Impact of COVID-19 pandemic on biochemistry laboratory test consumptions and diversity

COVID-19 pandemisinin biyokimya laboratuvarı test tüketimleri ve çeşitliliği üzerindeki etkisi

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ABSTRACT

Introduction: The disease caused by SARS-CoV-2, which the World Health Organization has considered as a pandemic, was named COVID-19 and has since spread worldwide. The COVID-19 pandemic has drastically changed the way we live and work. During events like COVID-19, it is very important to manage resources and supplies correctly in medical laboratories. This article aims to explore the changes in laboratory test demands during the COVID-19 pandemic.

Materials and Methods: The statistics of medical biochemistry laboratory test consumption between the pre-pandemic period (April 2019 - 2020) and the pandemic period (April 2020 - 2021) were evaluated using the hospital information system. Changes in the number of biochemistry tests were given as percentages.

Results: Total specimens received for testing in April 2020-2021 showed a decline of 63.22% compared to April 2019-2020. An increase in test demands of prognostic biomarkers for COVID-19; including fibrinogen, D-dimer, procalcitonin, CRP, troponin I, prealbumin, blood gas analysis was noted in contrast to the overall decline.

Conclusions: It was concluded that it is very important for clinical laboratory managers to be prepared and careful, as significant changes were detected in general routine biochemical test consumptions and COVID-19 prognostic biomarker test requests during the pandemic compared to the pre-pandemic period.

Keywords: COVID-19, laboratory, diagnostics, pandemic.

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ÖZET

Amaç: Dünya Sağlık Örgütü'nün pandemi olarak kabul ettiği SARS-CoV-2'nin neden olduğu hastalığa COVID-19 adı verildi ve o zamandan beri dünya çapında yayıldı. COVID-19 salgını, yaşama ve çalışma şeklimizi büyük ölçüde değiştirdi. COVID-19 gibi olaylar sırasında tıbbi laboratuvarlarda kaynak ve sarf malzemelerinin doğru yönetilmesi çok önemlidir. Bu makale, COVID-19 salgını sırasında laboratuvar test taleplerindeki değişiklikleri araştırmayı amaçlamaktadır.

Metod: Pandemi öncesi dönem (Nisan 2019 - 2020) ile pandemi dönemi (Nisan 2020 - 2021) arasındaki tıbbi biyokimya laboratuvarı test tüketim istatistikleri hastane bilgi sistemi kullanılarak değerlendirildi. Biyokimya test sayısındaki değişimler yüzde olarak verildi.

Bulgular: Nisan 2020-2021'de test için alınan toplam numuneler, Nisan 2019-2020'ye göre %63,22'lik bir düşüş gösterdi. Genel düşüşün aksine COVID-19 için prognostik biyobelirteçler olan fibrinojen, D-dimer, prokalsitonin, CRP, troponin I, prealbümin, kan gazı analizlerinin test taleplerinde artış tespit edildi.

Sonuç: Pandemi sırasında pandemi öncesi döneme kıyasla genel rutin biyokimyasal test tüketimlerinde ve COVID-19 prognostik biyobelirteç test taleplerinde önemli değişiklikler tespit edildiğinden laboratuvar yöneticilerinin hazırlıklı ve dikkatli olmasının çok önemli olduğu sonucuna varıldı.

Anahtar kelimeler: COVID–19, laboratuvar, tanısal testler, pandemi.

INTRODUCTION

The Coronavirus Disease 2019 (COVID-19) was identified as a global pandemic in 2020, which is a respiratory and systemic viral disease. The COVID-19 pandemic has caused changes in the use of healthcare resources, patient care and the clinical laboratories (1).

Identifying critically ill patients early, helps to reduce mortality and improve morbidity. Evaluation of COVID-19 with biochemical tests is very important in the follow-up of the disease and in the evaluation of its severity.

