Original Article

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Investigation of Drug-Related Problems and Influencing Factors of COVID-19 Patients in Hospital Settings: An observational Study

COVID-19 Hastalarında İlaçla İlişkili Sorunların Belirlenmesi ve İlişkili Faktörlerin İncelenmesi: Gözlemsel Bir Çalışma

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ABSTRACT

Objective: Clinical prognosis of COVID-19 may be severe and unexpected. Patients may quickly progress to respiratory failure, infections, multiple organ dysfunction, and sepsis. The main objective of this study is to investigate the pharmaceutical care need of COVID-19 patients and related factors.

Methods: A prospective observational study was conducted on COVID-19 patients. between September 2020, and May 2021. Patients' demographics, comorbid diseases, prescribed medicine, laboratory findings were recorded. Drug-related problems (DRPs) were identified by a clinical pharmacist according to recent guidelines, UpToDate® clinical decision support system and evidence-based medicine.

Results: The median age of 107 patients was 64 and 50.46% of them were male. The median number of comorbidities was 3[2-4] per patient. The majority of the patient had at least one comorbidity (88.79%) other than COVID-19 and the most frequent comorbidities were hypertension, diabetes mellitus. The total number of DRP recorded as 201 and at least one DRP was

ÖZ

Amaç: COVID-19 enfeksiyonun klinik tablosu ağır ve beklenmedik şekilde seyredebilmektedir. Hastalarda solunum yetmezliği, ikincil enfeksiyonları, çoklu organ yetmezliği ve sepsis tablosu görülebilmektedir. Bu çalışmanın amacı, COVID-19 hastalarında olası ilaçla ilgili sorunları (İLİS) ve ilişkili faktörleri araştırmaktır.

Yöntemler: Eylül 2020 ile Mayıs 2021 tarihleri arasında COVID-19 hastalarının katılımıyla prospektif gözlemsel bir çalışma tasarlanmıştır. Hastaların demografik özellikleri, komorbid hastalıkları, kullandıkları ilaçlar, laboratuvar bulguları kayıt altına alınmıştır. İLİS'lerin belirlenmesi klinik eczacı tarafından güncel kılavuzlara, UpToDate® klinik karar destek sistemlerine göre yapılmıştır.

Bulgular: Toplamda 107 hasta çalışmaya dahil edilmiştir, yaşların medyanı 64 [54,5-76.0] ve %50,46'sı erkek olarak kayıt altına alınmıştır. Medyan komorbidite sayısı 3 [2-4] olduğu gözlemlenmiştir. Hastaların çoğunluğunda COVID-19 dışında en az bir komorbidite (%88,79) mevcuttu ve en sık görülen komorbiditeler Hipertansiyon, Diyabetes Mellitus ve koroner

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seen in 75 out of 107 patients. The median number of DRPs was 2[0-8], respectively. In multivariate model number of comorbidities (OR=1.952; 95% CI: 1.07–3.54, p<0.05), number of medications (OR=1.344; 95% CI: 1.12-1.61, p<0.001), and serum potassium levels (OR=5.252; 95% CI: 1.57–17.56, p<0.001) were the factors related with DRP.

Conclusion: This highlights the DRPs and related factors in COVID 19 patients in hospital settings. Considering unknown features of the infection and multiple medication use, DRPs are likely to occur. It would be beneficial to consider the related factors in order to reduce the number of the DRPs.

Keywords: COVID-19, hospital, clinical pharmacist, Drug-related problems, pharmaceutical care need

arter hastalığı olarak belirlenmiştir. Toplam İLİS sayısı 201 olarak belirlenmiş ve 107 hastanın 75'inde en az bir İLİS görüldü. Medyan İLİS sayısı sırasıyla 2 [0-8] olarak kaydedilmiştir. Çok değişkenli regresyon modeline göre komorbidite sayısı (OR=1.952; %95 CI: 1.07–3.54, p<0.05), ilaç sayısı (OR=1.344; %95 CI: 1.12-1.61, p<0.001) ve serum potasyum seviyeleri (OR=5,252; %95 CI: 1,57–17,56, p<0,001) ile ilişkili faktörler olarak belirlenmiştir.

Sonuç: Bu çalışma COVID 19 hastalarında ilaçla ilgili sorunları ve ilişkili faktörleri incelemektedir. Enfeksiyonun bilinmeyen özellikleri ve ilaç kullanım ihtiyacı göz önüne alındığında İLİS'lerin ortaya çıkması muhtemeldir. İLİS sayısını azaltmak için ilgili faktörleri göz önünde bulundurmak faydalı olacağı kanaatindeyiz.

