RETROSPECTIV STUDY REGARDING THE EPIDEMIOLOGICAL ASPECTS OF COVID-19 INFECTION IN MOLDAVIA, ROMANIA

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Abstract:

The aim of this study is to carry out an epidemiological retrospective of COVID-19 with individualization of the peculiarities of manifestation on the territory of Moldova, the evolutionary peculiarities being in full agreement with the general status of the patient up to that moment. 779 patients with COVID-19, hospitalized between September 2020 and April 2021, 386 men (49.6%) and 393 women (50.4%), aged between 7 and 93 years, were investigated; the mean age of the patients was 52.26 ± 15.844 years, with no significant differences between men (52.26 ± 15.830 years) and women (52.26 ± 15.878 years). More than half of the patients (59.6%) are aged between 30-59 years; 8.3% are young people under 30 years old, and about a third (32.1%) are elderly, over 60 years old (table 1) – without statistically significant differences between the sexes (Pearson Chi - squared = 3.102, p = 0.875). There are certain correlations between the symptoms noticed in patients, their comorbidities and the appearance of lung changes on CT, respectively febrile or afebrile evolution. Among the characteristic symptoms of COVID-19, patients with comorbidities present more frequently cough, physical asthenia, inappetence and other than chest pain compared to those without comorbidities.

Key words: COVID-19, epidemiological retrospective , comorbidities;

INTRODUCTION

Population health status is a complex social and biological phenomenon that expresses the level and characteristics of health of members of a community as a whole. However, defining, precisely defining, and assessing this phenomenon is difficult because of its complexity and the various factors that affect it.

The level of health of the population at both national and global level has been seriously disrupted since 2020 by the outbreak of the coronavirus pandemic. The epidemiological aspects of Covid-19 infection are extremely important, on the general background found in all forms of manifestation there were elements of particularity in relation to the type of strain involved and especially the mode of manifestation of the clinical picture from individual to individual, from country to country[1-11].

On February 11, 2020, WHO announced that the official name of the new virus first identified in Wuhan, China, is "SARS-CoV-2. This virus is acute respiratory syndrome. It is part of the sub-family of viruses called Coronaviruses (CoV): 229E, NL63, OC43, HKU1, SARS-CoV, MERS-CoV.

Coronaviruses are known to be widespread in nature, causing respiratory tract diseases and gastroenteritis in humans and animals (birds, pigs, cattle, horses, rodents, bats, cats, dogs), some very severe and others mild or even without clinical symptoms. They are the second viral group, after rhinoviruses, responsible for inducing rhinopharyngitis, the common cold in humans[11-16].

The literature shows that SARS-CoV-2 is not the first virus in its sub-family to cause numerous deaths. From 2012 to November 2019, 2,494 cases of MERS-CoV infection and 858 deaths have been reported to the World Health Organization (WHO).

A virus such as SARS-CoV-2 is considered dangerous because of its virulence, speed of transmission, in a very short time. From December 2019 to March 2020, in just 4 months, 114,243 infections and 4,023 deaths have been confirmed in 25 countries[16-21].

The virus is transmitted in two main ways: through contact with an infected person, contact defined as a distance of about 1.8 meters, through droplets from the respiratory tract removed when a person sneezes or coughs; by touching contaminated surfaces, followed by touching the eyes, nose or mouth.

Not only elderly people are affected by COVID-19, but also young people and children. However, it appears that age category influences the severity of illness and the increased risk of death[21-32].

The aim of this study is to carry out an epidemiological retrospective of Sarcovirus 2 infection with individualization of the peculiarities of manifestation on the territory of Moldova, the evolutionary peculiarities being in full agreement with the general status of the patient up to that moment.

MATERIAL AND METHOD:

779 patients with COVID-19, hospitalized between September 2020 and April 2021, 386 men (49.6%) and 393 women (50.4%), aged between 7 and 93 years, were investigated; the mean age of the patients was 52.26 ± 15.844 years, with no significant differences between men (52.26 ± 15.830 years) and women (52.26 ± 15.878 years). More than half of the patients (59.6%) are aged between 30-59 years; 8.3% are young people under 30 years old, and about a third (32.1%) are elderly, over 60 years old (table 1) – without statistically significant differences between the sexes (Pearson Chi - squared = 3.102, p = 0.875).

