ORIGINAL ARTICLE

CONTENTS

Analysis and interpretation of Coronavirus infection children's incidence, contributing factors, risks of complications and their relationship

Olesya M. Horlenko, Khrystyna Hechko, Lyubomyra B. Prylypko, Mykhaylo Hechko, Fedir V. Horlenko, Adrian I. Tomey, Agneta V. Lenchenko
UZHHOROD NATIONAL UNIVERSITY, UZHHOROD, UKRAINE

ABSTRACT

Aim: To study and investigate the incidence of Coronavirus infection in children, the course of the disease, the risks of complications and their interrelationships

Materials and Methods: Study included the analysis and observation of children (n=55, aged 14.36±3.62 years) with confirmed Coronerovirus infection, who were observed in the CNE «CMCH» in Uzhgorod in outpatient conditions. A study of clinical presentations, a clinical and laboratory examination followed by a mathematical analysis of the symptoms data in children with an identified Coronavirus infection and in the dynamics up to week 30 (with survey intervals in 3 weeks) from the diagnosis verification was carried out

Results: A dynamic analysis of the clinical manifestation of symptoms in children with an identified Corona virus infection and within 30 weeks (with survey intervals of 3 weeks) from the beginning of the diagnosis verification was carried out. Complaints from the respiratory system were prevailed. The most long-lasting complaint was observed «changes in the sense of taste and smell» (from 35(63.6%) to 6(10.9%) up to 18 weeks inclusive. Other complaints «Cough, Rhinitis, Shortness of breath, Pain in the chest» was observed for 6 weeks. Sore throat, muscular and joint pain were persisted for 3 weeks. Fever was not identified at week 3. Illness with other viral respiratory diseases started at week 9 and was observed until week 30 (from 10(18.2%) to 19(34.5%)) with varying levels. A decrease in cases of IgM identification was observed within 6 weeks (from 55, 100% to 20, 36, 4%). On the 9th week, the presence of IgM was not established. There is also an increase in the number of cases of detection of IgG in patients with a level maximum of 6 weeks.

Conclusions: There is a positive effect of the CRP level on the occurrence of symptoms of cough, rhinitis, shortness of breath, chest pain, change in taste and smell, muscle and joint pain (r=0.33-0.55), with the most significant data for the symptom of pain in chest (p=0.00001). Ferritin level interactions mostly had a negative direction (r=-0.35-0.48, p=0.02-0.00001) on the development of symptoms, with the exception of rhinorrhea (r=0.48, p=0.00002) and chest pains (r=0.39, 0.003). According to multiple logistic regression analysis the chance of the symptom of a change in taste and smell increases due to an increasing in the level of Procalcitonin in 1.48 times. The chance of the symptom of shortness of breath increased due to an increasing in the Ferritin level in 1.025 times

KEY WORDS: Coronavirus infection (SARSCoV-2), symptoms, complication, correlational and multiple logistic regression analysis, children

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INTRODUCTION

The study of the prevalence of SARSCoV-2 among children in Ukraine in the first year of the pandemic showed that the part of registered cases was 0.7%, and the morbidity per 100,000 children was determined in 688.64 cases. The most vulnerable to SARS-CoV-2 age group infection among children in Ukraine was teenagers (63.8%). There is a similarity with the results of studies in the USA [1], where children over the age of 12 were predominated [2]. SARS-CoV-2 is characterized by an extraordinary speed of spread due to factors unique to the virus, characteristics of the child, and interaction with the environment [3]. More than 90% of children with COVID-19 have a mild course of the disease and do not require hospitalization. This contrasts with other respiratory viruses, where the disease in children is often more severe. Among the most common clinical signs of SARSCoV-2 in children are classic flu-like symptoms such as fever, sore throat, nasal congestion, and cough. In addition to damage in the upper respiratory tract, other organs can be affected, for example, the gastrointestinal and central nervous systems. Most children were asymptomatic, and only a few cases were severe, in contrast to adult patients [4]. At the same time, it was established that asymptomatic infection is registered in 15-42% of children [5,6]. It is important to note that this is likely an underestimate of the true occurrence, as asymptomatic children are applied much less often for testing than symptomatic children [7].

