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How Vitamin D Levels of Children Changed During COVID-19 Pandemic: A Comparison of Pre-pandemic and Pandemic Periods

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What is already known on this topic?

Vitamin D has immunomodulatory effects and this has effects on infections, including Coronavirus disease-2019 (COVID-19). Vitamin D deficiency has been reported to be associated with clinical severity in COVID-19 disease, in both adults and children.

What this study adds?

Vitamin D levels of healthy children (>6 years old) and adolescents decreased in the first year of the pandemic due to the pandemic-related restrictions.

Abstract

Objective: The synthesis of vitamin D is related to sun exposure, thus the restrictions during the Coronavirus disease-2019 (COVID-19) pandemic may have affected the levels of vitamin D in all age groups. The aim of this study was to evaluate vitamin D levels of healthy children and adolescents during the first year of the pandemic.

Methods: The study group included healthy children and adolescents who were admitted for general check-ups and evaluated with 25(OH)D levels. Then, it was divided into two groups: Group 1 "pre-pandemic", and Group 2 "pandemic". Vitamin D levels were recorded from the hospital database and were compared according to age groups, gender, and the season, retrospectively.

Results: The study group [mean age = 90.29 ± 59.45 median age = 79 interquartile range (IQR): 102 months, male/female: 1409/1624] included 3033 children and adolescents (Group 1/Group 2 n = 1864/1169). Although the mean 25(OH)D levels among preschool children did not differ between groups, the vitamin D levels of school-aged children and adolescents were significantly lower in the pandemic period than in the pre-pandemic period [Group 1 median = 16.50 (IQR: 10.5) vs Group 2 median = 15.9 (IQR: 11.3) in 6-12 age group (p = 0.026); Group 1 median = 13.30 (IQR: 10.2) vs Group 2 median = 11.20 (IQR: 9.7) in 12-18 age group (p = 0.003)]. Moreover, the 25(OH)D levels of adolescents showed seasonal variance with lower levels in winter, and unexpectedly, in summer.

Conclusion: Pandemic-related restrictions have caused significant decreases in vitamin D levels of school-aged children and adolescents. We suggest that children and adolescents should be given vitamin D supplementation in order to maintain sufficient levels of vitamin D during the pandemic.

Keywords: Vitamin D, COVID-19, children, pandemic

Introduction

In recent years, the interest in the extraskeletal effects of vitamin D, especially its immunomodulatory effects, has increased. Moreover, this interest has increased during the pandemic as the association of vitamin D and infections has previously been reported. Meta-analysis of randomized controlled trials has indicated that vitamin D has a protective effect against respiratory tract infections (1). Recently, the possible protective and/or preventive effect of vitamin D against Coronavirus disease-2019 (COVID-19) has also been reported (2,3).

A very recent study from Turkey revealed an association between vitamin D deficiency and clinical severity in

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pediatric COVID-19 cases (4). These authors suggested that prophylactic vitamin D supplementation may be considered in order to prevent deficiencies, especially in the adolescent age group. However, this study reported findings from children infected with COVID-19 and there is a lack of data about how the levels of vitamin D in the general population of children and adolescents changed during the pandemic.

In December 2019, after an epidemic of a new viral infectious disease was firstly reported from China, later identified as COVID-19 disease, the World Health Organization declared a pandemic of global health caused by Severe acute respiratory syndrome-Coronavirus-2 (5). After the disease was shown to spread rapidly in many different ways, but primarily through the respiratory tract, many countries implemented a series of social distancing policies, restricting travel and movement to reduce transmission, requested citizens to stay-at-home, and lockdowns. As the synthesis of vitamin D is directly modulated by sunlight, stay-at-home behavior and/or lockdowns to prevent COVID-19 spreads may have affected vitamin D levels in all age groups-adults, children, and adolescents.

The aim of this study was to determine the vitamin D levels of children and adolescents in the first year of the pandemic and compare the results with a one year period pre-pandemic. In addition, a further aim was to identify possible at risk groups for age, gender, and season that were more likely to be affected by lockdowns in terms of vitamin D levels.

