Research Article

COVID-19 – the challenge to treat a disease and not a positive RT-PCR test

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Abstract

The new pandemic disease COVID is quick spread worldwide.The primary method used for diagnosing of COVID-19 is detecting viral nucleic acids. The main problem with RT-PCR test is the false negative results. The negative RT-PCR does not exclude a SARS-CoV-2 infection and this method should not be used as the only diagnostic criteria. The RT-PCR result does not change the complex treatment of the disease. The aim of the current study is to compare the four groups clinical cases of the different parameters: RT-PCR test, rapid test, clinical picture, laboratory tests as hematology, inflammatory markers, coagulation status and chemistry and imaging examinations: Chest X-ray at and Chest CT scan. Complex therapeutic approach has been implemented: antibiotic, inflammatory, anticoagulants, oxygen therapy, hepatoprotectors, antimycotics, fibrinolytics, probiotics, essential oils, vitamins. During the follow-up period, a tendency for significant reduction and resorption of the pulmonary changes on the CT scans has been seen.

Keywords

Introduction

COVID-19 was identified as a disease in the city of Wuhan, province of Hubei, China in December 2019, when a group of patients were hospitalized with nonspecific symptoms such as high temperature, caught and dyspnea. Specific CT findings in the lungs of all these patients were found, suggesting the presence of atypical pneumonia. The additional analysis of the nucleic acids of known pathogens using polymerase chain reaction (PCR) was negative, thus the causative agent of pneumonia remained unknown. On the 10th January 2020 a bronchoalveolar lavage sample from a patient was analyzed and a new pathogen was identified resembling the genetic sequencing of a Betacoronavirus B. Approximately 80%, 50%, and 96% coincidence between the new virus and the genomes of SARS-CoV, MERS-CoV, and BAT-CoV RaTG13 (bat coronavirus) was established. On the 11th February 2020 the World Health Organization officially named the new disease COVID-19 and its causative agent – SARS-CoV-2. The quick spread of the new disease worldwide turned to be world health threat and challenge of any health system. As a consequence, a month later, the WHO declared COVID-19 a pandemic (Abbasi-Oshaghi et al. 2020; Cascella et al. 2020; Guan et al. 2020; Udugama et al. 2020; Wu et al. 2020; Zitek 2020).

The clinical presentation of COVID-19 is nonspecific, and there is no pathognomonic symptom to be used for diagnostic purposes. Guan et al. report febrile state in 44% of 199 patients at hospitalization; and 89% of them developed

it later during hospitalization (Guan et al. 2020). A representative extract of the study shows that in 68% of patients cough is the main symptom together with fatigue (38%), shortness of breath (35%) and expectoration (34%). All of these symptoms are typical for the entire spectrum of acute respiratory diseases (Cevik et al. 2020; Kim et al. 2020; Mizumoto et al. 2020; Shen et al. 2020; Wu Z et al. 2020).

Another characteristic feature of is the variability of the clinical presentation – some patients remain completely asymptomatic, while others develop severe forms of the disease with rapidly progressing pulmonary insufficiency, ARDS and multiorgan failure with fatal outcome. The infection is particularly dangerous for patients with concomitant diseases, immunocompromised and elder patients (Cevik et al. 2020; Mizumoto et al. 2020; Shen et al. 2020).

Symptoms may appear 2–14 days after exposure to the virus, ranging from mild symptoms to severe illness, especially in patients with cardiovascular diseases and after cardiac surgery (Abedinov et al. 2018). Preexisting cardiovascular diseases and cases after cardiac surgery (Abedinov et al. 2019a; Abedinov et al. 2019b; Tsaryanski et al. 2013b) are one of the very often risk factors, associated with worse outcomes and increased risk of death in patients with COVID-19. Very often mechanical abdominal ventilation is applied in patients with Covid 19 with acute hypoxic respiratory insufficiency like after cardiac surgery (Tsaryanski et al. 2013a, Tsaryanski et al. 2014).

The studies show that compared with SARS, MERS and influenza virus, SARS-CoV2 is spread more rapidly: partially due to the globalization of the human population, but also due to high virus variability. As a consequence, a significant portion of the population was affected promptly by the new disease (Kageyama et al. 2003; Cevik et al. 2020; Udugama et al. 2020).