Table 1. Prospective characteristics of the main symptoms in children with coronavirus infection

Parameters (n=55)	Oneset	3 weeks	6 weeks	9 weeks	12 weeks	15 weeks	18 weeks	21 weeks	24 weeks	27 weeks	30 weeks
IgM	55	55	20(36,4%)	-	-	-	-	-	-	-	-
IgG	-	22(44,0%)	55	55	55	55	55	55	55	55	55
Fever	55	-	-	-	-	-	-	-	-	-	-
Cough	29 (52,7%)	14(25,5%)	2(3,64%)	-	-	-	-	-	-	-	-
Sore throat	8(14,5%)	2(3,64%)	-	-	-	-	-	-	-	–	-
Rhinitis	33(60,0%)	8(14,5%)	4(7,25%)	-	-	-	-	-	-	-	-
Dispnea	21(38,2%)	3(5,45%)	3(5,45%)	-	-	-	-	-	-	-	-
Chest pain	39(70,9%)	23(41,8%)	2(3,64%)	-	-	-	-	-	-	-	-
Desorders in the taste and smell sensation	35(63,6%)	9(16,4)	6(10,9%)	6(10,9%)	6(10,9%)	6(10,9%)	6(10,9%)	-	-	-	-
Muscular and joint pain	48(87,3%)	19(34,5%)	-	-	-	-	-	-	-	-	-
Other viral respiratory diseases	-	-	-	10(18,2%)	14(25,5%)	2(3,64%)	4(7,25%)	1(1,82%)	2(3,64%)	6(10,9%)	19(34,5%)
Hospitalization	3(5,45%)	2(3,64%)	-	-	-	-	-	-	-	-	-

Table 2. Associated pathology in children with coronavirus infection

Associated pathology in children with Covid-19(n=55)	Number (%)
Reccuurnce respiratory diseases in anamneses	8 (14,5%)
Over weight	2(3,64%)
Anemia	5(9,1%)
Chronic respiratory pathology	0
Asthma	2(3,64%)
Cardiio- vascular diseases захворювання	1(1,82%)
Urinary tract pathology патологія	0
Digestivet ract pathology	0
Connective tissue diseases	0

AIM

To study and investigate the incidence of Coronavirus infection in children, the course of the disease, the risks of complications and their interrelationships

MATERIALS AND METHODS

Materials and methods of the study included the analysis and observation of children (n=55, aged 14.36±3.62 years) with confirmed Coronerovirus infection, who were observed in the CNE «CMCH» in Uzhgorod in outpatient conditions. A study of clinical presentations, a clinical and laboratory examination followed by a mathematical analysis of the symptoms data in children with an identified Coronavirus infection and in the dynamics up to week 30 (with survey intervals in 3 weeks) from the diagnosis identification was carried out.

RESULTS

A dynamic analysis of the clinical manifestations of symptoms in children with an identified Coronaviral infection and within 30 weeks (with survey in intervals of 3 weeks) from the beginning of the verification of the diagnosis was carried out (Table 1).

Consideriation of the obtained data presented that complaints from the respiratory system are prevail. The most long-lasting complaint was observed changes in taste and smell sensations (from 35(63.6%) to 6(10.9%) up to and including 18 weeks (Fig. 1).

Other complaints, as cough, rhinitis, dispnea, chest pain has been observed for 6 weeks. The dynamic of chest pain is shown on Fig. 2.

Sore throat and muscle and joint pain lasted 3 weeks. Fever was not identified on the 3rd week. The rate of hospitalization and the presence of complications was observed during the first 6 weeks. Pneumonia was

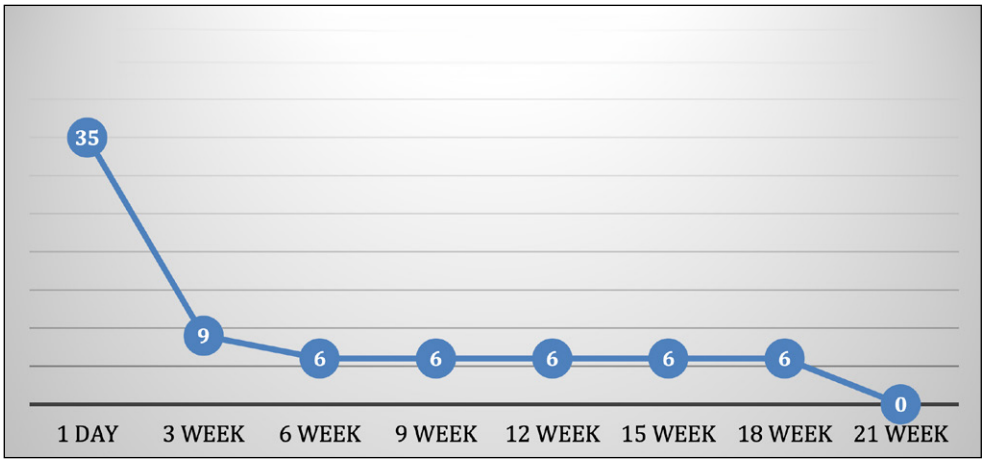

Fig.1. Dinamic of disorders in the taste and smell sensation.