Table 1. Structure of the investigated group by gender and age group

		Sex				Total	
		m		F			
		N	%	N	%	N	%
Age range	under 20 years	8	2.1%	7	1.8%	15	1.9%
	20-29 years old	24	6.2%	26	6.6%	50	6.4%
	30-39 years old	50	13.0%	44	11.2%	94	12.1%
	40-49 years old	89	23.1%	90	22.9%	179	23.0%

	50-59 years	87	22.5%	104	26.5%	191	24.5%
	60-69 years	73	18.9%	63	16.0%	136	17.5%
	70-79 years	36	9.3%	36	9.2%	72	9.2%
	over 80 years	19	4.9%	2. 3	5.9%	42	5.4%
Total		386	100.0%	393	100.0%	779	100.0%

RESULTS:

We carried out a comparative study of the symptoms recorded in patients and comorbidities, correlated with pulmonary complications and the evolution, characterized by febrile, subfebrile and afebrile states, in order to identify and quantify the risk factors that facilitate the onset of complications.

Among the 779 investigated patients, 205 (26.3%) were asymptomatic, the rest presenting between 1-9 monitored symptoms (fig. 1); the most frequently recorded symptoms were cough (40.2% of cases), followed by headache (21.6%), physical asthenia (21.3%) and fever (17.8%); 11.2% of patients had 1 symptom, 17.3% had 2 symptoms, 25.9% had 3 symptoms, and 19.2% had 4 or more symptoms.