The necessity of early start of treatment, epidemiological control and identification of severe forms, requires defining of the main diagnostic steps that could be used by the clinicians:

1. Detailed anamnesis with epidemiological focus and physical examination of the patient.
2. Complete laboratory tests, mainly: hematology, chemistry, inflammatory markers, coagulation status and ferritin.
3. Imaging examinations – pulmonary X-ray and CT.
4. Differential diagnostic with the other respiratory diseases
5. RT-PCR for confirmation of the diagnosis.

Serological tests for antibodies, the expression of the immune response to SARS-CoV-2 infection, can also be used in the diagnostic process. The positive result proves that the patient has "met" the virus. IgM antibodies represent active or recent infection. IgG antibodies become positive later during the infection and indicate long-term infection, however a recent infection cannot be completely overruled, especially in case IgM antibodies are also detected. In these later cases the patient can still be contagious – pathogen-carrier and, respectively, contagious. In viral infections IgG antibodies usually persist longer than IgM antibodies and ensure protection against re-infection. However, this is not yet proven to be the case for the SARS-CoV-2 infection (Poon et al. 2003; Abbasi-Oshaghi et al. 2020; Cascella et al. 2020; Guan et al. 2020; Grenache et al. 2020; Li et al. 2020; Yang et al. 2020; Wang et al. 2020; Wu Z et al. 2020; Zitek 2020).

Knowledge about the virus structure is required to be able to clarify the role of the RT-PCR test in the diagnostic approach. The genome of SARS-CoV-2 ranges from 27 to 32 kb It's proved that the CoV contains variable number (6–11) open reading frames (ORF). Two thirds of the viral RNA, located mainly in the first ORF – (ORF1a/b) participates in the translation of two polypeptides, pp1a and pp1ab, and codes 16 nonstructural proteins (NSP). The rest of the ORF code accessory and structural proteins. The main four structural proteins of SARS-CoV-2 are S-glycoprotein or spike protein; small E-protein (envelope protein); M-protein (matrix-protein) and N-protein (nucleocapsid proteins). The S-protein contains three main sections: large ectodomain, transmembrane "anchor" and short intracellular "tail They play a major role in the binding of the virus to the host-cells. The ectodomain contains two subunits – S1 (receptor binding subunit) and S2 (membrane fusion subunit). The name"coronavirus" was first used by June Almeida and David Tyrrell, and comes from the Latin "corona", "crown" wreath" and refers to the characteristic appearance of the virions on electron microscopy, resembling of the solar corona. The SARS-CoV2 genome contains as well several additional proteins, which inhibit the host innate immune response (Kageyama et al. 2003; Lim et al. 2016; Sexton et al. 2016; Schoeman and Fielding 2019; Shen et al. 2019; Wrapp et al. 2020; Wu A. et al. 2020; Pan et al. 2020; Xi et al. 2020; Yang et al. 2020).

The main method for diagnosing COVID-19 is the detection of nucleic acids. Several kits for SARS-CoV-2 detection via PCR (PT-PCT) are developed. RT-PCReaction represents reverse transcription of SARS-CoV-2 RNA into a complementary DNA (cDNA) and amplification of specific DNA targets (Poon et al. 2003; Tahamtan and Ardebili 2020).

In the genome of the viruses belonging to the SARS strain three conservative sequencing are detected: 1) *RdRP* gene (in ORF1ab region); 2) *E* gene and 3) *N* gene. The first two have high analytical sensitivity of detection (technical limit of respectively 3.6 and 3.9 copies per reaction), while the *N* gene possesses a lower analytical sensitivity of detection (8.3 copies/reaction). The World Health Organization recommends detection of at least two regions of the viral genome for confirmation of results. For example, screening for , followed by search for *RdRP* for confirmation. In case of a positive result for *N* gene and negative for *RdRP* gene, it's recommended additional examination (antibodies, sequencing) for final confirmation (Hui et al. 2004; Wu A. et al. 2020; Yang et al. 2020).

The PC Reaction itself is developed such that two primers are used: one is specific for the large group of coronaviruses, including SARS-CoV-2, and the second one is specific only for SARS-CoV-2. Following the optimization of the conditions for the reaction, the actual conductance of the PCR is done. The RT-PC Reaction can be performed in one or two steps. In the first case, the reverse transcription and amplification are done together, which ensures quick results. However, due to the difficulties in the optimization of simultaneously conducted two reactions, the outcome is a lower level of target amplicon. In the second case, the two reactions are performed sequentially, which provides higher sensitivity but takes more time and requires optimization of some additional parameters. It's also critical the controls to be carefully chosen, so that accurateness and reliability of the test is ensured (Freeman et al. 1999; Kageyama et al. 2003; Wang et al. 2020; Wu A. et al. 2020; Xi et al. 2020).

