Prevalence and intensity of dental caries in adolescents with juvenile idiopathic arthritis

Dmytro Komarov[1], Nataliia Savelieva[2]

[1] Phd student, Department of dentistry ESIPE, Kharkiv national medical university, Kharkiv, Ukraine

[2] Professor of the Department of dentistry ESIPE, Kharkiv national medical university, Kharkiv, Ukraine

Address for correspondence:

Dmytro Komarov

E-mail: dr.dmytrokomarov@gmail.com

Abstract: One of the central problems of modern dentistry is the analysis of the impact of juvenile idiopathic arthritis (JIA) - the most widespread heterogeneous rheumatic disease in pediatrics on a child's dental health. The prevalence of JIA in Ukraine is 0,37 cases per 1000 children under 17 years of age with a tendency to increase. JIA is a collective term that combines various forms of arthritis of unknown etiology, which debut in children under 16 and lasts for more than 6 weeks. The central idea in JIA management is that treatment, timeliness, and adequacy determine the disease's prognosis and the child's further development. The primary principles in the treatment of JIA manifestations remain the principles of basic therapy of the disease, necessarily with the use of disease-modifying antirheumatic drugs. Taking into account the negative dynamics of the incidence of JIA and scientific data about the impact of the disease on the condition of hard dental tissues, conducting research in this area is of particular scientific interest to us. This study aims to determine the prevalence and intensity of the carious process in adolescents suffering from JIA, taking into account the subtypes of rheumatological disease and the possible negative impact of basic drug therapy. As part of the study, a dental examination of 80 adolescent children suffering from JIA was conducted. The control group consisted of 20 healthy adolescents. By the study design, the study participants were divided primarily by the presence of JIA; the second division was based on the presence of a specific subtype of JIA in the study participants: groups with polyarticular rheumatoid factor positive (RF+) (n=29), oligoarticular (n=24), enthesitis-associated (n=12), polyarticular RF- (n=10), undifferentiated (n=5) variants of JIA and a control group (n=20). Another division of the study participants took place according to the basic medical support: groups of patients taking methotrexate at a dose of less than or equal to 15 mg (n=43) and greater than 15 mg (n=18), a group of patients receiving adalimumab (n=20) and a control group (n=20). An examination of the oral cavity, recording of the dental formula and determination of the prevalence and intensity of the carious process in the studied groups depending on the presence of JIA, basic medical support and subtype of the disease were performed. Statistical analysis of the data was performed using the STATISTICA 10.0 program. It was noted that patients with JIA have a 1,6-fold higher intensity of dental caries compared to children without JIA (p= 0,004). Analysis of the structure of the DMF+df index allows us to state that patients with JIA have carious lesions of permanent teeth on average 2 times more often compared to the control group (p= 0,004). Analysis of the effect of basic drug therapy on the caries intensity in general and separately on each

structural component of the DMF+df index showed that patients taking methotrexate at a dose of less than or equal to 15 mg have an average caries intensity of 1,25 times higher compared to patients who take adalimumab, and a 2-fold higher intensity of the carious process compared to children without general somatic pathology (p = 0,0096 and p = 0,0008, respectively). The study also showed that patients taking methotrexate at a dose of less than or equal to 15 mg have an average of 3 times higher frequency of carious lesions of permanent teeth (p = 0,0016). The analysis of the influence of the JIA subtype on the intensity of the carious process showed that patients with RF-negative polyarticular and oligoarticular variants of JIA have, on average, twice the intensity of caries compared to the control group (p = 0,0032 and p = 0,0065, respectively). In contrast, the JIA subtype does not affect the structure of caries incidence in adolescents.

Keywords: Adolescent, Dental Caries, Prevalence, Arthritis, Juvenile.

Introduction

Juvenile idiopathic arthritis (JIA) is "arthritis of unknown etiology that begins before the age of 16 and lasts at least 6 weeks and other known conditions are excluded" [1,2]. According to official statistics, the prevalence of JIA in Ukraine is 0,37 cases per 1000 people and there is a fairly pronounced tendency for its increase [3].

According to scientific research, JIA is considered the main rheumatological disease of childhood that leads to short-term and long-term disability [4]. The central place in the problem of JIA is occupied by the issue of treatment, the timeliness and adequacy of which determines the prognosis of the disease and, probably, the further life of the child [5].

