ISSN print: 1224-5984
ISSN online: 2248-3942

Rom Biotechnol Lett. 2021; 26(2): 2560-2565
doi: 10.25083/rbl/26.2/2560.2565

Received for publication, October, 28, 2020
Accepted, December, 9, 2020

Original paper

The Consistency between Covid-19 RT-PCR and IgM/IgG Quick tests results

IRINA-ANCA EREMIA[1,2#], ADRIANA BIDICĂ[2], REMUS-IULIAN NICA[3], EUGEN RADU[1,2], CĂTĂLIN-FLORIN CÎRSTOIU[1,2], CORINA-SILVIA POP[1,2], DANUT CIMPONERIU[4], SILVIA NICA[1,2#]

[1]"Carol Davila" University of Medicine and Pharmacy Bucharest, Faculty of Medicine, Bucharest, Romania
[2]Bucharest University Emergency Hospital, Bucharest, Romania
[3]Central Military Emergency University Hospital "Dr. Carol Davila", Bucharest, Romania
[4]University of Bucharest, Faculty of Biology, Bucharest, Romania

[#]Authors' contribution: Eremia Irina-Anca and Nica Silvia equally contributed to the manuscript

Abstract

The aim of this retrospective study was to analyze the results of tests for SARS-CoV-2 performed during 07.04.2020- 20.06.2020 in the Department of the Emergency from Bucharest University Emergency Hospital.

We detected 173 men and 133 women that were tested with both RT-PCR and serologic tests. The results were concordant for 287 samples (93,8%) that were collected from subjects for whom the diagnosis of COVID-19 was subsequently confirmed (10) or infirmed (277). We found that the most frequent signs and symptoms of patients with COVID-19 were at the respiratory (e.g. dyspnea), neurological (e.g. vertigo, cephalgia) and gastrointestinal (e.g. abdominal pain, vomiting, high volume of the abdomen) systems. There was no situation with positive RT-PCR and IgG and negative IgM results.

In our study the RT-PCR and quick serological tests were concordant in 93,8% of cases. The combination of RT-PCR and serological testing can enhance the accuracy of COVID-19 diagnosis.

Keywords SARS-CoV-2, RT-PCR, IgM/IgG serology tests.

To cite this article: EREMIA IA, BIDICĂ A, NICA RI, RADU E, CÎRSTOIU CF, POP CS, CIMPONERIU C, NICA S. The Consistency between Covid-19 RT-PCR and IgM/IgG Quick tests results. *Rom Biotechnol Lett*. 2021; 26(2): 2560-2565. DOI: 10.25083/rbl/26.2/2560.2565

*Corresponding author: NICA SILVIA, Bucharest University Emergency Hospital, 169, Splaiul Independentei, 050098, District 5, Bucharest, Romania
E-mail: silvia.nica@umfcd.ro

Introduction

Since the beginning of 2020, mankind has been facing a new virus which belongs to the beta-coronaviridae group, called SARS-CoV-2 (JIN Y, 2019). After an incubation period between 2 and 14 days, it can determine a disease named COVID-19. The disease is characterized mostly by respiratory symptoms and, in some cases, by gastro-intestinal and neurological manifestations (TANG YW, 2020).

SARS-CoV-2 testing can be carried out through two main ways: detection of the viral RNA genome based on RT-PCR techniques or serological detection of specific type M (IgM) and type G (IgG) immunoglobulins (TANG YW, 2020; GUO L, 2020). The RT-PCR testing has the advantage of sensibility. Thus, it can be used to detect viral RNA, even if the viral titer is very low, as in the nasopharyngeal swabs (EMERY SL, 2004). Consequently, the PCR molecular biology techniques can identify most of the infected individuals since the very first days of infection. A negative result does not overrule the SARS-CoV-2 infection (e.g. the viral titer is below the detection limit of the method or the sample is not compliant for genetic testing) and therefore it should not represent the sole criteria which guides the therapeutic strategy. The IgM-IgG combined assay has better utility and sensitivity compared with a single IgM or IgG test and can be used for the rapid screening of SARS-CoV-2 carriers, symptomatic or asymptomatic (Criteria to Guide Evaluation and Laboratory Testing for COVID-19, 2020). However, it is not exactly known how fast the body's immune response appears by producing antibodies, for how long these antibodies persist in the blood, if every infected individual produces detectable amount of antibodies or if their titer is correlated to the symptoms and what are the bases for the inter individual differences regarding these features (LI Z, 2020).