There is a variability of the examinations based on the viral burden of upper (URA) and lower (LRA) respiratory airways of different patients during different days of the disease course. For example, in the initially PCR-positive patients, samples from URA on day 18th and from LRA on day 20th of the disease, the PCR examination does not detect viral burden. A sample from the URA taken on day 25, the PCR is positive for *RdRp* and *E* genes. The time of detection of the first positive samples during the disease also varies across different patients. These data must be accounted for when interpreting the laboratory results (Wong et al. 2005; Pan et al. 2020).

The PCR method has become an accessible examination for virus identification. This contributes for the possibility of early diagnostics in complete lack of symptoms. In many of the affected countries, the PCR tests for coronavirus have become the gold standard and main method for control of morbidity. In the mass testing nasopharyngeal and oropharyngeal samples are used, however, it be accounted for that there is still not sufficient published evidence for the sensitivity and specificity of the RT-PCR testing. In vitro data suggest that the RT-PCR tests are highly specific for SARS_coV and do not become positive in the presence of other respiratory viruses. Similar to that, the in vitro sensitivity of the test is high, but these results are disputable in clinical practice and in vivo testing (Freeman et al. 1999; Kageyama et al. 2003; Wong et al. 2005).

The main problem in the use of the RT-PCR methodology is the risk of false negative results. In the clinical practice there are cases with typical clinical characteristics and specific CT-scan changes, but with negative PCR test results. Therefore, the negative RT-PCR test does not exclude the presence of coronavirus infection and should not be used as a single criterion for diagnostic purposes. The PCR result does not change the complex therapeutic approach as there is no etiological treatment of SARS-CoV infection yet. Thus can be concluded that the role of the positive PCR-test is predominant in the epidemiological control of the disease, than in the diagnostics and treatment of the patient (Freeman et al. 1999; Hui et al. 2004; Xi et al. 2020).

The aim of the current study is to compare the four groups clinical cases of the different parameters: RT-PCR test, rapid test, clinical picture, laboratory tests as hematology, inflammatory markers, coagulation status and chemistry and imaging examinations: Chest X-ray at and Chest CT scan.

Clinical case and methods

In this study clinical cases for four groups of patients at age in the range 48–56 years, were presented. The published results were concerning 40 participants in the trial. All of the clinical trials occurred in UMHATM „Pirogov". Patients were hospitalized and treated due to atypical pneumonia. Clinical cases were assessed and compared according to the above-mentioned diagnostic criteria for SARS-CoV2 infection. The positive RT-PCR test was not registered in two of the patients despite the established epidemiological connection. Despite the lack of proven etiological causative agent, the patients were isolated and treated with the same therapeutic scheme as the patients with proven SARS-CoV2 infection. Laboratory tests, radiography and computed tomography were used.

Results and discussion

In Table 1 are presented data for RT-PCR test, rapid test, clinical picture and concomitant diseases and on Table 2 are summarized results for hematology, inflammatory markers, coagulation status and chemistry. The imaging examinations for patients are described: Chest X-ray at admission (Table 3) and Chest CT scan (Table 4).

For patient 2 and patient 4 well-marked lumens of the distal bronchi are clear. For patient 3 higher position of the right diaphragm contour is observed.

The imaging examinations for Chest X-ray at different days are included on Table 5.

The parallel review of the clinical cases reveals some peculiarities. In all four patients overlapping clinical symptoms are observed. In all cases epidemiology link is detected. The correlation between the results of the 'rapid' tests and the PCR is interesting. In two of the patients the PCR test is negative while the rapid test (IgG & IgM) is positive. The opposite subordination is also true (Table 1). Considering the presented data, we could suppose that in cases with positive serological tests, the PCR samples are taken in a later stage of the disease development. In the contrary: the PCR-positive patients are most probably with fresh infection. Similarity in type and severity of pulmonary changes on the CT scans of the patients in various stages of the disease development is seen. This is suggesting of the importance of the individual immune response to the virus about disease severity, and indicating that changes are not linked only with the time passed since the infecting. The following laboratory parameters

Table 1. RT-PCR test, a rapid test, clinical picture and concomitant diseases.