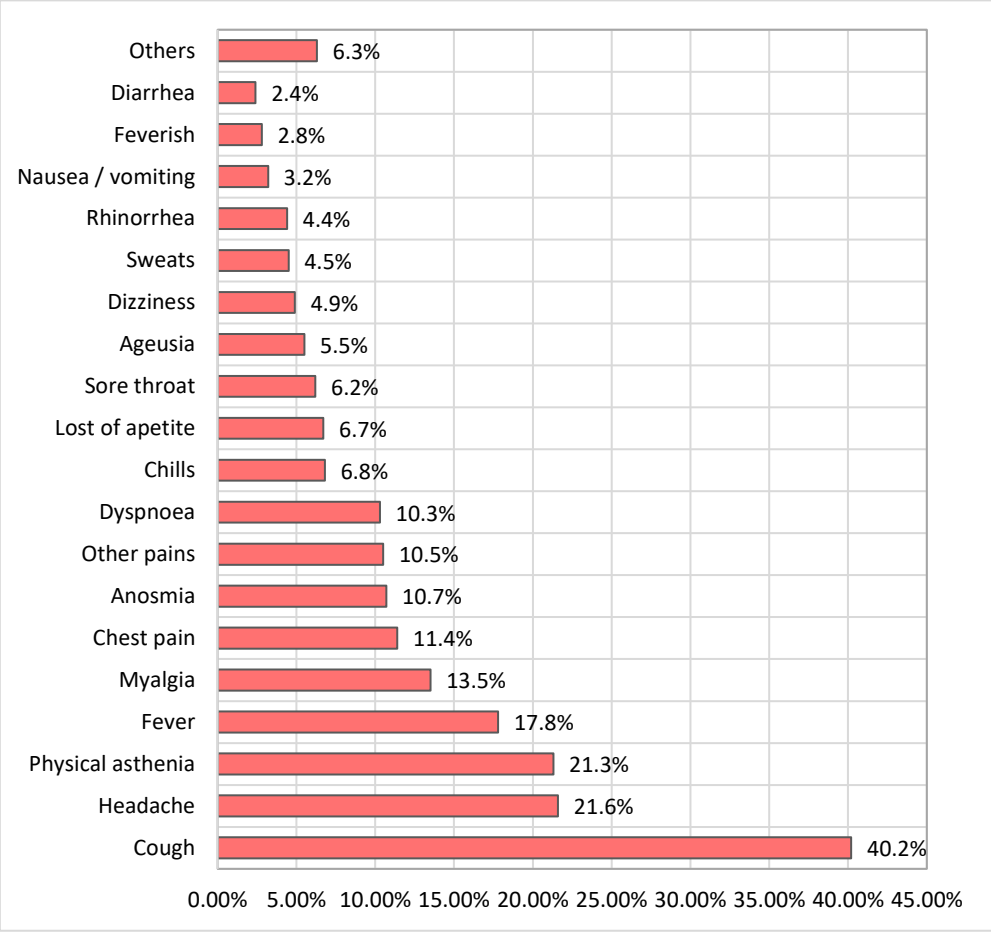

Fig. 1. The share of symptoms recorded in the batch

We analyzed the patients' symptoms comparatively by gender and age range, using the age of 60 years as a cutoff to identify the elderly (table 2).

In men, cases of fever are significantly more frequent than in women (21.8% versus 14.0%) and slightly more frequent are cases of chest pain (12.7% versus 10.2%), dyspnea (11.9 % vs. 8.7%), rhinorrhea (5.4% vs. 3.3%), and sweating (5.2% vs. 3.8%); on the other hand, in women, cases of physical asthenia (25.7% versus 16.8%), anosmia (13.7% versus 7.5%), odynophagia (8.4% versus 3, 9%) and diarrhea (3.8% vs. 1.0%); other slightly more common symptoms were headache (22.4% vs. 20.7%) and myalgias (14.2% vs. 12.7%). Also, the percentage of asymptomatic was slightly higher in women (27.0%) compared to men (25.6%). In patients under 60 years of age, cases of headache (25.3% versus 13.6%), anosmia (13.2% versus 5.2%), odynophagia (7.6% versus 3.2%) and rhinorrhea (6.0% versus 0.8%), and in patients over 60 years physical asthenia (30.8% versus 16.8%), dizziness (7.6% vs. 3.6%), loss of appetite (10.0% vs. 5.1%), and pain other than chest pain (17.2% vs. 7.4%), along with other manifestations (8.8% versus 5.1%). The percentage of asymptomatic patients is significantly higher among those under 60 (28.7%) compared to those over 60 (21.2%).

Table 2. Distribution of recorded symptoms, compared by gender and age range

	Sex					Age range				
	m		F		p	under 60 years		over 60 years		p
	n	%	n	%		n	%	n	%	
Rhinorrhea	21	5.4%	13	3.3%	,145	32	6.0%	2	0.8%	.001**
Dyspnoea	46	11.9%	34	8.7%	,133	49	9.3%	31	12.4%	,178
Chest pains	49	12.7%	40	10.2%	,270	62	11.7%	27	10.8%	,706
Cough	157	40.7%	156	39.7%	,781	202	38.2%	111	44.4%	.099
Fever	84	21.8%	55	14.0%	.005**	90	17.0%	49	19.6%	,379
feverish	9	2.3%	13	3.3%	,411	18	3.4%	4	1.6%	,156
Chills	26	6.7%	27	6.9%	,941	37	7.0%	16	6.4%	,758
Sweats	20	5.2%	15	3.8%	,358	2. 3	4.3%	12	4.8%	,776
myalgia	49	12.7%	56	14.2%	,525	80	15.1%	25	10.0%	,051
sore throat	15	3.9%	33	8.4%	.009**	40	7.6%	8	3.2%	,018*
anosmia	29	7.5%	54	13.7%	.005**	70	13.2%	13	5.2%	.001**
ageusia	18	4.7%	25	6.4%	,299	35	6.6%	8	3.2%	,051
Physical weakness	65	16.8%	101	25.7%	.003**	89	16.8%	77	30.8%	,000**
dizziness	15	3.9%	2. 3	5.9%	,203	19	3.6%	19	7.6%	.015*
DISORDERS	80	20.7%	88	22.4%	,572	134	25.3%	34	13.6%	,000**
loss of appetite	2. 3	6.0%	29	7.4%	,427	27	5.1%	25	10.0%	,011*
Nausea / vomiting	9	2.3%	16	4.1%	,168	16	3.0%	9	3.6%	,671
Diarrhea	4	1.0%	15	3.8%	,012*	10	1.9%	9	3.6%	,149
Other pains	39	10.1%	43	10.9%	,703	39	7.4%	43	17.2%	,000**
Other	24	6.2%	25	6.4%	,934	27	5.1%	22	8.8%	.047*
Asymptomatic	99	25.6%	106	27.0%	,675	152	28.7%	53	21.2%	.026*