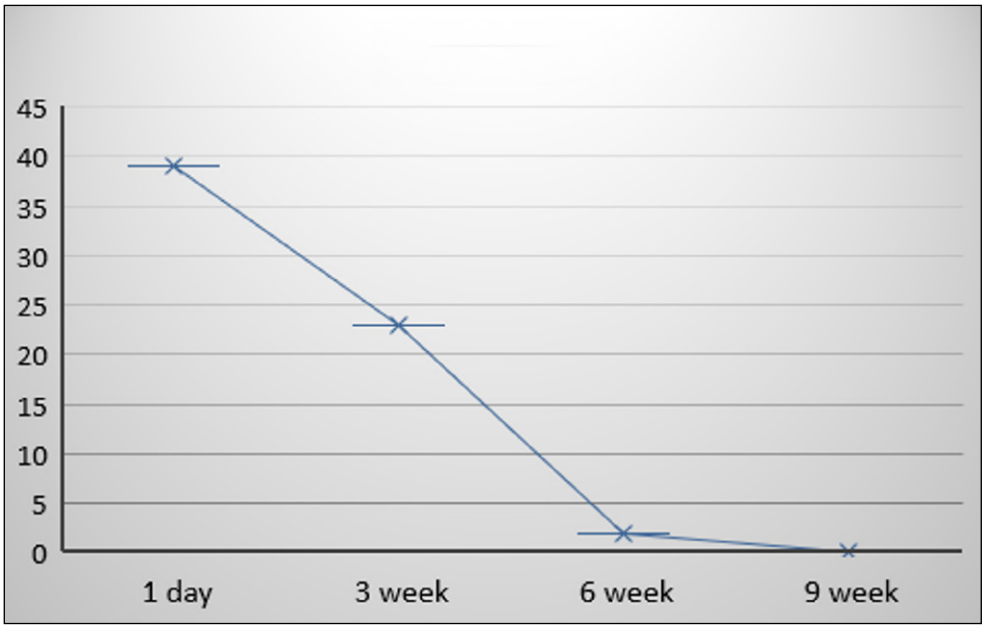

Fig. 2. Dynamics of chest pain.

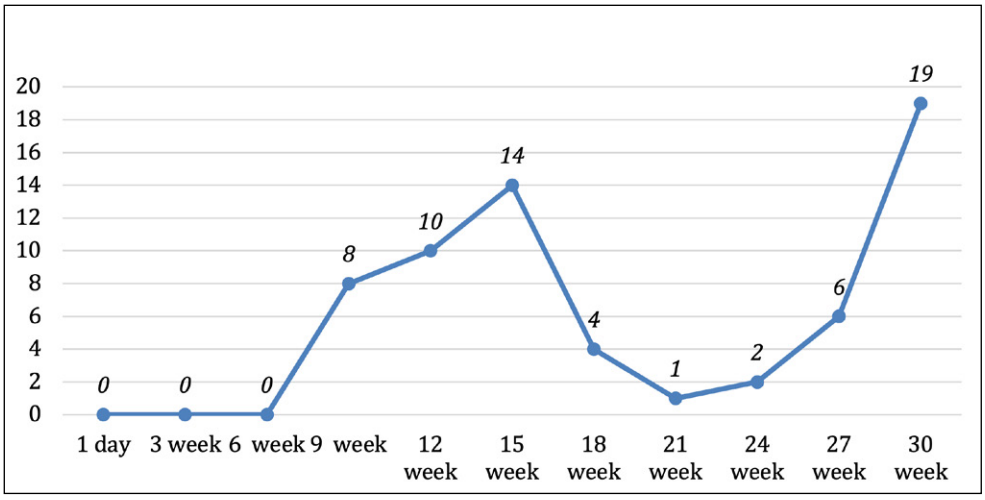

Fig. 3. Dinamics of other respiratory diseases in the postcovid perid.

diagnosed (3.5/45%) in the first 2 weeks and 2 cases (3.64%) in the 3rd week range.

Other viral respiratory diseases began from the 9th week and was observed until the 30th week (from 10 (18.2%) to 19 (34.5%)) with different levels, which are graphically illustrated on Fig. 3.