Methods

Study Design and Patients

The study population included 1-18 year-old children who attended the University of Health Sciences Turkey, Dr. Behçet Uz Pediatric Diseases and Surgery Training and Research Hospital, İzmir, Turkey between April 1, 2019, and April 1, 2021, and who were evaluated for vitamin D levels for routine health checks. Infants (<1 year of age) were not included in the study as they are eligible to receive prophylactic vitamin D in Turkey through a national vitamin D supplementation program. Children with a medical history of vitamin D-related metabolic disorders, such as skeletal or gastrointestinal system diseases, liver or kidney diseases, genetic syndromes, obesity, malnutrition, or malabsorption disorders were excluded from the study. Data on the date of birth, gender, hospital visit dates, and 25(OH)D levels available in the Hospital Information System (PROBEL) were obtained retrospectively. Then, patients selected for the study were divided into two groups according to the blood sampling date for the 25(OH)D measurement. Repeated measurements in the same subject were not included in the study. Group 1 included patients admitted in the 'pre-pandemic' period (April 1, 2019-March 31, 2020) while Group 2 included patients admitted in the 'pandemic' (April 1, 2020-April 1, 2021) period. Data of the 25(OH)D levels were compared between Group 1 and Group 2 according to age, gender, and also the season. Groups were divided into three age groups: 1-6 years (13-72 months; toddlers and preschool children); 6-12 years (73-144 months; school-age children); and 12-18 years (adolescents). To evaluate seasonal variability, the pre-pandemic/pandemic periods were divided into spring (March, April, May), summer (June, July, August), autumn (September, October, November), and winter (December, January, February).

Serum 25(OH)D levels were measured by an electrochemiluminescence immunoassay method using a standard kit available on the Abbott Architect System and analyzed using an automated biochemical analyzer, Abbott, I 2000, (Abbott Laboratories, Abbott Park, IL, USA). Serum 25(OH)D levels <12 ng/mL, between 12-20 ng/mL, and levels >20 ng/mL were defined as vitamin D deficiency, insufficiency, and sufficiency, respectively (6).

Lockdown Measures for Pediatric Age During the First Year of the Pandemic

After the global pandemic declaration in December 2019, the first patient with COVID-19 disease was reported on 11 March 2020 in Turkey. Then, on 16 March 2020, the Turkish Ministry of National Education declared the cessation of face-to-face education and offered online education for both elementary, secondary and high schools. In addition, the Government of Turkey announced that all children, adolescents, and young adults (<20 years old) were under curfew on weekdays and for the whole day at weekends (7). The restrictions for <20 year-old citizens continued until June 2020 along with >65 year-old citizens. Table 1 summarizes the opening and closure of schools following the lockdown periods during the study period.

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Ethics Committee of University of Health Sciences Turkey, Dr. Behçet Uz Pediatric Diseases and Surgery Training and Research Hospital, İzmir (protocol no: 554, decision no: 2021/09-02, date: 06.05.2021).

Statistical Analysis

The data were analyzed using the Statistical Package for the Social Sciences, version 21. Categorical data are presented as percentages whereas numerical data with Gaussian distribution are presented as mean ± standard deviation (SD)

and abnormally distributed data are presented as median [interquartile range (IQR)]. The chi-square or Fisher's exact test was used to compare proportions between groups, where appropriate. Student's t-test or Mann-Whitney U test, as appropriate, was used to analyze numerical data between different groups. For correlation analysis, the Spearman rank coefficient was calculated for variables without a normal distribution, and Pearson's linear correlation coefficient was used for variables with a normal distribution. A p value < 0.05 was considered statistically significant.

Results

The study group included 3033 children between 1 year and 18 years old [mean ± SD = 90.29 ± 59.45; median age = 79 (IQR: 102) months] The male to female ratio (M/F) was 1409/1624 with 46.5% of the study population male. Group 1 (pre-pandemic group) consisted of 1864 children [mean ± SD = 91.08 ± 59 months; median = 80 (IQR = 102)] months with a M/F of 856/1008 (45.9% male) while Group 2 (pandemic group) consists of 1169 children [mean ± SD = 89.43 ± 60 months; median = 77 (IQR: 103)] months with a M/F of 616/553 47% male). The main characteristics of the participants are presented in Table 2. The mean serum 25(OH)D level in the study group was 18.69 ± 9.98 ng/mL. The mean serum 25(OH)D level of girls participating in the study was 17.78 ± 10.11 ng/mL and lower than the mean serum 25 (OH) vitamin D level of boys 19.76 ± 9.72 ng/mL ($p < 0.05$).