The purpose of this retrospective study was to analyze the results of tests for SARS-CoV-2 performed during 07.04.2020 - 20.06.2020 in the Bucharest University Emergency Hospital.

Materials and Methods

For this retrospective study we queried the archive of Department of the Emergency from Bucharest University Emergency Hospital for subjects who were tested for SARS-CoV-2 between 07.04.2020 - 20.06.2020. We identified subjects that were tested by RT-PCR (n=3151) or using both RT-PCR and serologic tests (n=306).

Viral RNA was isolated using an automated system (Qiagen QIAsymphony SP) and CE-IVD reagents (QIAsymphony DSP Virus/Pathogen Midi kit, Qiagen, Hilden, Germany) from naso- and oropharyngeal swabs in VTM medium. Reverse transcription and real-time PCR target detection was performed using one the following reagent kits: Seegene Allplex 2019-nCov Assay (Seegene Inc, Seoul, Republic of Korea), PowerCheck 2019-nCoV Real-Time PCR Kit (Kogene Biotech, Seoul, Republic of Korea) or ViroReal Kit SARS-CoV-2 & SARS (ingenetix GmbH, Vienna, Austria). For data acquisition and analysis we used Roche LightCycler 480 II (Roche Applied Sciences, Penzberg, Germany) or Bio-Rad CFX96 Touch (Bio-Rad, California, USA) real-time PCR systems.

Serology tests to detect the presence of IgG-IgM antibodies to SARS-CoV-2 was performed with quick SARS-CoV-2 Antibody Test (colloidal gold immuno-chromatography).

The clinically and laboratory data for subjects with both tests were analyzed and the subjects were classified as suspicious (according to Guo Liya criteria) (LIYA G, 2020) or confirmed cases (if they have positive molecular tests for SARS-CoV-2, regardless of clinical signs and symptoms) (DEEKS JJ, 2020; *Ghidul de diagnostic în COVID-19*).

Results

In the Department of the Emergency from Bucharest University Emergency Hospital, between 07.04.2020-20.06.2020, 306 (8,9%) subjects were investigated using booth RT-PCR and serologic tests for SARS-CoV-2. This lot consists in 173 men and 133 women (average interval: new born - 91 years old). The distribution by age groups reveals that the bigger share was in the 41-50 and 61-70 years old sub-groups (Figure 1). Molecular and serological tests were concordant for 287 (93,8%) subjects (men: 59%, women: 41%) of which 10 were considered confirmed cases (Table 1).

Table 1. The correlation between COVID-19 status and results for serologically and RT-PCR tests

COVID-19 disease	Test results	PCR	IgM	IgG	Number of samples
Not confirmed	Concordant	-	-	-	277
	Discordant	-	+	+	1
		-	+	-	10
		+	+	-	3
Confirmed	Concordant	+	+	+	7
	Discordant	+	-	-	8

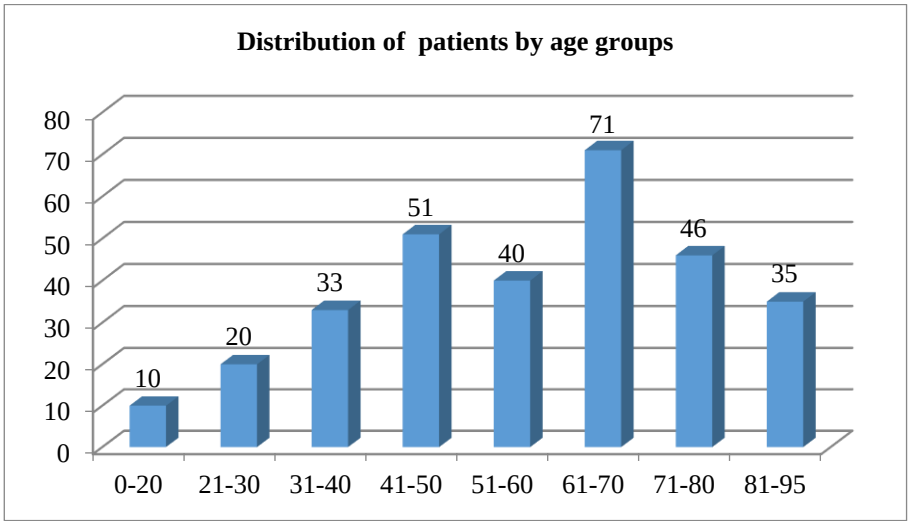

Figure 1. The distribution based on age groups for the studied subjects (n=306).