Risk stratification is difficult in patients with COVID-19 as signs and symptoms often lack specificity. The severity of COVID-19 disease can be evaluated with the results of many laboratory tests (2). The hyperinflammatory state caused by SARS-CoV-2 active infection can be evaluated with ferritin and C-reactive protein (CRP) (3,4), D-dimer is gaining importance in relation to disorders of hemostasis mechanisms in COVID-19 patients (5). Cardiac troponin may indicate pulmonary dysfunction or cardiac problems due to Covid-19 infection (6,7).

Also, COVID-19 severity and prognosis may be associated with lactate dehydrogenase (LDH), CRP, ferritin and procalcitonin (8). There is currently a need for reliable biomarkers associated with COVID-19 disease progression in patients with high risk (9).

Clinical laboratories play a critical role in the management of the pandemic (10). Quarantines and restrictions imposed by most countries have affected the course of routine laboratory services (11).

During the pandemic period, the delay of routine healthcare services and changing lifestyle are expected to lead to a significant decrease in routine biochemical testing demands and a rapid increase in testing requests for COVID-19 prognostic biomarkers. In extraordinary times like these, it becomes crucial for lab managers to anticipate changing test consumption and new demands for lab services. This study was planned to determine the changes in laboratory test numbers during the COVID-19 outbreak in our biochemistry laboratory.

MATERIALS AND METHODS

This cross-sectional study was carried out in the of Health Sciences University of Izmir Bozyaka Training and Research Hospital, Medical Biochemistry Laboratory. The study was approved by the ethical committee of the study hospital (08/07/2020, 15345988-

19). We analyzed the biochemistry laboratory test consumption statistics for the pre-pandemic period (1/04/2019 - 1/04/2020) and the pandemic period (1/04/ 2020 - 1/04/2021) using the hospital information system (HIS). These tests were include all routine biochemistry tests, immunochemistry tests, coagulation tests, HbA1c, blood gas analysis, urinalysis, troponin I. Statistics of test numbers were analyzed by months. At the same time, the changes according to the years were calculated. Changes in test numbers were shown as percentages. Data analysis was performed using Microsoft Excel (Microsoft, Washington, US) program.

RESULTS

In April 2020-2021, when the pandemic prevailed, the number of patients and biochemistry laboratory test numbers decreased significantly compared to the previous year. The total specimens received in biochemistry laboratory in pre-pandemic period; between 1/04/2020-1/04/2021 (n = 912009) showed a decline of approximately 63.22% compared to pandemic period; between 1/04/2019-1/04/2020 (n = 576612). An upward increase in COVID-19 prognostic biomarkers was noted in contrast to the overall decline in other tests.

Annual test numbers by months before and during the pandemic was shown in Tables I and II, respectively.

While a significant decrease was detected in the number of routine biochemistry and immunochemistry tests, fibrinogen, D-dimer, procalcitonin, CRP, troponin I, prealbumin, blood gas analysis increased despite the decreasing number of patients. The percentages change in the one-year test numbers and their significances before and during the pandemic are shown in Table III. Changes in the number of tests before and during the pandemic was shown in Figure I.

When the increases and decreases were examined from test to test, it was observed that there was a decrease in all tests in immunochemistry assays. Besides, there was a decrease in all routine biochemistry tests, except a slight increase in prealbumin test numbers 3.8% (3205 vs 3328). While a decrease was detected in emergency biochemistry tests (amylase, creatinine, CK, Cl, total bilirubin, lipase, Ca, AST, ALT, K, Na, glucose), CRP which is requested from the emergency department was increased 17.24% (72168 vs 84608) but there was a 21.01% (64236 vs 50737) decrease in routine CRP tests.

