawing, they were centrifuged for 15 minutes at 3,500 rpm, after which biochemical analyses were performed. Elastase activity in oral fluid was determined spectrophotometrically at a wavelength of 347 nm. The method is based on the hydrolysis of the synthetic substrate Boc-L-alanine-p-nitrophenyl ester by the enzyme, resulting in the formation of yellow p-nitrophenol. One katal was defined as the amount of enzyme activity that catalyzes the formation of one mole of p-nitrophenol [19]. Catalase activity was measured photometrically at a wavelength of 410 nm. The method is based on the ability of ammonium molybdate to form a yellow-colored complex upon reaction with hydrogen peroxide. One unit of catalase activity was defined as the amount of enzyme that catalyzes the decomposition of one mole of hydrogen peroxide [19].

The concentration of malondialdehyde (MDA) in oral fluid was determined photometrically at a wavelength of 530 nm using the thiobarbituric acid method [19]. Lysozyme activity in oral fluid was measured spectrophotometrically at a wavelength of 540 nm (after 15 and 180 minutes) using the indicator culture Micrococcus lysodeikticus ATCC 4698 [20]. Urease activity was determined based on the enzymatic breakdown of urea into ammonia, which reacts with Nessler’s reagent, producing a yellow color. Urease activity was expressed in micromoles of ammonia formed per minute per liter of oral fluid. Optical density was measured using an SF-56 spectrophotometer. The degree of dysbiosis (DD) was calculated as the ratio of specific urease activity to specific lysozyme activity [20].

Biochemical analyses were performed at the “Molecular Biology” Core Facility of the Central Research Laboratory at the Order of the Red Banner of Labour Medical Institute named after S. I. Georgievsky. During statistical analysis, the arithmetic mean, standard error, median (Me), and lower (Q1) and upper (Q3) quartiles were calculated. Statistical analysis included assessment of data distribution using graphical methods (histograms and comparison with a theoretical normal distribution curve), as well as evaluation of skewness and kurtosis. In addition, the one-sample Kolmogorov–Smirnov test was used to test the hypothesis that the data could be approximated by a normal distribution. Based on graphical analysis, parametric statistical methods were considered appropriate in most cases, which justified the use of confidence intervals and Student’s t-test. However, given the relatively small sample sizes, non-parametric methods were also applied to assess differences between groups. The Mann–Whitney U test was used as a non-parametric alternative to the independent samples t-test. Z values, asymptotic two-sided significance, and exact significance values were calculated. The two-sample Kolmogorov–Smirnov test was also used to assess differences in distribution shape. For small samples ($n \leq 30$), exact p-values were used instead of asymptotic ones. The level of statistical significance was set at $\alpha = 0.05$. Differences between groups were assessed using Student’s t-test for normally distributed data with equal variances. When these assumptions were not met, the Mann–Whitney U test was applied. Statistical analysis was performed using Microsoft Excel 2024 (Microsoft, USA). Further statistical processing was carried out using the R statistical computing environment. The packages stats, ctest, FactoMineR, and others were used. R is a free and open-source software environment for statistical computing developed under the GNU Project.

RESULTS

The analysis of medical documentation revealed significant differences in the Infectious Index (II) and Resistance Index (RI) between the groups: the II in the study group was 1.23±0.04, compared to 0.29±0.02 in the control group ($p<0.001$); the RI was 0.61±0.02 and 0.15±0.018 ($p<0.001$), respectively. The clinical examination identified a large number of filled and decayed primary teeth in 50 (96.15%) children with RRIs. The dmf index was 5.9±0.45, and dmfs was 6.3±0.56 ($p<0.001$). Additionally, carious lesions in the fissures and cervical areas of the first permanent molars were frequently diagnosed. The DMF index was 1.25±0.03, and DMFS was 1.45±0.02 ($p<0.001$).