Overall, in investigated lot 18 (5,87%) cases were confirmed with COVID-19 by molecular and serological tests. Women were more frequent in sub-group of patients with concordant than in those with discordant results at these tests (80% vs. 50%). The age of patients with concordant (59,40±17,86 years; 32-88 years old) or discordant (55,88±31,08 years; 1-91 years old) results at these tests were similar (p>0,05). We identified no subject with RT-PCR and IgG positive tests and IgM negative result (Table 1).

The most frequent signs and symptoms of patients with COVID-19 were identified at the respiratory, neurological and gastrointestinal systems. The respiratory signs and symptoms and fever were more common in COVID-19 patients which have RT-PCR "+"and serological "-" results whereas neurological, gastrointestinal and deterioration of general condition were more common in patients with both RT-PCR and serological "+" results (Figure 2).

The fibrinogen levels were similar in patients with both tests "+" (612,5±170,21; range: 360-799) and in those with discordant results (566±184,14; range: 262-744) (p<0,05).

The chest radiograph was available for 14 of the 18 patients with COVID-19. Lung changes have been identified in all cases. The most frequent radiological finding was airspace opacities which were detected in patients with concordant (6 from 7 patients) or discordant (6 from 8 patients) results for molecular and serological tests (Figure 3).

Six patients have different comorbidities: cardiovascular (3) or renal diseases, type 2 diabetes or obesity.

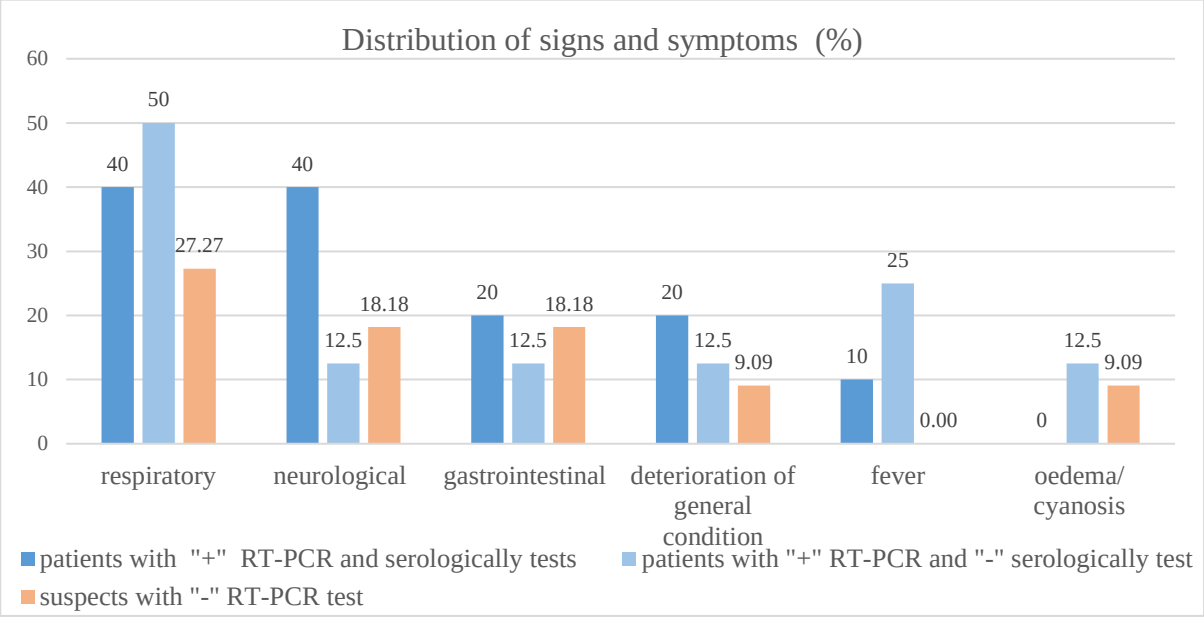

Figure 2. The distribution of the most common groups of signs and symptoms identified in patients with COVID-19 and suspects with discordant results.