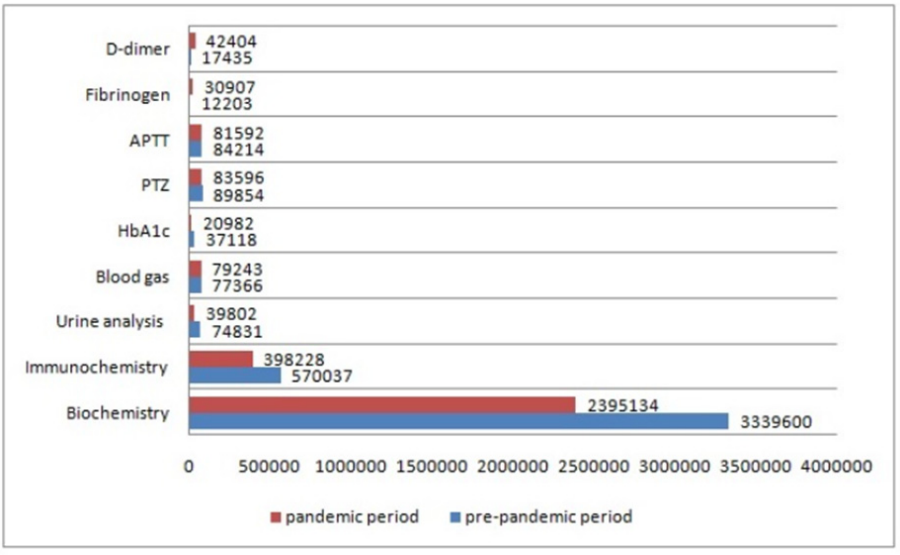

Figure 1. Changes in the number of tests before and during the pandemic

Table 1. Annual test numbers in pre-pandemic period by months.
Tablo 1. Pandemi öncesi dönemde aylara göre yıllık test sayıları.

	Biochemistry	Immune analysis	Urine analysis	Blood gas	HbA1c	PTZ	APTT	Fibrinogen	D-dimer
April 2019	290376	50170	6521	7258	3697	8181	7674	943	1566
May 2019	297958	50208	6457	7468	3935	8434	7858	1135	1750
June 2019	233176	36836	5245	6569	2518	7208	6834	1064	1562
July 2019	307336	50496	7037	6617	3359	7790	7311	936	1496
August 2019	251130	42120	5828	6036	2526	6954	6588	999	1544
September 2019	294337	53239	6906	5563	3374	7045	6624	1006	1412
October 2019	300323	54476	6898	5782	3370	6931	6429	857	1111
November 2019	286109	52217	6682	5695	3010	7100	6591	1003	1314
December 2019	289619	48026	6326	6036	2939	7352	6788	1000	1347
January 2020	299670	51842	6512	7257	3158	8110	7600	1318	1575
February 2020	285695	49906	6603	6549	3391	7895	7417	1070	1399
March 2020	203871	30501	3816	6536	1841	6854	6500	872	1359
TOTAL	3339600	570037	74831	77366	37118	89854	84214	12203	17435

PTZ: prothrombin time
APTT: activated partial thromboplastin time

Table 2. Annual test numbers by months in pandemic period.
Tablo 2. Pandemi döneminde aylara göre yıllık test sayıları.

	Biochemistry	Immune analysis	Urine analysis	Blood gas	HbA1c	PTZ	APTT	Fibrinogen	D-dimer
April 2020	93169	9626	959	5003	317	4258	4123	1183	2383
May 2020	101082	10280	1402	5539	380	4469	4353	1147	1839
June 2019	194180	29445	3651	6065	1832	5989	5730	1302	1835
July2020	205418	31394	3732	6666	1828	6551	6308	1475	2077
August 2020	227156	34293	3811	8258	1765	8383	8131	2949	4183
September 20120	252917	41794	4123	8235	2461	8716	8450	3601	4682
October 2020	228615	39705	3871	6355	2168	7419	7185	2380	3472
November 20120	216197	38588	3122	7042	1733	7980	7790	4194	5499
December 2020	203406	36015	2816	7976	1399	8388	8278	5474	6884
January 2021	201092	35953	3470	6032	1890	6749	6671	2737	3711
February 2021	203995	37681	3535	5417	1970	6738	6652	1881	2504
March 2021	267907	53454	5310	6655	3239	7956	7921	2584	3335
TOTAL	2395134	398228	39802	79243	20982	83596	81592	30907	42404