They did not register a distinction statistically significant neither between sexes, neither between the elderly patients and the others in the EAEC what the look classification symptoms after their number; it is possible however to notice that in men they are slightly common than in women, cases with 1-4 symptoms (70.4% versus 62.9%), in time what about women are fairly common cases with 5-9 symptoms (10.3% vs. 3.8%); in patients under 60 they are more common cases with 5-9 symptoms (7.3% versus 6.4%), and in patients over 60 there are common the cases with 1-4 symptoms (72.4% versus 63.9%) – table 3.

Table 3. Distribution symptoms according their number, compared by gender and age range

		Gender, p = .071				Age range, p = .069				Total	
		m		F		under 60 years		over 60 years			
		n	%	n	%	n	%	n	%	N	%
No symptoms	0	99	25.6%	106	27.0%	152	28.7%	53	21.2%	205	26.3%
	1	48	12.4%	39	9.9%	57	10.8%	30	12.0%	87	11.2%
	2	69	17.9%	66	16.8%	80	15.1%	55	22.0%	135	17.3%
	3	107	27.7%	95	24.2%	136	25.7%	66	26.4%	202	25.9%
	4	48	12.4%	47	12.0%	65	12.3%	30	12.0%	95	12.2%
	5	9	2.3%	29	7.4%	28	5.3%	10	4.0%	38	4.9%
	6	4	1.0%	7	1.8%	5	0.9%	6	2.4%	11	1.4%
	7	2	0.5%	3	0.8%	5	0.9%	0	0.0%	5	0.6%
	9	0	0.0%	1	0.3%	1	0.2%	0	0.0%	1	0.1%
Total		386	100.0%	393	100.0%	529	100.0%	250	100.0%	779	100.0%

Among the investigated patients, 500 (64.2%) presented various comorbidities, the most frequently recorded being HTN (51.4%) and DM type II (21.0%) - fig. 2. A quarter of the patients (25.0%) presented a single comorbidity, 17.3% presented 2 comorbidities, 12.3% presented 3 comorbidities and 9.5% presented 4-7 comorbidities - fig. 2.