Table 2. The most common signs and symptoms of patients confirmed with COVID-19 by RT-PCR "+" test

Patients with "+"RT-PCR test and	Dyspnea	Fatigability	Abdominal pain	High abdominal volume	Vomiting	Cephalgia	Vertigo
"+" serologic test	40%	20%	20%	12,5%	10%	10%	0
"-" serologic test	50%	12,5%	10%	12,5%	0	0	12,5%

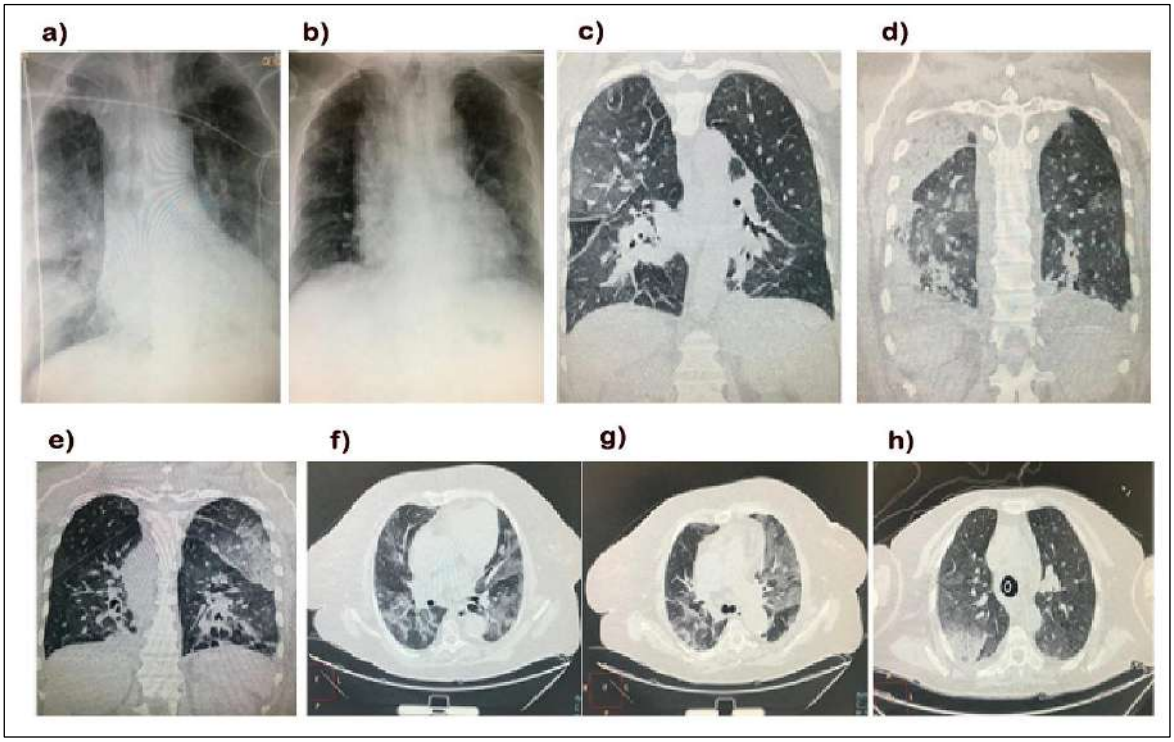

Figure 3. Suggestive radiological and Ct scan images for patients infected with SARS-CoV-2 infections. **a)** Multiple opacities of alveolitis confluent in the lower 2/3 predominantly on the right side; **b)** Alveolo-interstitial densifications URL (upper right lobe) and right basal micronodular infiltrations; **c)** Alveolar filling densifications in URL as matt glass; **d)** Bilateral matt glass densifications; **e)** Densifications presented as matt glass in the medium and inferior right and ILL (inferior left lobe); **f)** 2/3 lower diffuse veil beaches with peripheral distribution, on a background of an emphasized interstitial design; **g)** Superior left love alveolar filling focus, lower and upper lingular; **h)** Bilateral matt glass source of alveolar filling, dominant in the inferior left lobe and inferior right lobe.

Discussion

The specific IgM/IgG antibodies may be undetectable in the first days or weeks of infection with SARS-CoV-2 (GUO L, 2020). Consequently, it is considered that serological tests do not have a primary role in the diagnosis of the disease in the first week since symptom onset (DEEKS JJ, 2020). The accuracy of COVID-19 diagnosis can be enhanced by combination of serological and RT-PCR tests (Criteria to Guide Evaluation and Laboratory Testing for COVID-19; Li Z, 2020; ZHAO J, 2020). Quick serologic tests to detect these antibodies were used during the first period of the pandemic within the recent framework developed by states which faced the start of the pandemics earlier than Romania.