	Group 1	Group 2	Group 3	Group 4
Epidemio-logical connection	Medic	Travel to France	Contact with ill person, returned from abroad	Minority
Rapid test (IgM, IgG antibodies)	Negative	Positive (Ig M, Ig G)	Positive (Ig M, Ig G)	Negative
RT-PCR test	Positive	Negative	Negative	Positive
Clinical picture	Febrile above 38 °C, fatigue, loss of appe-tite, shortness of breath	Febrile below 38 °C, dry cough, muscle aches, fatigue, loss of appetite	Febrile above 38 °C, fatigue, muscle aches, cough, no shortness of breath	Febrile below 38 °C shortness of breath, cough, dizziness
Concomitant disease	None	Chronic hepatitis B	None	Arterial hypertension
RT-PCR test at discharge	negative	negative	negative	negative
Hospital stay	12 days	10 days	14 days	16 days

Table 2. Laboratory tests: hematology, inflammatory markers, coagulation status, chemistry.

	Group 1	Group 2	Group 3	Group 4
Hematology				
Leucocytes	10.4 g/l	7.54 g/l	8.30 g/l	7.3 g/l
Lymphocytes	1.2 g/l	1.48 g/l	1.90 g/l	1.9 g/l
Granulocytes	8.7 g/l	5.57 g/l	5.0 g/l	5.0 g/l
Erythrocytes	3.80 T/l	3.77 T/l	4.08 T/l	4.62 T/l
Hemoglobin	114 g/l	116 g/L	123 g/L	127 g/L
Hematocrit	0.34 l/l	1.34 l/l	0.37 l/l	0.38 l/l
Platelets	560 g/l	316 g/l	436 g/l	396 g/l
Inflammatory markers				
CRP	27.35	19.5	27.35	4.53
ESR	60 mm/h	52 mm/h	38 mm/h	28 mm/h
Coagulation status				
d-dimer	176 ng/ml	476 ng/ml	736 ng/ml	-
Fibrinogen	6.40 g/l	-	7.60 g/l	-
Chemistry				
ASAT	46 U/I	158 U/I	104 U/I	47 U/I
ALAT	37 U/l	183 U/l	84 U/l	37 U/l
LDH	393 U/l	375 U/l	412 U/l	389 U/l
Ferritin	688.20 ng/ml	529 ng/ml	368 ng/ml	453 ng/ml

Table 3. Imaging examinations for patients: Chest X-ray at admission.

Group 1	Both lungs have lower opacity with initial peripheral interstitial edema, more expressed in the right lung. Peribronchial changes, expanded lungs, clearly visible costophrenic angles, pleural adhesions in the left base and normal for the age configuration of cardiovascular structures are detected.
Group 2 Group 3	There are seen zones with reduced parenchymal opacity, type "ground glass opacification" bilateral basal and in the right upper pulmonary field, sharp and well visible diaphragm contours and clearly visible costophrenic angles. At polypositioning examination, the changes are tracked subpleural. Widened interlobular septal lines are sutuated bilaterally, in the axillary zones.
Groups 2, 3, 4	X-ray data show interstitial inflammatory changes, most probably with atypical viral genesis with branching opacities from the hilus shadows toward zones with more consolidated shadowing, mediastinum situated in the middle.
Group 4	There are observed diffuse compacted and reticulate increased interstitial structure of the lung parenchyma, more expressed on the right side, decreased parenchymal opacity axillary – type "ground glass opacification," extended interlobular septal lines axillary and blurred costophrenic angles.

Table 4. Imaging examinations for patients: Chest CT scan.