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The prevalence of dental caries in primary teeth among children in the control group was 82.8% (29 individuals), with lower caries intensity indices (dmf was 3.35±0.41, dmfs – 3.51±0.45). The intensity of caries in permanent teeth, according to the indices, was as follows: DMF – 0.43±0.11, DMFS – 0.51±0.13. Chronic catarrhal gingivitis was diagnosed in 46 children with RRIs (88.5% of cases), compared with 13 individuals (37.1%) in the control group. Significant differences were observed in the indices characterizing periodontal status. In the main group, the PMA index reached 22.9±1.6% ($p<0.001$), and the bleeding index was 0.19±0.03 points ($p<0.05$). Oral hygiene indices in children with RRIs were significantly worse than in the control group, with the Silness–Löe index being 1.9±0.08 points ($p<0.001$) and the K. Stallard index being 2.05±0.08 points ($p<0.01$). Based on the clinical examination results, the Dental Health Level (DHL) in children with RRIs was reduced to 66.7% (compared with 84.6% in the control group). The reduction in DHL in this group was primarily associated with a high intensity of untreated caries and a large number of primary teeth affected by complicated caries. The results of the biochemical analysis of oral fluid in children with RRIs are summarized in Table 1.

Table 1. Biochemical parameters of oral fluid in children with recurrent respiratory infections (Me (Q1; Q3))

Indicator	Study group n=31	Control group n=21	Significance of differences between groups
Catalase, mkat/L	0,101 [0,092; 0,111]	0,255 [0,221; 0,261]	p=0.000076*
MDA, mmol/L	0,45 [0,40; 0,52]	0,17 [0,13; 0,20]	p=0.002438*
Lysozyme, units/L	51,4 [47,3; 57,3]	76,2 [7,7; 85,4]	p=0.008614*
Urease, μkat/L	0,850 [0,742; 0,912]	0,206 [0,172; 0,219]	p=0.000001*
Elastase, μkat/L	2,45 [1,87; 3,10]	2,19 [1,72; 2,34]	p=0.597439

**Statistically significant differences at $p<0.05$*

Catalase activity in the oral fluid of children with RRIs was significantly lower than in the control group ($p<0.001$). A statistically significant increase in malondialdehyde (MDA) concentration was observed in children of the main group compared with controls ($p<0.001$), indicating the development of oxidative stress and a reduced capacity of the antioxidant system to counteract lipid peroxidation.

In the oral fluid of children with RRIs, urease activity- a marker of microbial load-was increased,

on average four times higher than in healthy peers, suggesting enhanced colonization of the oral cavity by opportunistic and pathogenic microorganisms. At the same time, a 1.5-fold decrease ($p<0.001$) in lysozyme concentration was observed, indicating weakening of local antimicrobial defense mechanisms.

The disruption of the oral microbiota profile in the main group was further confirmed by an increase in the dysbiosis degree (DD) index to 2.95, which was approximately two times higher than in the control group (DD = 1.44) and 2.9 times higher than the reference “normal” value of 1. Against this background, increased elastase activity, a marker of inflammation, was detected in the main group. It should be noted that even in the control group, elastase levels in oral fluid exceeded normative values, which may be explained by the presence of mild inflammatory changes in gingival tissues associated with suboptimal oral hygiene, including edema, hyperemia, and bleeding.

Children with RRIs exhibited disturbances in the acid–base balance of the oral cavity. The confidence interval of hydrogen ion fluctuations (ΔpH) in mixed saliva was 1.9 times higher than in the control group, amounting to 0.27±0.02 ($p<0.001$). A stable pH of oral fluid is a crucial component of oral homeostasis. Its disturbance in children with RRIs represents a risk factor for dental caries in permanent teeth and gingivitis.

DISCUSSION

We set out to test the hypothesis that preschool children with recurrent respiratory tract infections (RRIs) have a deterioration in oral health status and in local protective mechanisms. The results of our study revealed higher levels of dental caries in both primary and permanent teeth in these children compared with their healthy peers. These findings are consistent with those of other authors who have shown that children with RRIs are more susceptible to dental caries than generally healthy individuals[9,21].

Kaskova L.F. and co-authors associate this with the development of a cariogenic situation in the oral cavity, including a reduction in the structural and functional resistance of enamel, poor oral hygiene, and disturbances in the composition and properties of oral fluid[10, 22].