The rate of vitamin D deficiency [25(OH)D level < 12 ng/mL] and insufficiency (12-20 ng/mL) in the study group was 27.5% (833/3033) and 34.1% (1034/3033), respectively; and the rate of children with sufficient vitamin D levels [25(OH)D level > 20 ng/mL] was only 38.4% (1166/3033). When evaluating the groups in terms of sufficient 25(OH)D vitamin levels in different age groups, the rate of children with adequate levels of vitamin D in preschool children (1-6 years), school-aged children (6-12 years) and adolescents (12-18 years) were 23.7% (n = 718), 10% (n = 302) and 4.8% (n = 146), respectively. Moreover, a negative correlation was found between age (months) and 25(OH)D vitamin level (Group 1, $r = -0.396$ $p < 0.01$; Group 2, $r = -0.504$ $p < 0.01$), respectively.

Group 1 (pre-pandemic group) included 1864 children, 835 (44.8%) of whom were 1-6 years, 578 (31%) were 6-12 years and 451 (24.2%) were 12-18 years old. In Group 2 (pandemic group), there were 1268 children, 561 (48%) of them were 1-6 years while 339 (29%) were 6-12 years and 269 (23%) were 12-18 years old. When evaluated according to gender difference, in Group 1, the median 25(OH)D level of girls was 16.1 (IQR: 11.5) ng/mL and significantly lower than the median 25(OH)D level of boys [18.5 (IQR: 13.2) ng/mL] ($p < 0.01$). In Group 2, the median 25(OH)D level was 15.8 (IQR: 14.1) ng/mL in girls and 17.8 (IQR: 12.8) ng/mL in boys, and the difference was again significant ($p < 0.01$). Table 3 presents the mean values of vitamin D levels according to gender in different age groups.

In the study group, the mean 25(OH)D (ng/mL) levels were similar between groups (18.75 ± 9.76 in Group 1 vs 18.60 ± 10.31 in Group 2) when not accounting for age, gender, and seasonal differences ($p > 0.05$). However, to

Table 1. The periods of open and closed schedules of schools according to the Turkish Ministry of National Education during the study period in İzmir

	Spring	Summer	Autumn	Winter
Kindergarten	Open	Open	Open	Open
Elementary school	All classes closed except 02.03.2021-31.05.2021	All classes closed except 01.06.2021-03.07.2021	All classes closed except 28.09.2020-09.11.2020 1st classes open 01.09.2020-28.09.2020	All classes closed
Secondary school	All classes closed except Only 12. Class 05.04.2021-16.04.2021 26.04.2021-29.04.2021	All classes closed except 14.06.2021-02.07.2021	All classes closed	All classes closed

Table 2. The main characteristics of the study group

	Group 1 (pre-pandemic) (n = 1864)	Group 2 (pandemic) (n = 1169)	p
Age (months) mean ± SD median (IQR)	91.08 ± 59 80 (102)	89.43 ± 60 77 (103)	0.063
Gender (male/female)	856/1008	616/553	0.08
25(OH)D mean ± SD*	18.75 ± 10.4	18.60 ± 10.31	0.69

*ng/mL.
SD: standard deviation, IQR: interquartile range

evaluate the effect of lockdowns and closure of schools, the 25(OH)D levels of the children were compared according to age groups. Our results show that the 25(OH)D levels among toddlers and preschool children (1-6 years) did not differ between groups 1 and 2 [Group 1 median = 19.80 (IQR: 13.2) vs Group 2 median = 21.60 (IQR: 14.3); $p > 0.05$]. However, for school-aged children and adolescents, the levels of 25(OH)D were lower in the pandemic period (Group 2) than in the pre-pandemic period (Group 1). Iin school-aged children (6-12 years) for Group 1 the median value was 16.50 (IQR: 10.5) vs Group 2 with a median of 15.90 (IQR: 11.3; $p = 0.026$). In adolescents (12-18 years old) the Group 1 median value was 13.30 (IQR: 10.2) vs Group 2 with a median of 11.20 (IQR: 9.7; $p = 0.003$) (Table 4).