The accompanying pathology of the studied contingent of children was considered and peasented in Table 2.

According to table II, the most common concomitant

Table 3. Correlation relationships of clinical and laboratory parameters

Parameters		Correlation coefficient (r)	Statistical significance (p)
Cough	CRP	0,44	0,001
	Ferritin	-0,47	0,0004
Sore throat	Total protein	-0,29	0,03
	Na	-0,38	0,004
	Urea	0,34	0,01
	Creatinin	0,36	0,008
	Ferritin	-0,48	0,0002
	antiTPO	-0,51	0,0002
Rhinitis	CRP	0,54	0,00002
	Ferritin	0,48	0,0002
Dispnea	K	0,29	0,03
	CRP	0,33	0,02
	Ferritin	-0,27	0,04
	antiTPO	-0,51	0,00008
Chest pain	CRP	0,55	0,00001
	Ferritin	0,39	0,003
Desorders in the taste and smell sensation	K	0,28	0,04
	CRP	0,44	0,001
	Ferritin	-0,35	0,009
Muscular and joint pain	CRP	0,52	0,00004

diseases were recurrent respiratory diseases in the anamnesis (8, 14.5%) and anemia (5.9.1%). The dynamics of IgM in patients is presented (Fig. 4).

There is a decrease in cases of IgM identification within 6 weeks (from 55/ 100% to 20/36,4%). On the 9th week, the presence of IgM was not established.

There is also an increasing in the number of cases of IgG detection in patients with a maximum of 6 weeks (Fig. 5).

Correlation analysis of the obtained data was carried out and the relationship between clinical symptoms and laboratory indicators was identified (Table 3).

According to Table 3, each considered symptom was correlated with inflammatory markers, in particular CRP and Ferritin, except for Sore Throat and Muscle and Joint pain, separately. There is a positive effect of the CRP level on the occurrence of symptoms of Cough, Rhinitis, Dispnea, Chest pain, change in taste and smell, muscle and joint pain (r=0.33-0.55), with the most significant data for the symptom of Chest pain (p=0.00001). Ferritin level interactions mostly had a negative direction (r=-0.35-0.48, p=0.02-0.00001) on the development of symptoms, with the exception of Rhinitis (r=0.48, p=0.00002) and Chest pain (r=0.39, 0.003). Also interesting is the fact that the level of mineral K has a weak effect on the severity of the symptom of Dispnea and Disorder in taste and smell sinsation. The symptom of Sore Throat is characterized by the most numerous multidirectional relationships, in particular, the negative direction with Total Protein (r =-0.29, p=0.03), Na (r =-0.38, p=0.004), Ferritin (r =-0.48, p=0.000003) antiTPO (r =- 0.51, p=0.0002) and positive direction with Urea (r =0.34, p=0.01), Creatinine (r =0.36, p=0.008). We also performed a multiple logistic regression analysis for interpretation of the development and formation of the symptom of taste and smell sensations change from the studied inflammatory markers [8]. It was proved that the coefficient of Procalcitonin level is statistically significant (p=0.0455). The influence of the Procalcitonin level was evaluated by the value of the Odds ratio (unit ch) (ORu) and the Odds ratio (range) (ORr) for it. The chance of the taste and smell sensation disorder in increases due to an increase in the level of Procalcitonin in 1.48 times (ORu = 1.008-2.184). The range of chances (ORr) for Procalcitonin was 73.846 (1.093-4989.745). It was also found that The coefficient of Ferritin level (p=0.028) in the risk of developing Dispnea in patients with Coronaryvirus disease was statistically significant. The chance of the symptom of Dispnea increases due to an increase in the Ferritin level in 1.025 times (ORu = 1.003-1.047). The chance range (ORr) for Ferritin was 25.12547 (1.437-439.399). Other values of inflammatory markers were not reliable in our sample.