PTZ: prothrombin time
APTT: activated partial thromboplastin time

Table 3. Changes in the number of tests as a percentage before and during the pandemic and their significances
Tablo 3. Pandemi öncesi ve pandemi sırasında test sayılarının yüzde olarak değişimi ve önemleri

	Biochemistry	Immun analysis	Urine analysis	Blood gas	HbA1c	PTZ	APTT	Fibrinogen	D-dimer
Change (%)	-28.28	-30.14	- 46.81	+2.43	- 43.47	- 6.96	- 3.11	+153.27	+143.21
p	p<0.05	p<0.05	p<0.05	p<0.05	p<0.05	p<0.05	p<0.05	p<0.05	p<0.05

PTZ: prothrombin time
APTT: activated partial thromboplastin time

There was a significant increase in procalcitonin test numbers 63.54% (7073 vs 11567). Troponin I increased by 13.42% (33880 vs 38428). The number of blood gas analysis tests was also increased by 2.42% (77366 vs 79243).

It was observed that the decrease in the number of routine tests during the pandemic process was observed mostly in April and May, the highest increases in Covid-19 biomarker tests were between August to September.

DISCUSSION

The COVID-19 was designated as a pandemic on 11 March 2020 and has created an unprecedented demand for healthcare resources (12,13). Various guidelines have been published focusing on diagnosis and treatment methods in the pandemic. Furthermore, biomarkers were needed to identify high risk patients and to monitor disease progression. With rapid increase in COVID-19 cases, the need for specialized testing, the development of new tests, the management of reagent deficiencies, and the risk of staff shortages due to COVID-19 infection have emerged (14). Biochemical laboratory tests are helpful in diagnosis, staging, prognosis and monitoring of therapeutic interventions in COVID-19 patients. Several studies have reported hematologic and blood chemistry alterations in patients infected by SARS-CoV-2 (15,16).

In this study, we investigated the changes in laboratory test usage. This study demonstrated a significant increase in testing requests for COVID-19 prognostic biomarkers, whereas there was a significant decrease in overall routine biochemical testing requests during the pandemic.

According to our study, the highest percent increase was noted for fibrinogen, followed by D-dimer, procalcitonin, CRP, troponin I, prealbumin and blood gas analysis, which are the laboratory tests related to COVID-19 diagnosis and management. In our hospital, like most institutions, outpatient services were restricted from time to time and elective outpatient surgery procedures were postponed. In this study, it was observed that the decrease in the number of tests during the pandemic process was observed mostly in April and May in 2020, when the restrictions were applied the most strictly. It was determined that the highest fibrinogen and D-Dimer increases were between August to September 2020, the months when the number of COVID-19 positive cases increased the most in our country.

Like our study, Ahmed et al. stated that the total number of samples taken in 2020 was 33% less than in 2019 and an upward increase was noted for COVID-19 prognostic biomarkers in contrast to a decrease in total sample numbers (8). The total samples coming to our biochemistry laboratory in the pre-pandemic period decreased by 63.22% compared to the pandemic period.

Yücel et al. reviewed the biochemistry laboratory test consumption statistics, they found that in April 2020, patient number and biochemistry laboratory test demands decreased significantly compared to April of

the previous year. The average decrease in the number of requests was 68.3%, which was similar to our ratio. During the COVID-19 pandemic their fibrinogen, D-dimer and procalcitonin test demands were increased, the results of this study were similar to ours, but we did a one-year comparison (17).

Thomas et al. found marked changes in coagulation testing. Fibrinogen, D-dimer, prothrombin time (PT), international normalized ratio (INR) and partial thromboplastin time (APTT) test demands were increased (14). Similarly, we found that fibrinogen and D-dimer test demands were increased, but PT and APTT counts were decreased in our study. Fibrinogen and D-dimer tests were the most requested tests in our region in pandemic. The occurrence of coagulopathy in COVID-19 patients is a poor prognostic feature and significantly high D-dimer levels have been observed. Accordingly, it is recommended to closely monitor D-dimer levels in patients. Some other studies also suggest to monitor PT, fibrinogen and platelet counts (18-20).