The main goal of JIA treatment is to achieve clinical remission [6]. The main goal of treatment is to control the activity of JIA [7]. Until the time goal is achieved, drug therapy should be changed at least every 3 months [6].

The primary treatment for JIA manifestations today remains the principles of basic therapy of the disease, which include disease-modifying antirheumatic drugs [8].

The main dilemma of JIA treatment is that, on the one hand, the lack of drug support for patients with this disease leads to impaired growth and development of the child's body (Garner AJ et al.) [9], and on the other hand, the use of disease-modifying antirheumatic drugs, as the authors indicate, can cause serious side effects [10].

Analysis of the results of scientific studies related to the investigation of caries in patients with JIA showed rather ambiguous results. Thus,

Pylypyuk O.Yu. in her PhD thesis states that children with JIA have 2-3 times higher intensity of caries compared with healthy individuals. She also notes that patients with JIA demonstrate a tendency to the prevalence of decompensated forms of caries in the structure of dental morbidity as opposed to compensated ones in the control group [11].

Similar results were obtained by Welbury, R. et al. Thus, they emphasized the increase in the frequency of caries in all age groups of children with JIA compared to children in the control group [12].

Savioli, C. et al., studying this problem in Brazil, also noted a difference in the DMF index in children with JIA, that correlates with the tendencies cited above [13].

At the same time, Gil E. et al., analyzing the prevalence of caries in children with JIA living in Norway, compared to the control group, did not find any differences in the prevalence of this dental disease. At the same time, they did not reject the hypothesis of the presence of potential correlations between the indicators characterizing JIA and the activity of caries [14]. Taking into account the negative dynamics of the incidence of JIA, the lack and certain controversy of data in the literature on the impact of the disease on the condition of hard dental tissues (Walton A.G. et al.) [15], conducting research in this area is of particular scientific interest to us.

Aim

To determine the prevalence and intensity of caries in adolescents with JIA, taking into account the subtypes of the rheumatological

disease and the possible negative impact of basic drug therapy.

Materials and methods

The study, which was conducted at the Department of Cardiorheumatology of the State Institution "Institute of Child and Adolescent Health Care, AMS of Ukraine", involved 80 children aged 10 to 17 years with a diagnosis of JIA, verified by a pediatric rheumatologist. Patients received treatment according to the guidelines of medical care for children in the specialty "Pediatric Cardiorheumatology". The control group consisted of 20 adolescents aged 10 to 17 years without concomitant general somatic pathology. Before being involved in the study, informed consents were signed by the participants and their parents or caregivers. The research protocol was developed in accordance with The Declaration of Helsinki (2013) principles and was approved by the Ethics and Bioethics Commission of Kharkiv National Medical University on October 12, 2022 (protocol № 2). All participants in the experiment underwent a basic dental examination and a dental formula record. To determine the intensity of the carious process during the period of alternating occlusion, the index DMF+df, permanent- DMF (where d- decayed temporary tooth, f- filled temporary tooth, D- carious lesion of a permanent tooth, F- filled permanent tooth, M- missed permanent tooth) was used. Prevalence of caries in children with JIA and the control group was calculated as the percentage of people with carious, filled and extracted teeth from the total number of respondents in the group.

According to the study design, the distribution of participants occurred three times. Firstly, patients were divided according to the presence (n = 80) or absence (n = 20) of JIA. Within the next division, 4 groups were created according to the basic therapy of JIA: patients with JIA receiving methotrexate (MTX) at a dosage of less than or equal to 15 mg (n = 43), patients with JIA receiving MTX at a dosage of more than 15 mg (n = 18), patients with JIA receiving MTX and adalimumab (n = 19) and the control group (n = 20). The third distribution was based on the presence of a certain subtype of JIA in the patient: patients with polyarthritis

rheumatoid factor positive (RF+) (n = 29), polyarthritis RF- (n = 10), enthesitis-related (n = 12), undifferentiated (n = 5), oligoarthritis (n = 24) variants of JIA and the control group (n = 20). In each of the distributions, the groups were comparable in age and sex.