The deficiency, insufficiency and sufficiency proportions during pre-pandemic and pandemic periods in different age groups are presented in Table 5. In this study population the rate of vitamin D deficiency was significantly higher in the pandemic period than in pre-pandemic period in the adolescent age group (12-18 years) [42.6% in Group 1 vs 53.2% in Group 2]. In addition, the rate of vitamin D insufficiency in the pre-pandemic period (35.9%) was significantly higher than in pandemic period (28.6%) while the rate of vitamin D sufficiency was similar between groups in this age group (21.5% in Group 1 vs 18.5% in Group 2). The rates of the deficiency, insufficiency and sufficiency ratios of vitamin D did not differ significantly during pre-pandemic and pandemic periods in other age groups ($p > 0.05$).

Table 6 presents the seasonal variation of 25(OH)D levels in both groups by age. When the mean 25(OH)D levels of both groups were evaluated by season, no significant difference was determined between the groups in the 1-6 years and 6-12 years age groups in all seasons ($p > 0.05$). However, in the 12-18 age group, the mean 25(OH)D levels in Group 2 were significantly lower during winter and summer than in Group 1. In winter in Group 1 the median value was 10.3 (IQR: 8.3) vs Group 2 with a median of 8.7 (IQR: 6.8) ng/mL ($p = 0.016$) while in summer the mean values were Group 1 19.83 ± 7.12 ng/mL vs Group 2 14.67 ± 6.62 ng/mL ($p = 0.03$).

Discussion

This study examined the effect of the restrictions applied in the pandemic on vitamin D levels in children by taking into account seasonal variability, gender, and age groups. We found that the rate of vitamin D insufficiency and deficiency was high among children during both pre-pandemic and pandemic periods. However, children between 6-12 and 12-18 years old had even lower levels of vitamin D in the pandemic period than in the pre-pandemic period. Thus, they were affected negatively, probably because of the closure of schools and stay-at-home restrictions during the COVID-19 pandemic. In addition, this negative effect showed seasonal variance in adolescents, as the mean levels

Table 3. Vitamin D levels according to gender in different age groups during pre-pandemic and pandemic periods

	Pre-pandemic			Pandemic		
	Girls	**Boys**	**p**	**Girls**	**Boys**	**p**
1-6 years, n (%)	440 (53)	395 (47)		267 (47.5)	294 (52.5)	
25(OH)D ng/mL*	18.9 (12.3)	20.5 (13.4)	0.13	21.1 (14.6)	21.7 (13.9)	0.07
6-12 years, n (%)	313 (54)	265 (46)		179 (52)	160 (48)	
25(OH)D ng/mL*	15.7 (9.4)	17.4 (11.2)	0.013	15.2 (11.6)	16.5 (10)	0.03
12-18 years, n (%)	300 (66)	151 (34)		170 (63)	99 (37)	
25(OH)D ng/mL*	13.9 (10.6)	15.3 (9.6)	0.001	10.1 (8.9)	13.9 (10.6)	0.001
Total, n (%)	1008 (54)	856 (46)		616 (53)	553 (47)	
25(OH)D ng/mL**	16.1 (11.5)	18.5 (13.2)	0.001	15.8 (14.1)	17.8 (12.8)	0.001

*Median (IQR), **mean ± SD.
SD: standard deviation, IQR: interquartile range

Table 4. 25(OH)D levels of the children between groups according to age groups

	Pre-pandemic	Pandemic	p
1-6 years (n)	835	561	0.97
25(OH)D ng/mL*	19.80 (13.2)	21.60 (14.3)	
6-12 years (n)	578	339	**0.026**
25(OH)D ng/mL*	16.50 (10.50)	15.90 (11.3)	
12-18 years (n)	451	269	**0.003**
25(OH)D ng/mL*	13.30 (10.2)	11.20 (9.7)	

*Median (IQR).
IQR: interquartile range

of vitamin D were lower especially during the summer and winter months.