10-25% of COVID-19 patients requiring hospital care have venous and thromboembolic complications. D-dimer elevations are most common in patients with coagulopathy. Patients with D-dimer concentrations above 1 mg/L have an approximately 18-fold increased risk of death. Fibrinogen concentrations may increase or decrease depending on the stage of disease progression (21). We found in our study that D-Dimer and fibrinogen test requests showed the highest increase compared to the pre-pandemic period.

Thomas et al. detected an increase in the test demands for procalcitonin and LDH, also cardiac troponin T and N-terminal probrain natriuretic peptide. Similarly, we found an increase in the use of procalcitonin and troponin I, but our LDH and proBNP demands were lower in pandemic. The reason for the increased troponin I test requests may be because of myocardial damage which is common in severe COVID-19 patients (22). Elevations in troponin levels have been reported in 7-17% of hospitalized COVID-19 patients (23). We also found that troponin I test demands increased 13.42% in our hospital.

Procalcitonin is used to distinguish bacterial infections from viral infections. Procalcitonin measurements are valuable for demonstrating bacterial superinfections or complications of COVID-19 (24). Procalcitonin values were found to be high in Covid-19 patients who had severe disease. The risk of serious COVID-19 infection associated with elevated procalcitonin reported in a meta-analysis was 5 times higher (25). Consistent with this information we found a remarkable increase in test demands of procalcitonin in pandemic (63.54%).

CRP is an acute phase protein and reflects the hyperinflammatory state caused by active infection with SARS-CoV-2 (3,4). Systemic inflammation can occur resulting in elevated CRP levels (26). We found 17.24% increase in emergency demands of CRP.

In our study, we found 2.42% increase in the number of blood gas analyzes. It has been observed that there has been an increase in the number of blood gas tests due to the frequent occurrence of respiratory failure in COVID-19 patients and the need for blood gas monitoring.

Isolation rules, restrictions, fear of people coming to the hospital due to the risk of contamination, the change in the course of routine services provided in the hospital have caused delays in non-emergency health problems and the decrease in the number of patients has also led to a decrease in the number of tests in pandemic. Although we monitor our laboratory test numbers and expiration dates on a monthly basis, we have had to pay extra attention and take precautions during this process. With the pandemic, all laboratories should show the necessary adaptation and start to take the necessary precautions.

Delays in making new diagnoses may be a health problem other than the pandemic.

Also, the inability of chronic patients to attend regular check-ups may be another problem.

Although acceptance of non-COVID-19 patients continued in our hospital, the number of patients decreased due to restrictions. Due to the diagnosis and follow up of outpatient and inpatient COVID-19 patients, a significant increase in COVID-19-specific test requests has been observed.

Clinical laboratory managers must be very careful and prepared during the pandemic period due to changing testing expenses and possible disruptions in international trade. Due to the decreasing test usage, there may be problems in terms of expiration dates. In addition there may be a stock problem for tests with increased use for COVID-19 patients. Also, delayed healthcare needs will rapidly increase hospital admissions once restrictions are lifted. Therefore, the necessary preparations should be planned in advance by the laboratories.