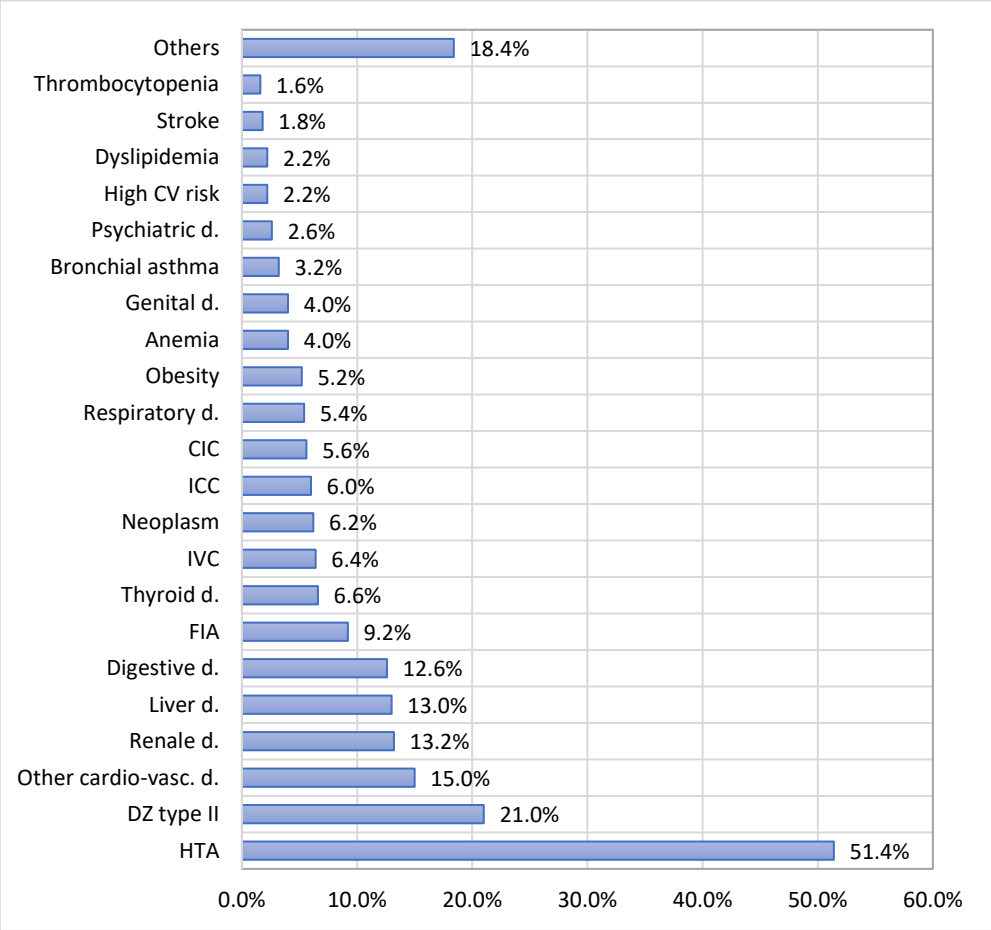

Fig. 2. Distribution of comorbidities in the study group

In patients with comorbidities, significantly increased percentages of cough (43.2% versus 34.8%), physical asthenia (25.6% versus 13.6%), loss of appetite (8.4% versus 3 .6%), pains other than chest pain (12.8% versus 6.5%) and other sporadic symptoms (8.2% versus 2.9%) – tachycardia, dysphagia, insomnia, psycho - motor agitation , paresthesias, jaundice, nitrogen retention syndrome and even syncope (2 cases). Patients without comorbidities present significantly more frequently anosmia (15.4% vs. 8.0%), odynophagia (8.6% vs. 4.8%), and rhinorrhea (7.5% vs. 2.6%); as expected, the percentage of asymptomatic patients is also slightly higher among those without comorbidities (29.7%) compared to others (24.4%) – table 4.

Table 4. Distribution of recorded symptoms, compared to patients with/without comorbidities

	Comorbidities										
	ABSENCES		present		p		ABSENCES		present		p
	n	%	n	%			n	%	n	%	
Rhinorrhea	21	7.5%	13	2.6%	.001**	anosmia	43	15.4%	40	8.0%	.001**
Dyspnoea	22	7.9%	58	11.6%	,102	ageusia	18	6.5%	25	5.0%	,395
Chest pains	34	12.2%	55	11.0%	,618	Physical weakness	38	13.6%	128	25.6%	,000**
Cough	97	34.8%	216	43.2%	,021*	dizziness	10	3.6%	28	5.6%	,210

Fever	50	17.9%	89	17.8%	,966	DISORDERS	66	23.7%	102	20.4%	,289
feverish	12	4.3%	10	2.0%	,063	loss of appetite	10	3.6%	42	8.4%	,010*
Chills	21	7.5%	32	6.4%	,549	Nausea / vomiting	6	2.2%	19	3.8%	,210
Sweats	11	3.9%	24	4.8%	,580	Diarrhea	7	2.5%	12	2.4%	,925
myalgia	41	14.7%	64	12.8%	,458	Other pains	18	6.5%	64	12.8%	.006**
sore throat	24	8.6%	24	4.8%	.034*	Other	8	2.9%	41	8.2%	.003**
						Asymptomatic	83	29.7%	122	24.4%	,104

No statistically significant differences are observed between patients with comorbidities and others regarding the classification of symptoms according to their number; among patients with comorbidities, cases with 1-4 symptoms are slightly more frequent (68.6% versus 63.1%), cases with 5-9 symptoms being noticed in similar percentages both in them (7.0%) and in those without comorbidities (7.2%) – table 5.