Group 1	There are observed data for various in size focal "ground-glass opacifications" in the pulmonary parenchyma of segments 1, 2, 3, 4, 5, 8 and 9 bilateral, reaching subpleural areas and some delimited by the interlobar pleura. In segments 6 and 10 bilateral, changes with the same structure are seen, but with tendency for confluence and formation of patchy structure with underlined thickening of the inter-and intralobular septs. Widened bronchi and vessels in the affected regions of segments 6 and 10 are visible. The changes detected in the pulmonary parenchyma resemble atypical pneumonia with viral genesis. Lymph nodes are with size of 12 mm around the trachea and no data for pleural effusion are seen.
Group 2	No CT data for enlarged lymph nodes bilateral are seen. In lungs, focal "ground-glass opacifications" in the pulmonary parenchyma of segments 2 and 3 in the right side and segments 1, 2 and 4 in the left, situated axillary and reaching the subpleural zones and marked by the interlobal pleura is observed. Bilateral dorsal and peripheral axillar, mainly in segments 6, 9 and 10 extensive "ground-glass opacifications" changes with crazy-paving, with marked thickening of the inter and intralobular septs are visible. Changes are marked by the interlobal pleura cranially. Mediastinum is without pathological changes with no significantly enlar-ged (above 10 mm) mediastinal lymph nodes. Trachea and main bronchi are clear, without data for compression or dislocation. Pleura is with no effusion. Spondylosis changes in the thoracic part of the spine are seen. CT data show changes in the pulmonary parenchyma indicative for atypical pneumonia with viral origin.
Group 4	CT examination of the thorax detects various focal "ground-glass opacifications" with expressed thickening of the inter and intralobular septs in the lung parenchyma bilateral, in all segments, reaching the subleural zones and marked by the interlobal pleura, situated both centrally and peripherally. Tendency for merging of the separate foci exists. Data for early changes in the lung parenchyma representative for atypical pneumonia with viral origin are visible and no data for enlarged lymph nodes or pleural effusion are seen.

Table 5. Imaging examinations for patients – Chest X-ray at different days.

	Group 1
Day 7	In comparison with the previous X-ray examination a worsening of the radiological findings is seen.
	Group 2
Day 7	Both lungs are with normal opacity. There are observed: enhanced and rough interstitial lung pattern and branching and small nodular opacities in the distal parts, expanded lungs, shadowing type "ground-glass opacifications" in the right axillary zone with lower edge the small interlobe and clearly visible costophrenic angles. The findings are worsening in comparison with those at admission. Cardiovascular structures are normal for the age configuration.
Day 24	Bilateral expanded lungs without X-ray data for infiltrative changes are detected. There are observed: hila – non-enlarged and normal structure, clearly visible costophrenic angles, mediastinum situated in the middle. Cardiovascular structures are normal for the age configuration.
	Group 3
Day 7	In comparison with the previous X-ray examination, the changes described in the left axillar and subpleural zones have decreased in size, but the have higher intensity. The described finding is most probably due to the formation of fibrosis along the interstitial structures. In the right axillar zone the changes in the parenchyma show a tendency for consolidation. There are visible: sharp and well visible diaphragm contours, notable relaxation of the right diaphragm contour, thickening of the interlobal pleura in the right side, clearly visible diaphragm contours and costophrenic angels and mediastinum situated in the middle.
	Group 4
Day 9	In comparison with the previous X-ray examination, the described changes have decreased in size, but are more compact. Cardiac structures are situated in the middle.
Day 13	There are no significant changes compared with the previous X-rays. There are detected persistent small "ground glass opacification" in the right, well marked interstitial and hilus structure, blurred diaphragm contours from breathing and no data for hydro- or pneumothorax.
Day 41	Expanded lungs, massive bilateral fibrotic changes, more expressed in the basal left zone are detected. In comparison with the X-day done on 11 May the infiltrative axillar shadows are significantly resorbed. There are observed: clearly visible costophrenic angles. Cardiovascular structures are situated in the middle A CT examination is needed for a more precise analysis.

Table 6. Imaging examinations for patients 1 and 2 for Chest CT scan at different days.

	Chest CT scan on day 10 for Group 1 and on day 24 and day 57 for Group 2
	There is observed mediastinum without pathological changes, single bifurcation lymph nodes up to 8 mm – non-significantly enlarged, clear,trachea and main bronchi, without data for compression or dislocation and no data for Pleura and pericardial effusion. CT data show changes in the pulmonary parenchyma indicative of atypical pneumonia with viral origin in the initial stage of resorption with formation of pulmonary fibrosis.
	Group 1
Day 10	In comparison with the previous CT scan dated Apr 13, 2020, bilateral changes "ground-glass opacifications" were resorbed to a significant extend, and in these zones irregular reticular opacities, as well as irregular zones of parenchymal consolidation were seen, mainly in the dorsal areas bilaterally. Spondylosis changes in the thoracic portion of the spine are observed.
Chest CT scan 32 days post discharge	In comparison with the previous CT scan, almost complete resorption of the changes in the pulmonary parenchyma is seen bilaterally. On the left, in the parenchyma of the 9th to 10th lung segment, there is a focal zone, a type of frosted glass with a mosaic structure /crazy paving/, with an axial size of 59.3/44.5 mm - most likely a new one. There are no pleural effusions bilaterally. The mediastinum normally presents for age, with no pathological changes. The lymph nodes persist paratracheally, subcarinally, paraortally, perihilerally to the left and axillary bilaterally, with a maximum size of 11 mm. Preserved integrity and density of the covered bones is observed.
	Group 2
Day 24	In lung changes "ground-glass opacifications" type are seen in the bilateral peripheral, situated axillary an dorsal, reaching to the subpleural zones and deli-mited by the interlobar pleura. In the dorsobasal segments massive irregular thickening, as well as irregular foci of parenchymal consolidation are detected.
Day 57	In comparison with the previous CT scan, the bilateral massive reticular thickenings, as well as the irregular in form foci of consolidation of the parenchyma are now resorbed to a significant extend. Single irregular reticular interstitial thickening, as well as discrete changes type "ground-glass opacifications" are detected bilaterally in the basal zones and in segments 3 and 6.