Anahtar Sözcükler: COVID-19, hastane, klinik eczacı, İlaçla İlgili Sorunlar, farmasötik bakım ihtiyacı

Introduction

Coronavirus disease (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Suspicion of COVID-19 is firstly reported as pneumonia with unknown etiology on December 31th in China [1]. An increase in pneumonia cases detected on 31 December 2019 was identified on January 7th, 2020, as a new Coronavirus that has not previously been detected in humans. After this date, the number of patients increased rapidly, including infected health care professionals. The first case of the COVID-19 in Turkey was confirmed on March, 11th, 2020 [2,3]. Current situation of Turkey on January 13rd, 2022, more than 9.4 million confirmed cases, 82361 death patients and the numbers are increasing each day [3]. The rapid global spread of COVID-19 continues, which remains a danger throughout the world however, an accurate and certain treatment is still investigating by the scientists.

The treatment of COVID-19 is complex and requires different groups of drugs and regimens. However despite all effort and clinical studies a conclusive consensus on treatment is still lacking [4]. Individualized treatment measures were referring to clinical severity and conditions. In many cases, multiple medication use was inevitable. The most prescribed drugs for the treatment of COVID-19 were antivirals, antibiotics, analgesics and antipyretics, corticosteroids, tocilizumab, anakinra, and convalescent plasma, etc. [4].

Since the concept of pharmaceutical care emerged, one of the primary services of pharmacists is to ensuring optimal drug use and minimize adverse events occurred as a result of medications [5]. The pharmacist-led cognitive services, which are defined as *"the use of specialized knowledge by the pharmacist for the patient or health professionals for the purpose of promoting effective and safe drug therapy"* aims to optimize pharmacotherapy [6].

The pharmacist should evaluate the medication therapies using their skills about pharmacotherapy as their daily routine [7]. As an expert on drug use and pharmacotherapy pharmacist has an essential role in identifying and resolving the Drug-Related Problems (DRPs). The term DRPs could be defined as any events or circumstances related to pharmacotherapy that could interfere with the health outcomes [8]. According to the definition of the Pharmaceutical Care Network Europe (PCNE), DRP is *"An event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes*" [9]. Potential or actual DRPs may be harmful for the patient and increase the healthcare costs [10]. In a recent study held by Liew et al., up to 60 % potentially inappropriate prescribing observed in patients above the age of 65 years [11].

The prevention and resolving of DRPs requires a professional experience and collaboration among the healthcare professionals. The pharmacists are one of the most qualified healthcare professionals to identify and prevent DRPs due to their pharmacotherapy knowledge, and regular communication with patients [5]. During the medication review process DRPs should be identified and classified by a clinical pharmacist. To optimize the drug therapy, an evaluation of the indications, dosage, adherence, adverse events, and therapeutic effects of all drugs should be assessed and recorded [7]. Despite increased attention and DRPs identification, management and prevention of this issue is still a challenge.

Aim of the study

The main objective of this study is to investigate the pharmaceutical care need of COVID-19 patients in hospital settings. The primary outcomes of the present study were (i) the identification DRPs and influencing factors, (ii) the evaluation of the impact of DRPs on mortality and morbidity of the COVID-19 patients.

Method

Study Design and Sample Size

A prospective observational was study conducted on COVID-19 patients who were admitted to pulmonology service at a tertiary-care university hospital in Istanbul, Turkey between September 2020, and May 2021. The patients in need of intensive care were excluded. The patients with COVID-19 indication enrolled in this study were diagnosed according to the World Health Organization and Turkish ministry of Health interim guidance [12]. A sample size of 85 was required within a 5% margin of error and confidence intervals (CI) of 95% [13].

Data Collection

The patients' demographic factors (age, gender, body weight), comorbid diseases, prescribed medicine (dosing, frequency, and treatment duration) and duration of hospital stay were recorded. In addition, blood pressure, heart rate, oxygen saturation, respiratory rate, and laboratory findings (e.g., creatinine, uric acid, fasting blood glucose, hemogram, LACE+ index, Quick COVID-19 Severity Index [qCSI], COVID-GRAM Critical Illness Risk Score) on admission were recorded [14–16]. Meanwhile, the number of prescribed medicine or over-the-counter medications were collected. The identification of DRPs made by the pharmacists according to recent guidelines, UpToDate® and Medscape® clinical decision support system, and evidence-based medicine. Potential Drug-Drug interactions (pDDI) determined by UpToDate®. Among detected pDDIs only X (Avoid combination), D (Consider therapy modification) and C (Monitor therapy) categories are taken into consideration.