A limited number of tests for SARS-CoV-2 virus were available in Romania during the time covered by this study. Consecutively, they were used primarily for the patients with medical-surgical emergencies, who required immediately treatment measures. From the standpoint of clinical criteria for COVID-19 a high percent of them (~80%) were non-symptomatic. Thus, quick serological tests have been carried out to obtain an indicative information regarding the possible SARS-CoV-2 infection in the detriment of RT-PCR based test which requires few hours for analysis (GUO L, 2020).

In our study RT-PCR and serological tests were concordant for 287 samples (93,8%) that were collected from subjects for whom the diagnosis of COVID-19 was subsequently confirmed (10) or infirmed (277) (Table 1).

The infection with SARS-CoV-2 may be asymptomatic or can predispose to a broad spectrum of respiratory (e.g. dry cough, dyspnea, fever, increased sweating, thoracic pain) or non-respiratory symptoms (e.g. fatigability, myalgia, anosmia and ageusia). The symptomatic forms may have mild, moderate (~80% of the cases) or severe manifestations (e.g. bilateral pneumonia, respiratory failure, acute respiratory distress). There are also patients with gastrointestinal symptoms (e.g. nausea, vomiting, diarrhea), which occur mostly in pediatric patients (TANG YW, 2020; LI Z, 2020; YANG J, 2020). Concordant with previous study we found that the most common signs and symptoms of patients with COVID-19 were at the respiratory (e.g. dyspnea), neurological (e.g. vertigo, cephalgia) and gastrointestinal (e.g. abdominal pain, vomiting, high volume of the abdomen) systems although most of our patients were adults (17 of them were ≥ 22 years old, median age: 61,5). The frequency of these manifestations is different from that reported in other larger studies (LI Z, 2020; LI Y, 2020). The respiratory signs seem to be more common in COVID-19 patients which have RT-PCR "+" and serological "-" results whereas neurological, gastrointestinal were more common in patients with both RT-PCR and serological "+" results (Figure 2).

Fibrinogen is a nonspecific inflammatory marker, and its growth above normal value can be found in many acute diseases or not, as well as in acute episodes of chronic pathologies. Elevated level of fibrinogen was reported to be associated with a progression of COVID-19 to a severe phenotype (ELSHAZLI RM, 2020. Taking into account the fact that the positive patients have been transferred to infectious diseases hospitals, specialized in treating COVID-19 patients, we do not have any deaths reported for this sub-group.

The patients with RT-PCR "+" and serological "-" tests mostly had chest X-rays suggestive for SARS-CoV-2 infections. Radiological and Ct scan images for patients infected with SARS-CoV-2 are represented by alveolar opacities disseminated in both lungs, sometimes only at their periphery, and "veil" images arranged randomly, most often unilaterally.

Most of the 10 subjects with "+" IgM antibodies and "-" RT-PCR have had some COVID-19 suggestive symptoms (fever, shortness of breath, fatigability, cough), but did not have an epidemiological framework (LI Y, 2020).

The combination between COVID-19 infection and other comorbidities, such as hypertension, diabetes mellitus, obesity, COPD, leads to medium and severe forms of disease, some of which have the patient's death as outcome (GUO L, 2020; ESPINOSA OA, 2020; PARVEEN R, 2020). Cardiovascular diseases (3), obesity and type 2 diabetes mellitus were also present in our lot of patients who were Covid-19 positive.

Conclusions

In our study the RT-PCR and quick serological tests were concordant in 93,8% of cases. The combination of these testing methods can enhance the accuracy of COVID-19 diagnosis especially for cases with mild symptoms or non-symptomatic. The most frequent signs and symptoms of patients with COVID-19 were at the respiratory (e.g. dyspnea), neurological (e.g. vertigo, cephalgia) and gastrointestinal (e.g. abdominal pain, vomiting, high volume of the abdomen) systems had a different distribution in patients with "+" or "-" serological results.

Acknowledgements

This work was partially supported by the Executive Agency for Higher Education, Research, Development and Innovation Funding (UEFISCDI) through grant PN-III-P2-2.1-SOL-2020-0090" Advanced Techniques and Increased Performance in Early Detection of SARS-CoV-2" (POC-SARS-CVo2)".