Statistical analysis was performed using the STATISTICA 10.0 program. Shapiro-Wilk normality test (W test) was used to analyze the distribution of quantitative characteristics in each group. For samples with non-normal distribution, the values of the median (Me), upper and lower quartiles Me (Lq; Uq) were indicated. Taking into account a non-normal distribution of data, the Mann-Whitney U-test (UMV) was used to test the significance of the differences in the mean values of independent groups in the case of pairwise comparisons, and with three or more comparisons, the Kruskal-Wallis H-test with posterior comparisons by UMV was used. To assess the statistical significance of the differences in relative indicators Pearson's chi-square test was used taking into account the fact that when the expected phenomenon took a value from 5 to 9, the Yates correction was used. When comparing relative indicators, the Fisher exact test was used. A $p<0,05$ value was considered statistically significant; for multiple comparisons of quantitative characteristics, the Holm-Bonferroni and Benjamini-Hochberg methods were used.

Results

Analyzing the prevalence of caries in this study, we found that in the group of children with JIA out of 80 adolescents, only 6 people did not have signs of carious lesions of the teeth (92,5%), and in the control group, among the 20 examined, only two did not have carious disease (90%). Thus, both groups demonstrate quite similar indicators, which may be interpreted as a high prevalence of caries. The Fisher exact test ($p = 0,659$) indicates the impossibility of rejecting the null hypothesis, i.e., there is no statistically significant difference in the prevalence of caries between the JIA and control groups in this study.

Having analyzed the intensity of the caries process in the group of children with JIA, we found that the median value is 4,0 with an

interquartile range from 2,0 to 6,0. The intensity of caries in the control group was 2,5 (1,0;4,0), respectively. Further analysis of the data set using UMV showed a statistically significant difference in the data obtained (p = 0,004), and therefore we can state that patients with JIA in this study had an average of 1,6 times higher intensity of the carious process compared to children without somatic pathology (Table 1). Analysis of the structure of the intensity of the carious process in the above groups did not reveal statistically significant differences in the components "d", "f", "F", and "M", however, the intensity of carious lesions of permanent teeth was 2 times higher in the group of adolescents with JIA compared to those somatically healthy with p = 0,004 (Table 2). In general, we see that adolescents of both groups have carious lesions and dental fillings mainly in permanent teeth, and therefore it is necessary to carry out effective prevention of diseases of the hard tissues of permanent teeth.

As a next step, the impact of basic JIA therapy on the intensity of the caries was assessed. Kruskal-Wallis test was performed (H (3, N = 100) = 14,45, p = 0,002) to indicate the presence of significant differences between the compared groups. Then pairwise comparisons were made between groups using a posterior UMV with a level of statistical significance adjusted according to the Holm-Bonferroni method. It was found that patients receiving MTX at a dosage of less than or equal to 15 mg had a 1,25-fold higher intensity of the carious process compared to patients receiving adalimumab, and a 2-fold higher intensity of the carious process compared to the control group, and the above differences are statistically significant (Table 3). The analysis of the structure of the DMF+df index depending on the type of basic medication did not reveal statistically significant differences in the components "d", "f", "F", "M", however, the Kruskal-Wallis test (H (3, N=100)= 13,51, p= 0,004) showed the presence of significant differences in the component of carious lesions of permanent teeth. A series of posterior pairwise comparisons with the level of statistical significance adjusted according to the Holm-Bonferroni method allows us to conclude that in this study, patients receiving MTX at a dosage of less than or equal to 15 mg were three times more likely than children in the control group to have carious lesions of permanent teeth (p=0,0016) (Table 4).

As the next step, the analysis of the influence of JIA subtypes on the intensity of caries was performed. The Kruskal-Wallis test showed the result H (5, N=100) = 11,03, p = 0,049, which indicates the presence of significant differences in the compared groups. A series of pairwise posterior comparisons using UMV with the level of statistical significance adjusted according to the Benjamini-Hochberg method allows us to state that patients with RF-negative polyarticular and oligoarticular variants of JIA have on average twice the intensity of the caries process compared to that in healthy children of the control group (Table 5). The analysis of the DMF+df index did not reveal statistically significant differences between the groups, which allows us to conclude

Table 1. Prevalence and intensity of the carious process in children with JIA and the control group

	Patients with JIA (n=80)	Controls (n=20)	p
Prevalence of caries	92,5 %	90 %	p= 0,659
Intensity of caries	4,0 (2,0;6,0)	2,5 (1,0;4,0)	p UMV=0,004