REFERENCES

1. Jafri L, Ahmed S, Siddiqui I. Impact of COVID-19 on laboratory professionals-A descriptive cross sectional survey at a clinical chemistry laboratory in a developing country. Annals of Medicine and Surgery 2020;57: 70-75.
2. Elena A, Mariia C, Ludovica S, Sara P, Felicia SF, Alberto D, et al. Comprehensive Appraisal of Laboratory Biochemistry Tests as Major Predictors of COVID-19 Severity. Arch Pathol Lab Med. 2020; 144(12):1457-64.
3. Liu F, Li L, Xu M, Wu J, Luo D, Zhu YS, et al. Prognostic value of interleukin-6, C-reactive protein, and procalcitonin in patients with COVID-19. J Clin Virol. 2020;127:104370.
4. Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet. 2020;395(10229):1033–34.
5. Tang N, Li D, Wang X, Sun Z. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. J Thromb Haemost. 2020;18(4):844–7.
6. Lippi G, Lavie CJ, Sanchis-Gomar F. Cardiac troponin I in patients with coronavirus disease 2019 (COVID-19): evidence from a meta-analysis. Prog Cardiovasc Dis. 2020;63(3):390–1.
7. Guo T, Fan Y, Chen M, Wu X, Zhang L, He T, et al. Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19). JAMA Cardiol. 2020;5(7):1–8.
8. Ahmed S , Ghani F . Trend analysis of lab tests requisitions of COVID-19 prognostic biomarkers at a clinical chemistry reference laboratory-an observational study. Ann Med Surg (Lond). 2020;60:522-5.
9. Ponti G, Maccaferri M, Ruini C, Tomasi A, Ozben T. Biomarkers associated with COVID-19 disease progression. Crit. Rev. Clin. Lab Sci. 2020;1-11.
10. G. Lippi, Plebani M. The critical role of laboratory medicine during coronavirus disease 2019 (COVID-19) and other viral outbreaks. Clin. Chem. Lab. Med. 2020;58(7):1063-9.
11. Ahmed S, Jafri L, Majid H, Khan AH, Ghani F, Siddiqui I. Challenges amid COVID-19 times-Review of the changing practices in a clinical chemistry laboratory from a developing country. Annals of Medicine and Surgery 2020;55:300-4.
12. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med. 2020;382:727–33.
13. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. J Emerg Med. 2020;58(4):711–2.
14. Thomas JSD, David RP , David F, Wade LS. Impact of COVID-19 Pandemic on Laboratory Utilization. J Appl Lab Med. 2020;5(6):1194-1205.
15. Zhu W, Xie K, Lu H, Xu L, Zhou S, Fang S. Initial clinical features of suspected Coronavirus Disease 2019 in two emergency departments outside of Hubei, China. J. Med. Virol. 2020;92(9):1525-32.
16. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020;395 (10229):1054-62.
17. Yucel M, Avsar C. The effect of COVID-19 pandemic on biochemistry laboratory test consumption numbers and variety. Turkish Journal of Biochemistry 2020;45(3):1-3.
18. Tang N, Li D, Wang X, Sun Z. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. J Thromb Haemost. 2020;18:844–7.
19. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020; 382:1708-20.
20. Thachil J, Tang N, Gando S, Falanga A, Cattaneo M, Levi M, et al. ISTH interim guidance on recognition and management of coagulopathy in COVID-19. J Thromb Haemost. 2020;18:1023–6.
21. Marcel L, Jecko T, Toshiaki I, Jerrold HL. Coagulation abnormalities and thrombosis in patients with COVID-19. The Lancet Haematol. 2020;7(6):438-40.

22. Lippi G, Plebani M. Laboratory abnormalities in patients with COVID-2019 infection. Clin Chem Lab Med. 2020;58(7):1131-4.

23. Wiersinga WJ, Rhodes A, Cheng AC, Peacock SJ, Prescott HC. Pathophysiology, Transmission, Diagnosis, and Treatment of Coronavirus Disease 2019 (COVID-19): A Review. JAMA. 2020;324(8): 782–93.

24. Lippi G, Plebani M. Procalcitonin in patients with severe coronavirus disease 2019 (COVID-19): a meta-analysis. Clin Chim Acta 2020;505:190-1.

25. Ahmed S, Siddiqui I, Jafri L, Hashmi M, Khan AH, Ghani F. Prospective evaluation of serum procalcitonin in critically ill patients with suspected sepsis-experience from a tertiary care hospital in Pakistan. Ann Med Surg. 2018;35:180–4.

26. Lippi G, Plebani M. The critical role of laboratory medicine during coronavirus disease 2019 (COVID-19) and other viral outbreaks. Clinical Chemistry and Laboratory Medicine (CCLM) 2020; 58(7):1063-9.