Vitamin D deficiency remains a significant global public health problem despite the availability of supplementation and numerous published guidelines for its prevention (8,9,10,11,12,13). The subject continues to be an important problem both in our country, in Europe, and the World (14,15,16,17,18,19). The results of our study show that the rate of vitamin D deficiency remains around a quarter of healthy children. The rate of vitamin D insufficiency (12-20 ng/mL) and deficiency (< 12 ng/mL) in the study group were found to be 34.1 % and 27.5 %, respectively. The Global Consensus Recommendations on Prevention and Management of Nutritional Rickets have recently reported that vitamin D deficiency is preventable and suggests supplementation and food fortification with vitamin D to prevent deficiency (20). In our country, a free vitamin D supplementation program was initiated by the Ministry of Health in 2005 and free vitamin D drops have been distributed to all newborn babies within the framework of this program, following the recommendations of the Endocrinology and Diabetes Association Bone Health Group (21,22). As all infants in this age group in Turkey are eligible to receive prophylactic vitamin D, regardless of the pandemic, infants < 1 year of age were not included in this study.

Table 5. The deficiency, insufficiency and sufficiency rates of 25(OH)D during pre-pandemic and pandemic periods in different age groups

			Pre-pandemic n (%)	Pandemic n (%)	p
25(OH)D*	1-6 years	< 12	149 (17.8)	98 (17.5)	0.115
		12-20	274 (32.8)	157 (28.0)	
		> 20	412 (49.3)	306 (54.5)	
	6-12 years	< 12	144 (24.9)	107 (31.6)	0.074
		12-20	233 (40.3)	131 (38.6)	
		> 20	201 (34.8)	101 (29.8)	
	12-18 years	< 12	192 (42.6)	143 (53.2)	**0.22**
		12-20	162 (35.9)	77 (28.6)	
		> 20	97 (21.5)	49 (18.2)	

*ng/mL.

Table 6. The seasonal variation of 25(OH)D levels according to age group

	Preschool	School-aged	Adolescent
Spring			
n (Group 1/Group 2)	194/147	123/104	81/62
25(OH)D, ng/mL			
Group 1	17.8 (12.8)*	14.4 (7.9)*	12.1 (7.8)*
Group 2	17.7 (11.8)*	13.7 (9.5)*	10.55 (8.4)*
p	0.92	0.61	0.25
Summer			
n (Group 1/Group 2)	112/43	61/24	68/23
25(OH)D, ng/mL			
Group 1	25.1 (9.9)*	22.68 ± 6.22**	19.83 ± 7.12**
Group 2	27.1 (13)*	21.81 ± 8.99**	14.67 ± 6.62**
p	0.20	0.62	**0.03**
Autumn			
n (Group 1/Group 2)	183/139	131/67	111/66
25(OH) D, ng/mL			
Group 1	23.6 (11.4)*	20.9 (10.8)*	17.07 ± 8.08**
Group 2	26.1 (7.7)*	23.3 (10.8)*	18.28 ± 8.19**
p	0.21	0.05	0.33
Winter			
n (Group 1/Group 2)	346/232	263/144	191/118
25(OH)D, ng/mL			
Group 1	16.9 (13.1)*	14.4 (8.8)*	10.3 (8.3)*
Group 2	17.8 (14.3)*	13.4 (9)*	8.7 (6.8)*
p	0.48	0.12	**0.016**

*Median, IQR, **mean ± SD.
SD: standard deviation, IQR: interquartile range

It was previously reported that levels of vitamin D are significantly lower in girls, adolescents, those with low physical activity, during the winter season, and in areas with little or no sun exposure (23-30). Our results were in keeping with these findings; the vitamin D levels of girls were significantly lower than boys especially in 6-12 and 12-18 years old children and adolescents. In addition, in our study population, vitamin D levels were negatively correlated with age. This negative correlation was present in both the pre-pandemic and pandemic periods

As the synthesis of vitamin D is directly modulated by sun exposure, stay-at-home orders and/or lockdowns to prevent COVID-19 spreads may have affected vitamin D levels in both children and adolescents. İzmir, where the current study was conducted, is on the coast of western Anatolia, located on 38.25°N latitude and is temperate and sunny during most of the year (31). However, despite the geographic location with an agreeable and relatively sunny climate for vitamin D synthesis, vitamin D insufficiency and deficiency was a problem before the pandemic and continues to be a problem after the pandemic in this region (32).