All assessment about DRPs which have clinical significance was performed by clinical pharmacists. The DRPs and clinical significance were evaluated using the Hepler and Strand drug-related problems classification system [17]. Data were collected using convenience sampling methods. This study has been reported according to recommendation of Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) standards (Figure 1). [18]

Statistical Analysis

As descriptive statistics, mean, median, standard deviation, and interquartile range [IQR] or count and percentages are given for continuous variables. The frequency, percentage are given for categorical variables. The normality of continuous variables was tested using the Kolmogorov-Smirnov test. The difference among groups was analyzed with an independent t-test or Mann-Whitney U test. Chi square tests are used to investigate the relationship between categorical variables. The univariate logistic regression analysis was used to determine which variable(s) are significant by using $p < 0.20$. The significant variables are included in the binary logistic regression analysis. The missing data were excluded from the analysis all the data were analyzed by using SPSS version 22® and Jamovi version 1.6.

Ethical Approval

The study protocol was approved by the ministry of health and the local ethics committee of Bezmialem Vakif University's clinical research ethics committee. The ethical approval was given by the Bezmialem Vakif University clinical research ethics committee with (approval number of 5/42, 06.05.2020). Informed consent was obtained from all individual participants included in the study.

Results

Demographics, Medications, and Drug-Related Problems (DRPs)

The total number of patients were 107, the median [IQR] age of patients was 64 [54.5-76.0] and 50.46% of them were male. The median [IQR] score of Body Mass Index (BMI) was 25.4 [23.7-27.7]. The median number of comorbidities [IQR] was 3 [2-4] per patient. The majority of the patient had at least one comorbidity (88.79%) other than COVID-19. The median [IQR] number of medicines prescribed, and hospital stay was 12.8 [8-16] and 9 [6-15], days respectively. The most frequently prescribed medicines were favipiravir, enoxaparin, pantoprazole, paracetamol, and dexamethasone (Figure 2). The total number of DRP was recorded as 201, and at least one DRP was seen in 75 out of 107 patients. The mean and median [IQR] number of DRPs were 1.93±1.91/patient and 2 [0-8] respectively (Table 4). According to our results 140 of the DRP was consist of pDDIs. One the most abundant pDDIs was increased bleeding due to concomitant use of dexamethasone and enoxaparin.

Medical conditions which are possessed by participants are summarized in Table 1. Among 107 patients, nearly half of them were diagnosed with hypertension (HT) (n = 54, 50.47%). The second and the third most common comorbidity were recorded as Diabetes Mellitus (DM) (n = 30, 28.47%) and coronary artery diseases (CAD) (n =25, 23.365) respectively (Table 1). Among patients with detected DRP out of 75, 44 patients had HT, 25 patients had DM and 24 patients had CAD (Table 1).

Vital Signs and Biochemical Findings

Baseline clinical and vital findings of the participants were recorded and presented in Table 3 and 4. The median [IQR] of body temperature of patients was recorded as 37 [36.4-37.5]. Among our sample median [IQR] the number of heartbeats per minute and oxygen saturation (spO_2) were 87 [78-96.5] and 93 [88-95] respectively. The median [IQR] systolic and diastolic blood pressure values were 131 [119-145] and 76 [65-82] respectively. The median [IQR] respiratory rate of the participant was 20 [16-22]. Participants' basal biochemical values are given in Table 4.

Factors associated with the Drug-Related Problems

Univariate analysis exploring the factors associated with DRP are presented in Table 5. The number of comorbidities (OR=2.097, 95% CI: 1.43-3.08; p<0.001), number of medications (OR=1.32, 95% CI: 1.17-1.49; p<0.001), serum Urea mg/dL levels (OR=1.035, 95% CI: 1.01-1.06; p<0.05), serum BUN levels (OR=1.00, 95% CI: 1.00-1.00; p<0.05), serum potassium levels (OR=2.409, 95% CI: 1.16-5.00; p<0.05), serum lymphocyte ratio (OR=0.967, 95% CI: 0.936-1.00; p<0.05), Quick COVID severity index score (OR=1.23, 95% CI: 1.01-1.353; p<0.05), and LACE+ index score (OR=1.23, 95% CI: 1.07-1.42; p<0.001) were associated with the DRPs. Binary logistic regression analysis for DRPs is presented in Table 5.