Information on the direct correlation between early childhood caries and the frequency of acute upper respiratory tract infections across different age groups is of significant importance for public health practice [13, 14, 15]. Therefore, the relationship between RRIs and the condition of the oral cavity appears to be bidirectional.

Frequent episodes of acute respiratory infections alter the structure of the oral microbiocenosis [8]. During acute respiratory diseases, there is a reduction in the relative abundance of microorganisms typical for this ecological niche, alongside an increase in opportunistic flora (such as Staphylococcus aureus, β-hemolytic streptococci, and others) and colonization by microorganisms not typical for the oral cavity [23].

As a result of frequent respiratory infections, local immunity is suppressed, which contributes to the development of oral dysbiosis [5,6]. Continuous antigenic stimulation and inflammatory processes lead to changes in the composition and properties of saliva. A decrease in the levels of lysozyme, lactoferrin, and specific antibodies (sIgA) in oral fluid during respiratory illness weakens the control over pathogenic microorganisms, allowing them to dominate the biotope. A reduction in the anti-adhesive activity of saliva in adolescents with RRIs, even during periods of clinical well-being, has been demonstrated in the study by Generalova E.V. (2023) [24]. It is known that the anti-adhesive properties of saliva integrally reflect the function of key components of local defense, such as secretory immunoglobulin A, lysozyme, lactoferrin, and others. Our study demonstrated suppression of lysozyme activity and increased urease activity in mixed saliva in children with RRIs.

Acute respiratory infections are also the main reason for prescribing antibiotics and anti-inflammatory drugs [25]. These medications negatively affect oral fluid homeostasis and microbial balance. Their frequent use leads to the elimination of beneficial commensals such as *Streptococcus salivarius* and creates ecological niches for the growth of opportunistic fungi (for example, species of the genus *Candida*) and Gram-negative bacteria. For instance, it has been shown that children with RRIs exhibit a significant increase in the adhesion index of *Candida albicans* to a single buccal epithelial cell. A correlation was observed between microbiota composition, the activity of the inflammatory process in the oral and gastrointestinal mucosa, and the severity of tissue involvement [7]. Dysbiosis of the oral microbiome increases colonization of the oral cavity by opportunistic and pathogenic microorganisms, which may subsequently enter the upper and lower respiratory tract, leading to respiratory diseases. In turn, these diseases may further destabilize the oral microbiota balance. This creates a vicious cycle that contributes to the deterioration of both oral and respiratory health [26].

An imbalance in the oral and nasopharyngeal microecology leads to the development of oxidative stress and inflammation. In our study, this was confirmed by increased lipid peroxidation (as indicated by malondialdehyde levels), increased activity of the proteolytic enzyme elastase, and decreased activity of the antioxidant enzyme catalase.

However, when interpreting the results of this study, several limitations should be considered. The relatively small sample size and single-center design may limit the generalizability of the findings. In addition, potentially important influencing factors were not assessed, including dietary habits, oral hygiene practices, fluoride exposure, and prior antibiotic use. Future multicenter longitudinal studies with larger sample sizes are needed to confirm these findings and further clarify the relationship between recurrent respiratory infections and oral health status in children.

CONCLUSION

A low level of oral health (66.7%) was identified in children with RRIs. The high prevalence and intensity of dental caries, together with the severity of gingival inflammation and weakened local nonspecific defense factors, highlight the need for the development of targeted therapeutic and preventive measures aimed at improving oral health.

Authors' Contributions

All authors contributed substantially to the work presented and gave final approval of the version for publication. Kolesnik K.A.: Conceptualization, Methodology, Writing—review and editing. Romanenko I.G.: Supervision. Dzhemileva L.E.: Investigation, Writing—original draft. Severinova S.K.: Investigation. Sadikov A.R.: Investigation, Formal analysis.

DECLARATIONS

Conflict of Interest
The authors declare no conflict of interest.
Funding
No external funding was received for this study.
Ethical approval
The study was reviewed and approved by University Ethical Committee (and in accordance with those of the World Medical Association and the Helsinki Declaration.
Consent for publication
Patients were informed verbally and in writing about the study and gave written informed consent.

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