Although the vitamin D levels were similar in Group 1 and 2 without taking age, gender, and seasonal differences into consideration, as we hypothesized that limited sun exposure due to lockdowns, closure of schools, and stay-at-home calls may have decreased vitamin D levels among specific age groups, we firstly compared the levels of vitamin D according to age subgroups. Our results showed that vitamin D levels of 6-12 year-old and 12-18 year-old children were significantly lower in the pandemic period (Group 2) than in the pre-pandemic period (Group 1). In a similar study of the relationship between serum levels of vitamin D and pandemic-related restrictions in children in Guangzhou, it was reported that vitamin D deficiency increased in the pandemic period in children under 6 years of age (33). Controversially, in another study conducted among 18-19 year-old male adolescents, the authors reported that they did not identify any difference in vitamin D levels before and during the pandemic in their study population (34). During the pandemic, the timing of the closure of schools, the season during the stay-at-home periods, and the duration of lockdowns vary from country to country (33,34,35). As soon as the first case was reported from our country, schools stopped face-to-face education. Moreover, children under 18 years were restricted in going out which led to limited sun exposure, especially in school-aged children.

In a very recent study, Bayramoğlu et al (4) reported that vitamin D insufficiency (38.4%) and deficiency (41.7%) were evident among adolescent COVID-19 patients and suggested prophylactic use of vitamin D in this age group. Our results add that vitamin D levels are also lower in healthy adolescents in the pandemic period than in the pre-pandemic period, and this decrease has caused an increased rate of vitamin D deficiency in this age group. We also add that the vitamin D levels were lower, not only in adolescents but also in school-aged children during the pandemic. Thus, we suggest that these age groups are affected due to pandemic-related restrictions and should be offered prophylactic vitamin D to prevent vitamin D insufficiency and deficiency. As for toddlers and preschool children (1-6 years), the vitamin D levels were similar between groups. In our opinion, the reason for this result might be that this age group either has no schooling or has been attending kindergarten which were not closed due to pandemic-related restrictions. Thus, we believe, sun exposure in this age group did not change between the pre-pandemic and pandemic periods. However, considering the continuing effect of COVID-19 related restrictions, this age group should also be offered prophylactic use of vitamin D to maintain sufficient levels of vitamin D.

There are many published studies reporting seasonal variations of vitamin D levels due to sun exposure (36). Rustecka et al (35), reported that the vitamin D levels in children decreased during the COVID-19 pandemic and the rate of children with vitamin D deficiency has increased in all seasons, except winter, in Poland. They also stated that although the characteristic seasonal variability was observed before the pandemic, no seasonal variability was observed during the pandemic. In our study, vitamin D levels were significantly lower in the pandemic period than pre-pandemic levels in 12-18 year old adolescents during winter and summer. Unexpectedly, in addition to the characteristic seasonal decrease in winter, the levels of vitamin D were also decreased during summer, indicating that adolescents could not benefit from sunlight because of restrictions.

Study Limitations

The most important limitation of this current study is its retrospective design. As we evaluated hospital records of children, we did not have data about nutritional intake, vitamin D supplementation status, physical activity, and body mass index of the children, all of which are known to affect vitamin D levels directly. Second, vitamin D levels are closely related to geographic properties, specifically the local climate and lockdown restrictions also varied between regions. Thus, the results are not generalizable. A strength of this current study, which goes some way to mitigating the lack of additional data, is the size of the study cohort, all of whom were without chronic disease and who could be correctly identified by hospital records.

Conclusion

We report that school-aged children (6-12 years) and adolescents (12-18 years) are at risk of vitamin D deficiency and insufficiency in both the pre-pandemic and pandemic periods in our country. Moreover, pandemic-related restrictions have caused significant decreases in vitamin D levels in these age groups. Thus, we suggest that children and adolescents should be given vitamin D supplementation in order to maintain sufficient levels of vitamin D. In addition, due to the continuing effects of the pandemic, since the time spent outdoors and, consequently, sun exposure is limited, dietary intake of vitamin D (fish, food fortified with vitamin D) should be supported to prevent vitamin D deficiency in all age groups.

Ethics

Ethics Committee Approval: The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Ethics Committee of Dr. Behçet Uz Pediatric Diseases and Surgery Training and Research Hospital, İzmir (protocol no: 554, decision no: 2021/09-02, date: 06.05.2021).

Informed Consent: Retrospective study.

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Authorship Contributions

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