Table 2. Structure of caries intensity in adolescents with JIA and controls

	d	f	D	F	M
Patients with JIA (n=80)	0 (0;0)	0 (0;0)	2 (1;4)	0 (0;2)	0 (0;0)
Controls (n=20)	0 (0;0)	0 (0;0)	1(0;1)	0 (0;2)	0 (0;0)
p UMV	0,42	0,96	0,004	0,66	0,80

Table 3. Intensity of the carious process in JIA patients dependent on medication

	JIA patients, taking MTX ≤15 mg (n=43)	**JIA patients, taking MTX >15 mg (n=18)**	**JIA patients, taking MTX+adalimumab (n=19)**	**Controls (n=20)**
Caries intensity	5,0 (3,0;8,0)	4,0 (2,0;6,0)	4,0 (2,0;5,0)	2,5 (1,0;4,0)

$p_{MTX \leq 15mg – MTX > 15mg} = 0,198$; $p_{MTX \leq 15mg – adalimumab} = 0,0096^*$;

$p_{MTX \leq 15mg – controls} = 0,0008^*$; $p_{MTX > 15mg – adalimumab} = 0,256$;

$p_{MTX>15mg – controls} = 0,049$; $_{adalimumab – controls} = 0,243$

* – statistically significant p value corrected using Holm-Bonferroni method

Table 4. Structure of caries intensity in adolescents with JIA dependent on medication

	d	**f**	**D**	**F**	**M**
JIA patients, taking MTX ≤15 mg (n=43)	0 (0;0)	0 (0;0)	3(1;5)	1 (0;2)	0 (0;0)
JIA patients, taking MTX >15 mg (n=18)	0 (0;0)	0 (0;0)	2(1;4)	1 (0;2)	0 (0;0)
JIA patients, taking MTX+adalimumab (n=19)	0 (0;1)	0 (0;0)	1(0;3)	0 (0;1)	0 (0;0)
Controls (n=20)	0 (0;0)	0 (0;0)	1(0;1)	0 (0;2)	0 (0;0)
Kruskal-Wallis test	H (3, N=100) = 2,17, p= 0,54	H (3, N=100) = 0,58, p= 0,89	H (3, N=100) = 13,51, p= 0,004	H (3, N=100) = 1,77, p= 0,62	H (3, N=100) = 1,68, p= 0,64

$p_{MTX \leq 15mg – MTX > 15mg} = 0,50$; $p_{MTX \leq 15mg – adalimumab} = 0,025$;

$p_{MTX \leq 15mg – controls} = 0,0016^*$; $p_{MTX > 15mg – adalimumab} = 0,118$;

$p_{MTX>15mg – controls} = 0,126$; $p_{adalimumab – controls} = 0,204$

*– statistically significant p value corrected using Holm-Bonferroni method

Table 5. Intensity of the carious process in JIA patients dependent on disease subtype

	JIA polyarthritis RF+ (n=29)	**JIA polyarthritis RF- (n=10)**	**JIA enthesitis-related (n=12)**	**JIA undifferentiated (n=5)**	**JIA oligoarthritis (n=24)**	**Controls (n=20)**
Caries intensity	4,0 (2,0;6,0)	5,0 (4,0;5,0)	5,0 (3,0;7,5)	5,0 (4,0;5,0)	5,0 (3,0;6,5)	2,5 (1,0;4,0)

$p_{poly RF+ -poly RF-} = 0,26$; $p_{poly RF+ – enth-rel} = 0,31$; $p_{poly RF+ – undif} = 0,44$;

$p_{poly RF+ – oligo} = 0,24$; $p_{poly RF+ – controls} = 0,16$; $p_{poly RF- – enth-rel} = 0,59$;

$p_{poly RF- undif} = 0,95$; $p_{poly RF- – oligo} = 0,60$; $p_{poly RF- – controls} = 0,0032^*$;

$p_{enth-rel – undif} = 0,95$; $p_{enth-rel – oligo} = 0,76$; $p_{enth-rel – controls} = 0,02$;

$p_{undif – oligo} = 1,0$; $_{undif – controls} = 0,08$; $p_{oligo – controls} = 0,0065^*$

*– statistically significant p value corrected using Benjamini-Hochberg method

that the JIA subtype has no influence on the structure of caries intensity in adolescents in this research (Table 6).