Table 5. Distribution symptoms considering their number, compared to patients with / without comorbidities

		Comorbidities, p = .519			
		ABSENCES		present	
		n	%	n	%
No symptoms	0	83	29.7%	122	24.4%
	1	32	11.5%	55	11.0%
	2	44	15.8%	91	18.2%
	3	67	24.0%	135	27.0%
	4	33	11.8%	62	12.4%
	5	17	6.1%	21	4.2%
	6	2	0.7%	9	1.8%
	7	1	0.4%	4	0.8%
	9	0	0.0%	1	0.2%
Total		279	100.0%	500	100.0%

86.5% of patients (674) were examined with lung CT, to identify possible complications; 125 patients (18.5%) showed no changes. In the others, the ground glass appearance was most frequently observed (59.9%) and that of accentuated interstitial drawing (8.9%), along with condensation (7.1%), fibronodular sequelae (7.1%) and confluence (6.7%) – fig. 3.

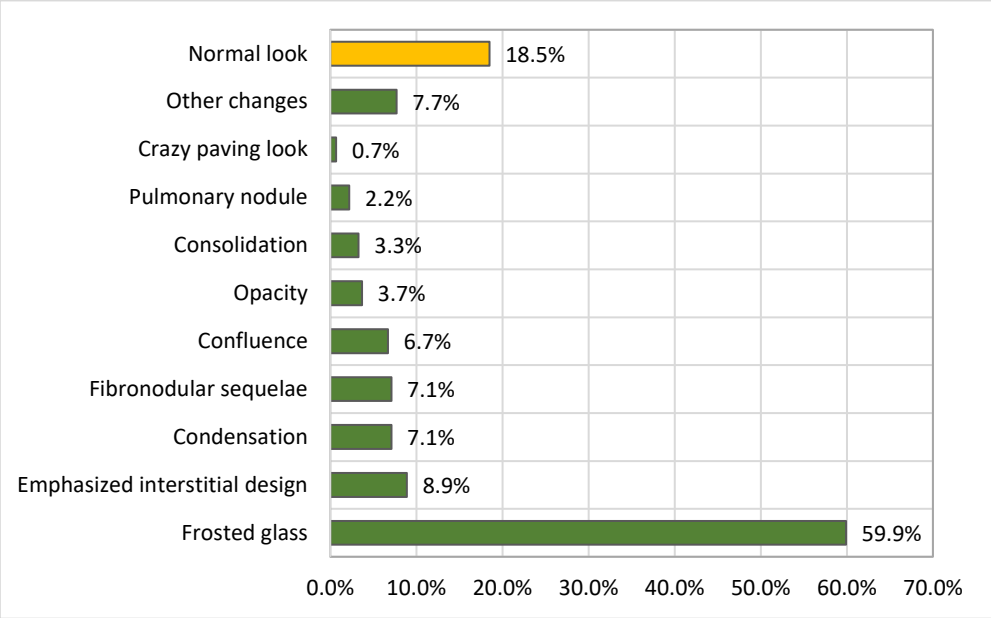

Fig. 3. Distribution of CT changes in the study group

There are no statistically significant differences between the sexes regarding the proportion of patients with modified CT; instead, 37.7% of them are over 60 years of age, compared to only 12.8% of those with normal appearance; therefore age over 60 years has an associated risk OR = 4.123 of causing pulmonary complications – table 6.

Table 6. Distribution by gender and age range, compared to patients with/without CT with altered appearance

		CT – modified layout							
		not		Yes		p	OR	95% CI	
		n	%	n	%			l.inf.	l.sup .
Sex	male	57	45.6%	280	51.0%	,276	-	-	-
	female	68	54.4%	269	49.0%				
Age	under 60 years	109	87.2%	342	62.3%	,000**	4,123	2,373	7,164
	over 60 years	16	12.8%	207	37.7%				

We compared the presence of symptoms and comorbidities in patients with normal and modified CT, in order to identify possible correlations; we also included in the study patient gender and age group, which may also have significant influences. In cases where we identified statistically significant differences in the weight of symptoms in patients with modified CT compared to others, we also calculated the risks associated with the respective symptoms, OR (Odds Ratio) – table 7.

Symptoms present in significantly increased percentages in patients with modified CT compared to others were chest pain, cough, fever, physical asthenia and loss of appetite; among these, the highest associated risk is found for inappetence (OR = 6.027), followed by physical asthenia (OR = 2.809) and cough (OR = 2.342). It also found that 41.6% of patients with normal CT were asymptomatic, compared to only 21.1% of those with altered CT – a difference that was also

statistically significant and associated with subunit risk, meaning that the absence of symptoms acts as a factor protection for lung changes.