Conflict of Interest

The authors have no conflict of interest to declare.

References

1. JIN Y, WANG M, ZUO Z, FAN C,, ZUO Z, et al. Diagnostic value and dynamic variance of serum antibody in coronavirus disease 2019. *Int J Infect Dis*. 2020; 94: 49-52. doi: 10.1016/j.ijid.2020.03.065
2 ANG YW, SCHMITZ JE, PERSING DH, STRATTON CW. Laboratory diagnosis of COVID-19: current issues and challenges. *J Clin Microbiol*. 2020; 58(6): e00512-20. doi: 10.1128/JCM.00512-20
3. GUO L, REN L, YANG S, XIAO M et al. Profiling early humoral response to diagnose novel coronavirus disease (COVID-19). *Clin Infect Dis. 2020*. 71(15): 778-785. doi: 10.1093/cid/ciaa310
4. EMERY SL, ERDMAN DD, BOWEN MD, NEWTON BR, et al. Real-time reverse transcription-polymerase chain reaction assay for SARS-associated coronavirus. *Emerg Infect Dis*. 2004; 10(2): 311-316. doi: 10.3201/eid1002.030759
5. Criteria to Guide Evaluation and Laboratory Testing for COVID-19, US Center for Disease Control and Prevention, 2020, https://emergency.cdc.gov/han/2020/HAN00429.asp
6. LI Z, YI Y, LUO X, XIONG N, et al. Development and clinical application of a rapid IgM-IgG combined

antibody test for SARS-CoV-2 infection diagnosis. *J Med Virol*. 2020; 10.1002/jmv.25727. doi: 10.1002/jmv.25727

7. LIYA G, YUGUANG W, JIAN L, HUAIPING Y et al. Studies on viral pneumonia related to novel coronavirus SARS-CoV-2, SARS-CoV, and MERS-CoV: a literature review. *APMIS*. 2020; 128(6): 423-432. doi: 10.1111/apm.13047
8. DEEKS JJ, DINNES J, TAKWOINGI Y, DAVENPORT C et al. Antibody tests for identification of current and past infection with SARS-CoV-2. *Cochrane Database Syst Rev*. 2020; 6(6): CD013652. doi: 10.1002/14651858.CD013652
9. Comisia de Microbiologie Medicală a Ministerului Sănătății, Comisia de Microbiologie Medicală a Colegiului Medicilor din România – Ghidul de diagnostic în COVID-19. https://www.srm.ro/media/2020/04/recomandarea-comisiilor-de-microbiologie-medicala-diagnostic-sars-2.pdf.
10. ZHAO J, YUAN Q, WANG H, LIU W, et al. Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019. *Clin Infect Dis*. 2020; ciaa344. doi: 10.1093/cid/ciaa344
11. LI Y, YAO L, LI J, CHEN L, ET al. Stability issues of RT-PCR testing of SARS-CoV-2 for hospitalized patients clinically diagnosed with COVID-19. *J Med Virol*. 2020. 92(7): 903-908. doi: 10.1002/jmv.25786
12. YANG J, ZHENG Y, GOU X, PU K, et al. Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: a systematic review and meta-analysis. *Int J Infect Dis. 2020*. 94: 91-95. doi: 10.1016/j.ijid.2020.03.017
13. ELSHAZLI RM, TORAIH EA, ELGAML A, EL-MOWAFY M, et al. Diagnostic and prognostic value of hematological and immunological markers in COVID-19 infection: A meta-analysis of 6320 patients. *PLoS One*. 2020; 15(8): e0238160. doi: 10.1371/journal.pone.0238160
14. ESPINOSA OA, ZANETTI ADS, ANTUNES EF, LONGHI FG, ET al. Prevalence of comorbidities in patients and mortality cases affected by SARS-CoV2: a systematic review and meta-analysis. *Rev Inst Med Trop Sao Paulo*. 2020; 62: e43. doi: 10.1590/S1678-9946202062043
15. PARVEEN R, SEHAR N, BAJPAI R, AGARWAL NB. Association of diabetes and hypertension with disease severity in covid-19 patients: A systematic literature review and exploratory meta-analysis. *Diabetes Res Clin Pract*. 2020. 166: 108295. doi: 10.1016/j.diabres.2020.108295