The results obtained in this research correlate with those reported by Gil E. et al. [14], and we also did not find a statistically significant difference in the prevalence of caries between children with JIA and those without comorbidity. Also, our analysis allows us to distinguish the disease subtype and its basic medical support

Table 6. Structure of caries intensity in adolescents with JIA dependent on disease subtype

	d	f	D	F	M
JIA polyarthritis RF+ (n=29)	0 (0;0)	0 (0;0)	2,0 (1,0;4,0)	1,0 (0;1,0)	0 (0;0)
JIA polyarthritis RF- (n=10)	0 (0;0)	0 (0;0)	3,0 (2,0;4,0)	0 (0;1,0)	0 (0;0)
JIA enthesitis-related (n=12)	0 (0;0,5)	0 (0;0,5)	2,0 (0;5,0)	2,0 (0;2,0)	0 (0;0)
JIA undifferentiated (n=5)	0 (0;0)	0 (0;0)	1,0 (1,0;2,0)	3,0 (0;3,0)	0 (0;0)
JIA oligoarthritis (n=24)	0 (0;1,5)	0 (0;0,5)	2,5 (0;3,0)	0 (0;1,0)	0 (0;0)
Controls (n=20)	0 (0;0)	0 (0;0)	1(0;1)	0 (0;2)	0 (0;0)
Kruskal- Wallis test	H (5, N=100) = 10,23, p= 0,07	H (5, N=100) = 3,57, p= 0,61	H (5, N=100) = 10,72, p= 0,06	H (5, N=100) = 6,39, p= 0,27	H (5, N=100) = 2,6, p= 0,75

as specific factors that influence the course of caries. Also, our results correlate with those obtained by a Ukrainian researcher [11] in the context of the presence of differences in the intensity of caries between the studied groups, which in our opinion, can serve as a basis for the development and implementation of a rational program for the prevention of dental diseases in adolescents with JIA.

We believe that further large-scale multicenter clinical studies aimed at studying the impact of juvenile idiopathic arthritis on the condition of dental hard tissues are warranted. Such studies, in particular, using a larger sample of patients and standardized assessment methods, will allow us to more objectively confirm our conclusions and expand our scientific understanding of the relationship between systemic rheumatic diseases and dental health.

Conclusions

The data obtained during the study indicate that the basic therapy and the subtype of JIA have an impact on the caries intensity and the structure of the DMF+df index in the caries of permanent teeth component.

We see further prospects for the study in conducting multicenter prospective studies that will be concerned with the search for correlations between JIA-specific disease factors and caries disease, which will contribute to increasing the effectiveness of prevention programs and providing high-quality dental care to this group of patients.

Author Contributions (CRediT taxonomy)

1. Conceptualization: Komarov Dmytro (ORCID: 0000-0003-2364-1962); Savelieva Nataliia (ORCID: 0000-0002-9670-0997);

2. Methodology: Komarov Dmytro; Savelieva Nataliia ;

3. Validation: Komarov Dmytro;

4. Formal Analysis: Komarov Dmytro;

5. Investigation: Komarov Dmytro;

6. Resources: Komarov Dmytro;

7. Data Curation: Komarov Dmytro;

8. Writing – Original Draft Preparation: Komarov Dmytro;

9. Writing – Review & Editing: Komarov Dmytro; Savelieva Nataliia;

10. Visualization: Komarov Dmytro;
11. Supervision: Savelieva Nataliia;
12. Project Administration: Komarov Dmytro; Savelieva Nataliia;

All authors have read and approved the final version of the manuscript.

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Поширеність та інтенсивність каріозного процесу у дітей підліткового віку, які хворіють на ювенільний ідіопатичний артрит

Дмитро Комаров[1], Наталія Савєльєва[2]

[1] Аспірант кафедри стоматології Навчально-наукового інституту післядипломної освіти, Харківський національний медичний університет, м. Харків, Україна

[2] Професор кафедри стоматології Навчально-наукового інституту післядипломної освіти, Харківський національний медичний університет, м. Харків, Україна