Table 7. Imaging examinations for patients 3 and 4 for Chest CT scan at differents days.

Day	Group 3
Day 10	There are detecred: in lungs – focal changes type "ground glass opacification" in the parenchyma, situated bilateral in the axillar zones, more expressed in the lower lobes, thickening of the inter- and intralobular septs, bilateral parenchymal consolidation in the dorsal zones. Mediastinum is without pathological changes and with no significantly enlarged (above 10 mm) mediastinal lymph nodes. Trachea and main bronchi are clear, without data for compression or dislocation. Pleura is without data for effusion. CT data for changes in the pulmonary parenchyma indicative for atypical pneumonia with viral origin.
Day 72	Without CT data for enlarged axillar lymph nodes bilateral. Lungs parenchyma, without pathological changes. Bilateral subpleural discrete changes type 'ground glass opacification' with lower intensity in comparison with the previous examination. Places with fibrotic changes and crazy paving. Mediastinum is without pathological changes. Trachea and main bronchi are clear, without compression or dislocation. Pleura and pericardium are without data for effusion. Not significant lymphadenomegaly is detected.
	Group 4
Day 42	There is dynamic in the shadows, expressed in reverse development of the of the foci of consolidation, situated in the peripheral lung zones bilateral, most intense in the middle and lower lung lobes. There are significant reverse development in regard to the thickening of the interlobular septs and still remaining scattered "ground-glass opacifications" changes in all lung segments bilateral, but significantly smaller in size and with less intensity. Atypical interstitial pneumonia in the stage of resorption is observed.

can be indicated as predictors of disease severity: elevated transaminases, d-dimers and fibrinogen, high CRP, lymphocytopenia, elevated LDH and ferritin (Table 2).

For an optimal recovery in all patients, the necessary hospital stay is over 10 days. Complex therapeutic approach has been implemented in all four cases, consisting of: symptomatic and supportive medicines, antibiotic treatment for preventing superimposed bacterial infections, control of inflammation, anticoagulant and stress ulcer prophylaxis, oxygen therapy, hepatoprotective treatment, antimycotics, probiotics, essential (ethereal) oils, vitamins, intravenous fluids, prolonged intake of food sup-

plements with fibrinolytic activity. In addition were given bronchodilators to patient 3 and antiemetics to patient 4.

The imaging examinations for Chest CT scan at different days are presented for patients 1 and 2 (Table 6) and for patients 3 and 4 (Table 7).

In all presented cases the outcome of the disease is favorable. During the follow-up period, a tendency for significant reduction and resorption of the pulmonary changes on the CT scans has been seen. All four patients are with good general condition and without reduction of physical capacity. At discharge and during the follow-up all patients were with negative PCR-tests.

Conclusion

RT-PCR tests should be carefully interpreted. Negative results from oro- and nasopharyngeal PCR tests, combined with clinical, laboratory and radiology changes indicating possible SARR-CoV2 infection, the diagnosis of COVID 19 cannot be overruled. The attention and efforts of the good clinician should be directed towards the treatment of the disease rather than the positive PCR test. The following laboratory parameters can be indicated as predictors of disease severity: elevated transaminases, d-dimers and fibrinogen, high CRP, lymphocytopenia, elevated LDH and ferritin. The fight against COVID 19 requires complete dedication and significant efforts from the treating physician, especially in the conditions of lack of etiological treatment and constantly changing guidance and recommendations for treatment. The basic clinical postulates remain on the forefront despite the new for the mankind disease.

Acknowledgements

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