Table 7. Distribution of recorded symptoms, compared to patients with/without CT with altered appearance

	CT – modified layout							
	not		Yes		p	OR	95% CI	
	n	%	n	%			l.inf.	l.sup .
Rhinorrhea	8	6.4%	21	3.8%	,two hundred	-	-	-
Dyspnoea	8	6.4%	62	11.3%	,106	-	-	-
Chest pains	8	6.4%	70	12.8%	.045*	2,137	1,001	4,565
Cough	32	25.6%	245	44.6%	,000**	2,342	1,515	3,620
Fever	14	11.2%	105	19.1%	.036*	1,875	1,034	3,400
feverish	4	3.2%	16	2.9%	,865	-	-	-
Chills	7	5.6%	44	8.0%	,357	-	-	-
Sweats	3	2.4%	30	5.5%	,152	-	-	-
myalgia	20	16.0%	77	14.0%	,570	-	-	-
sore throat	11	8.8%	29	5.3%	,133	-	-	-
anosmia	13	10.4%	57	10.4%	,995	-	-	-
ageusia	5	4.0%	33	6.0%	,379	-	-	-
Physical weakness	13	10.4%	135	24.6%	.001**	2,809	1,532	5,151
dizziness	5	4.0%	28	5.1%	,607	-	-	-
DISORDERS	24	19.2%	126	23.0%	,363	-	-	-
loss of appetite	2	1.6%	49	8.9%	.005**	6,027	1,446	25,125
Nausea / vomiting	2	1.6%	18	3.3%	,318	-	-	-
Diarrhea	3	2.4%	13	2.4%	,983	-	-	-
Other pains	10	8.0%	59	10.7%	,361	-	-	-
Other	6	4.8%	39	7.1%	,352	-	-	-
Asymptomatic	52	41.6%	116	21.1%	,000**	,376	,249	,567

We identified statistically significant differences between patients with normal CT and those with pulmonary changes in the number of symptoms; thus, 71.1% of patients with modified CT have 1-4 symptoms, and of these, 31.0% have 3 symptoms; on the other hand, only 53.6% of patients with normal CT have 1-4 symptoms, and only 14.4% have 3 symptoms. Also, 7.8% of patients with modified CT have 5-9 symptoms, compared to 4.8% of those with normal CT - table 8.

Table 8. Distribution symptoms taking into account their number, compared to patients with / without CT with altered appearance

		CT – modified appearance, p = .000**			
		not		Yes	
		n	%	n	%
No symptoms	0	52	41.6%	116	21.1%
	1	14	11.2%	59	10.7%
	2	21	16.8%	97	17.7%
	3	18	14.4%	170	31.0%
	4	14	11.2%	64	11.7%
	5	5	4.0%	28	5.1%
	6	0	0.0%	10	1.8%
	7	1	0.8%	4	0.7%
	9	0	0.0%	1	0.2%
Total		125	100.0%	549	100.0%

The ROC analysis for the number of symptoms reveals an AUC coefficient (Area under Curve) of 0.622, with a confidence interval between 0.565 ¸0.678, statistically significant (p = .000**), but still indicating a rather poor discriminatory power for identifying lung changes. The identified cut - off value is 1.50, corresponding to a sensitivity of 0.681 and a specificity of 0.528 (fig. 4) – therefore it can be considered that the risk of pulmonary changes increases in patients with more cumulative symptoms, compared to those with only one symptom.