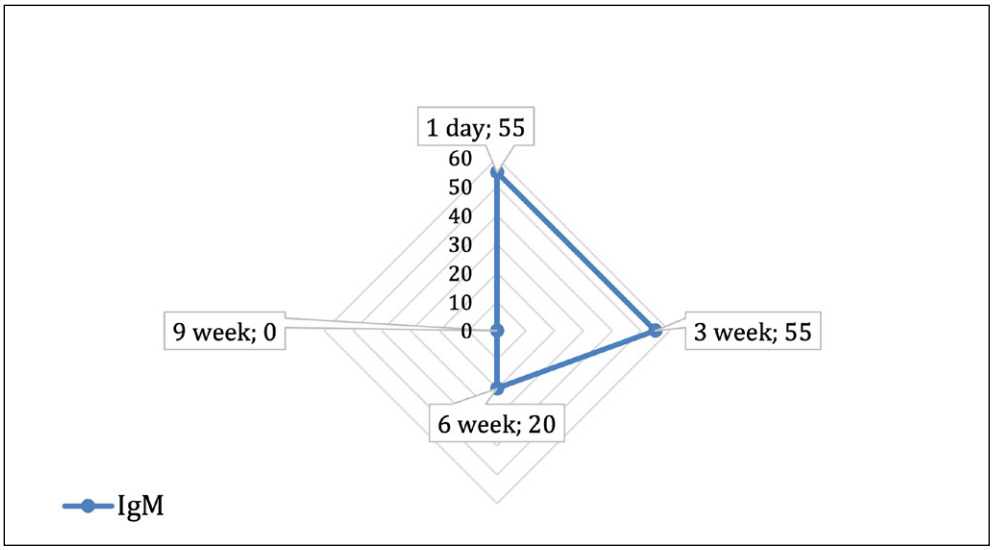

Fig. 4. The dynamics of IgM in patients.

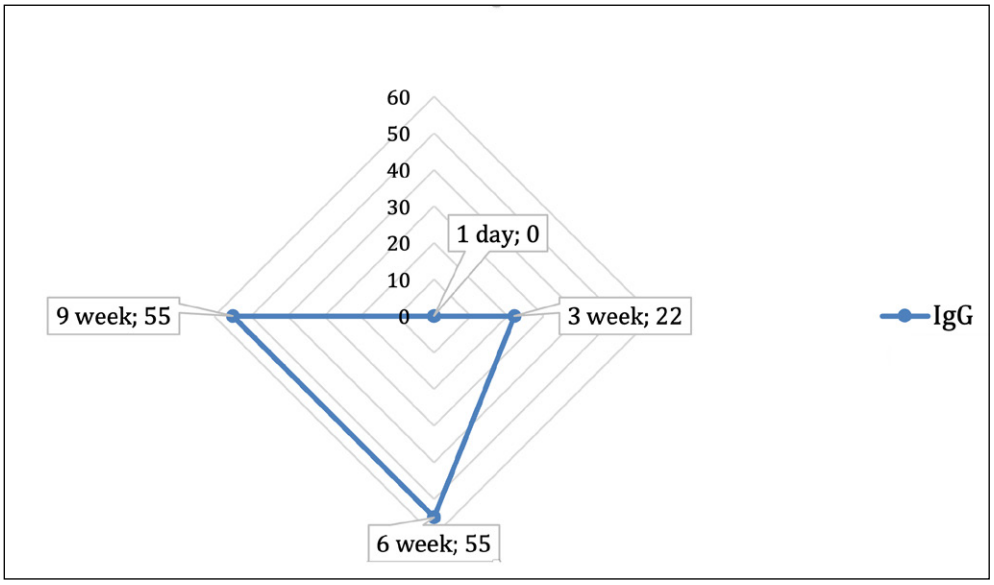

Fig. 5. Dynamics of IgG detection in the examined contingent.

DISCUSSION

SARS-CoV-2 is characterized by a predominance of complaints from the respiratory tract. When the virus binds to the ACE2 receptor, which is present in the lungs as well as in many other organs, the inflammatory response can occur and leading to multiple organ damage and long-term disease symptoms. The reaction of each organism to a viral factor is unique and can be considered as a set of contributing factors for the development of those or other clinical presentations. The persistence of the virus or viral fragments determines the triggering of the immune response, the duration of the disease and the possibility of developing complications [9]. Studies of inflammatory markers of the disease, as levels of Ferritin, CRP, Procalcitonin and proteins of the Acute phase response proved correlations with the severity of Coronaryvirus infection. Research of the functions and influence of each marker on the course of the disease, the intensity of manifestations and the possibility of complications is ongoing [10]. There are several hypotheses for the relatively low morbidity and mortality of SARS-CoV-2 among children, which are largely related to differences in immune responses compared to adults, as well as differences in the distribution of Angiotensin-Converting enzyme 2 (ACE2), which potentially limits viral entry. and subsequent inflammation, hypoxia and tissue damage [11]. The authors suggest that mucosal immunity in children can prevent SARS-CoV-2 infection [12]. This finding is now supported by further studies showing an increased innate antiviral response in the upper respiratory tract in children compared to adults [13]. Higher levels of IFN-α2, IFN-γ, IP-10, IL-8 and IL-1β , proteins in nasal fluid are also observed in children compared to adults [14]. These results are direct evidence of a more intense early immune response of the Respiratory tract mucous membranes in children compared to adults, and suggest that this contributes to easier There are