Address for correspondence:
Dmytro Komarov

E-mail: dr.dmytrokomarov@gmail.com

Анотація: однією з центральних проблем сучасної стоматології є вивчення впливу на стоматологічне здоров'я дитини ювенільного ідіопатичного артриту (ЮІА) – найбільш поширеного гетерогенного хронічного ревматичного захворювання у педіатрії. Поширеність ЮІА в Україні становить 0,37 випадки на 1000 дітей віком до 17 років з тенденцією до зростання. ЮІА – збірне поняття, що об'єднує різні форми артритів невідомої етіології, які дебютують у дітей до 16 років і тривають понад 6 тижнів. Центральне місце у проблемі ЮІА займають питання лікування, від своєчасності та адекватності якого залежить прогноз захворювання і, напевне, подальша доля дитини. Первинним у лікуванні проявів ЮІА залишаються принципи базисної терапії захворювання неодмінно із застосуванням хворобомодифікуючих протиревматичних препаратів. Зважаючи на негативну динаміку захворюваності на ЮІА та обмаль даних в літературі щодо впливу захворювання на стан твердих тканин зубів, проведення досліджень в цьому напрямку представляє для нас особливий науковий інтерес. Метою даного дослідження є визначенняпоширеностііаінтенсивностікаріозногопроцесувдітейіпідліткового віку, які хворіють на ЮІА з урахуванням субтипів ревматологічного захворювання та можливого негативного впливу медикаментозної базової терапії. В рамках виконання дослідження проведене стоматологічне обстеження 80 дітей підліткового віку, які хворіють на ЮІА. Група контролю складалась з 20 соматично здорових підлітків. Згідно з дизайном дослідження було проведено розподіл учасників дослідження в першу чергу за наявністю у них ЮІА; другий розподіл базувався на наявності у учасників дослідження певного субтипу ЮІА: групи пацієнтів з поліартикулярним позитивним за ревматоїдним фактором (РФ+) (n=29), олігоартікулярним(n=24), ентезит-асоційованим (n=12), поліартикулярним РФ- (n=10), недиференційованим (n=5), варіантами ЮІА та група контролю (n=20). Ще один розподіл учасників дослідження відбувся відповідно до базового медикаментозного супроводу: групи пацієнтів, які приймають метотрексат у дозуванні менше чи рівному 15 мг (n=43) та більшому за 15 мг (n=18), група пацієнтів, яка прходить лікування адалімумабом (n=20), та контрольна група (n=20); Було проведено: огляд ротової порожнини, запис зубної формули, визначення показників поширеності та інтенсивності каріозного процесу в досліджуваних групах в залежності від наявності ЮІА, базового медикаментозного супроводу та субтипу захворювання. Статистична обробка масиву отриманих даних проведена з використанням програми STATISTICA 10.0. Визначено, що пацієнти з ЮІА мають у 1,6 разів вищу інтенсивність каріозного процесу в порівнянні з дітьми без ЮІА (р= 0,004). Аналіз структури індексу КПВ+кп дозволяє стверджувати, що пацієнти з ЮІА мають каріозні ураження постійних зубів в середньому в 2 рази частіше в порівнянні з контрольною групою (р=0,004). Аналіз впливу базової медикаментозної терапії на показник інтенсивності карієсу та окремо на кожен структурний компонент індексу КПВ+кп показав, що пацієнти, які отримують метотрексат у дозуванні менше чи рівному 15 мг мають інтенсивність карієсу в середньому в 1, 25 разів вищу в порівнянні із пацієнтами, які отримують адалімумаб, і у 2 рази більшу інтенсивність каріозного процесу в порівнянні з дітьми без загальносоматичної патології (р=0,0096 та р=0,0008 відповідно). В дослідженні також продемонстровано, що пацієнти, які отримують метотрексат у дозуванні менше чи рівному 15 мг, мають в середньому в 3 рази більшу частоту каріозного ураження постійних зубів (р=0,0016). Проведений аналіз впливу субтипу ЮІА на показник інтенсивності каріозного процесу показав, що пацієнти з РФ-негативним поліартикулярним та олігоартикулярним варіантами ЮІА мають в середньому у два рази більшу інтенсивність карієсу в порівнянні з групою контролю (р=0,0032 та р=0,0065 відповідно), в той же час субтип ЮІА жодним чином не впливає на структуру захворюваності на карієс у дітей підліткового віку.

Ключові слова: підлітки, зубний карієс, поширеність, артрит ювенільний.