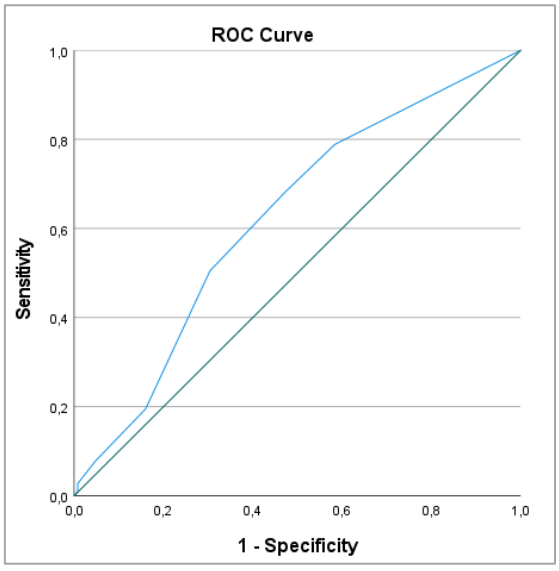

Fig. 4. No. symptoms vs. CT change – ROC curve

The percentage of patients with comorbidities among those with lung changes (69.8%) is statistically significantly higher than the similar percentage among patients with normal lung appearance (47.2%). From the list of monitored comorbidities, statistically significant differences were recorded between patients with altered lung appearance and those with normal lung appearance in the case of HTN (37.0% vs. 16.0%), AIF (7.5% vs. 0.8%), Type 2 DM (16.4% vs. 2.4%), renal disease (9.1% vs. 3.2%), and psychiatric disease (1.3% vs.

4.8%). The risk calculation shows that, in general, the presence of comorbidities is associated with an important risk of pulmonary changes, OR = 2.581, and among the comorbidities, the highest risk corresponds to AIF (OR = 10.008), followed by DM type 2 (OR = 7.974) and respectively HTN (OR = 3.080) and kidney diseases (OR = 3.031), with similar risks; the presence of psychiatric conditions is not relevant for pulmonary changes, the recorded risk being sub-unit - table 9.

Table 9. Distribution of recorded comorbidities, compared to patients with/without CT with altered appearance

	CT – modified layout							
	not		Yes		p	OR	95% CI	
	n	%	n	%			l.inf	l.sup
Comorbidities	59	47.2%	383	69.8%	,000**	2,581	1,738	3,833
HTN	20	16.0%	203	37.0%	,000**	3,080	1,852	5,122
ClC	3	2.4%	22	4.0%	,391	-	-	-
ICC	4	3.2%	24	4.4%	,554	-	-	-
AF	1	0.8%	41	7.5%	.005**	10,008	1,363	73,463
IVC	2	1.6%	27	4.9%	.099	-	-	-
Other af . cardio-vasc	10	8.0%	53	9.7%	,566	-	-	-
High CV risk	3	2.4%	7	1.3%	,405	-	-	-
Stroke	1	0.8%	8	1.5%	1,000	-	-	-
DZ type II	3	2.4%	90	16.4%	,000**	7,974	2,481	25,627
Obesity	4	3.2%	17	3.1%	1,000	-	-	-
Bronchial asthma	4	3.2%	10	1.8%	,306	-	-	-
Af . respiratory	3	2.4%	21	3.8%	,596	-	-	-
Af . digestive	8	6.4%	49	8.9%	,360	-	-	-
Af . liver	11	8.8%	47	8.6%	,931	-	-	-
Af . kidney	4	3.2%	50	9.1%	.028*	3,031	1,074	8,555
Anemia	2	1.6%	17	3.1%	,551	-	-	-
Thrombocytopenia	0	0.0%	7	1.3%	,359	-	-	-
Dyslipidemia	1	0.8%	9	1.6%	,698	-	-	-
Af . thyroid	3	2.4%	28	5.1%	,193	-	-	-
Af . genital	1	0.8%	18	3.3%	,226	-	-	-
Af . psychiatric	6	4.8%	7	1.3%	,020*	,256	.085	,776
Neoplasm	4	3.2%	2. 3	4.2%	,611	-	-	-
Other	10	8.0%	71	12.9%	,126	-	-	-

CONCLUSIONS:

There are certain correlations between the symptoms noticed in patients, their comorbidities and the appearance of lung changes on CT, respectively febrile or afebrile evolution. Among the characteristic symptoms of COVID-19, patients with comorbidities present more frequently cough, physical asthenia, inappetence and other than chest pain compared to those without comorbidities.

Also, the symptoms present in significantly increased percentages in patients with modified CT compared to the others were chest pain, cough, fever, physical asthenia and loss of appetite, and the characteristic comorbidities were HTN, AIF, DM type II and renal diseases; however, the

multivariate analysis identifies 4 significant predictors for the occurrence of pulmonary complications, namely age over 60 years, the presence of cough, at least 2 cumulative symptoms and type II diabetes.

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