several hypotheses for the relatively low morbidity and mortality of SARS-CoV-2 among children, which are largely related to differences in immune responses compared to adults, as well as differences in the distribution of angiotensin-converting enzyme 2 (ACE2), which potentially limits viral entry. and subsequent inflammation, hypoxia and tissue damage [11]. The authors suggest that mucosal immunity in children can prevent SARS-CoV-2 infection [12]. This finding is now supported by further studies showing an increased innate antiviral response in the upper respiratory tract in children compared to adults [13]. Higher levels of IFN-α2, IFN-γ, IP-10, IL-8 and IL-1β proteins in nasal fluid are also observed in children compared to adults [14]. These results provide direct evidence of a more intense early immune response of the respiratory tract mucosa in children compared to adults, and suggest that this contributes to easier clinical outcomes.

CONCLUSIONS

1. The complaints by the Respiratory system prevail according our data. The most long-lasting complaint was observed as taste and smell sensation disorder (from 35/63.6%) to 6/10.9%) up to 18 weeks including. Other complaints, as Cough , Rhinitis Dispnea, Chest Pain were observed for 6 weeks. Sore throat and muscular and joint pain persisted for 3 weeks. Fever was not identified at week 3. Ilness with other viral respiratory diseases have started at week 9 and was observed until week 30 (from 10(18.2%) to 19(34.5%)) with varying levels.
2. A decrease in cases of IgM identification was observed within 6 weeks (from 55/ 100% to 20/36, 4%). The presence of IgM was not revealed on the 9th week,. There is also an increase in the number of cases of detection of IgG in patients with a maximum on 6th week.
3. Each considered symptom correlated with inflammatory markers, in particular with (CRP and Ferritin), with the exception of Sore Throat and Muscle and joint pain and most significant was the symptom of Chest pain (r=0.00001). Positive effects of CRP level on the occurrence of all symptoms (r=-0.33-0.0,55 p=0.02-0.00001), with exception of Sore throat. Ferritin level interactions mostly had a negative direction (r=-0.35-0.48, p=0.02-0.00001) on the development of symptoms, with the exception of Rhinitis (r=0.48, p=0.00002) and Chest pain (r=0.39, 0.003).
4. According to the data of the conducted Multiple Logistic Regression analysis for the interpretation of the development and formation of the next symptom as Taste and Smell sensations disorder under the influence of the studied inflammatory markers. It was proved that the coefficient of Procalcitonin level is statistically significant (p=0.0455). The influence of the Procalcitonin level was evaluated by the value of the Odds ratio (unit ch) (ORu) and the Odds ratio (range) (ORr) for it. The chance of the taste and smell sensation disorder in increases due to an increase in the level of Procalcitonin in 1.48 times (ORu = 1.008-2.184). The range of chances (ORr) for Procalcitonin was 73.846 (1.093-4989.745).
5. The coefficient of Ferritin level (p=0.028) in the risk of developing Dispnea in patients with Coronaryvirus disease was statistically significant. The chance of the symptom of Dispnea increases due to an increase in the Ferritin level in 1.025 times (ORu = 1.003-1.047). The chance range (ORr) for Ferritin was 25.12547 (1.437-439.399).

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

CORRESPONDING AUTHOR

Olesya M. Horlenko
Uzhhorod National University
1 Narodna squ., 88000 Uzhhorod, Ukraine
e-mail: ohorlenko@gmail.com

ORCID AND CONTRIBUTIONSHIP

Olesya M. Horlenko: 0000-0002-2210-5503 A D F
Khrystyna Hechko: 0000-0003-4989-7659 A B D
Lyubomyra B. Prylypko: 0000-0002-4131-5450 C D
Mykhaylo Hechko: 0000-0003-2793-5044 B C
Fedir V. Horlenko: 0000-0002-0496-2069 E F
Adrian I. Tomey: 0000-0002-60958937-2069 B E
Agneta V. Lenchenko: 0000-0001-7954-7540 B E

A – Work concept and design, B – Data collection and analysis, C – Responsibility for statistical analysis, D – Writing the article, E – Critical review, F – Final approval of the article

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