A binomial logistic regression was performed to ascertain the effects of the number of medications, the number of comorbidities, BUN, serum potassium levels, lymphocytes ratio, LACE+ Index, score, Quick COVID severity Index, serum urea level, on the likelihood that participants have a drug-related problem. The logistic regression model was statistically

Table 1. Patient Characteristics

Total number of patients	Total n=107	DRP Present (n=75)	DRP not Present (n=32)	*p*
Gender n (%)				*N.S*
Female	53 (49.53 %)	38 (35.51%)	15 (14.02%)	
Male	54 (50.46 %)	37(34.58%)	17(15.88%)	
BMI (Median [IQR])	25.4 [23.7-27.7]	24.9 [23.7-28.2]	25.9 [23.7-27.4]	*N.S*
Weight (kg)	75 [15, 65.0-80.0]	72 [65-80]	75 [70-80]	
Height (m)	1.66 [0.135, 1.62-1.75]	1.65 [1.60-1.75]	1.68 [1.65-1.75]	
Age (Median [IQR])	64 [54.5-76.0]	68 [58-76.0]	60 [50.5-67.0]	*p<0.05*
No. of Comorbidities (Median [IQR])	3 [2-4]	4 [2-5]	2 [1.75-3]	*p<0.001*
1 (n, %)	12 (11.21 %)	4 (5.33%)	8 (5.33%)	
2 (n, %)	29 (27.10 %)	19 (25.3%)	10 (31.25%)	
3 (n, %)	20 (18.69 %)	11 (14.6%)	9 (28.12%)	
4 (n, %)	25 (23.36 %)	22 (29.3%)	3 (9.37%)	
5 (n, %)	13(12.14 %)	12 (16.0%)	1 (3.12%)	
6 (n, %)	8 (7.47 %)	8 (10.6%)	0 (0%)	
Comorbidities				NA
COVID-19	107 (100 %)	75 (100%)	32 (100%)	
Hypertension	54 (50.47 %)	44 (58.6%)	10 (31.25%)	
Diabetes Mellitus	30 (28.04 %)	25 (33.3%)	5 (15.6%)	
Coronary Artery Disease	25 (23.36 %)	24 (32.0%)	1 (3.12%)	
Cancer	23 (21.50 %)	23 (30.6%)	7 (21.87%)	
Chronic Obstructive Lung Disease	20 (18.70 %)	18 (24.0%)	2 (6.25%)	
Cerebrovascular Disease	11 (10.28 %)	10 (13.3%)	1 (3.12%)	
Chronic Kidney Disease	8 (7.47 %)	7 (9.33%)	1 (3.12%)	
Neurological Diseases	8 (7.47 %)	7 (9.33%)	1 (3.12%)	
Psychiatric Diseases	7 (7.65 %)	7 (9.33%)	0 (0%)	
Others	32 (29.90 %)	20 (26.6%)	12 (37.5%)	
Hospital Stay in days (Median, [IQR])	9 [6-15]	10 [6-17.5]	7 [5-11]	*p<0.001*
Number of Medication (Median, [IQR])	12.8 [8-16]	14 [10.5-19]	7 [5-10]	*p<0.001*
Quick COVID severity Index	2 [0-5]	2 [0-5.5]	0 [0-2]	*p<0.001*
COVID GRAMM Critical Index	140 [117-164]	144 [127-164]	125 [108-164]	*p<0.001*
Charlson Comorbidity Index	4 [0-5]	4 [2-6]	2 [1-4]	*p<0.001*
LACE+ Index	13 [10-16]	14 [12-16]	10.5 [9-13.3]	*p<0.05*

significant, $\chi^2(8) = 57.842$, $p < 0.0001$. The model explained 59.7% (Nagelkerke R^2) of the variance in drug-related problems and correctly classified 84.1% of cases. Sensitivity was 92.1%, specificity was 64.52%, positive predictive value was 61.5% and negative predictive value was 74.3%. Of the eight predictor variables only four were statistically significant: number of comorbidities, number of medications, serum potassium levels and lymphocyte ratio (as shown in Table 5). Increased number of comorbidities (OR = 1.952; 95% CI: 1.07–3.54, p<0.05), number of medications (OR = 1.344; 95% CI: 1.12-1.61, p<0.001), and serum potassium levels (OR = 5.252; 95% CI: 1.57–17.56, p<0.001) was associated with an increased likelihood of exhibiting DRP. But increasing lymphocyte ratio (OR = 0.953; 95% CI: 0.91-0.99, p<0.05) was associated with a reduction in the likelihood of exhibiting DRPs.

Discussion

In this study, we investigated the DPRs of COVID-19 patient and related factors in hospital settings. Hospitalized COVID-19 patients have multi comorbidities and need multiple medications[4]. Currently many scientists investigating alternative medicine for COVID-19 infections. However, there is no exact treatment alternative for COVID-19 which approved by different authorities. On the other hand, the ethical aspects of these options are still questionable [19].

Many of the participants were prescribed with antivirals, antibiotics, analgesics, antipyretics, and anti-thrombotic drugs. Based on primary findings the number of comorbidities, serum potassium levels, lymphocyte ratio, and the number of medications were associated with the number of DRPs. The identified risk factors should be assessed by pharmacist to prevent DRPs in COVID-19 patients.

According to Pradhan et al and Imam et al. HT and DM were the most common comorbid disease among COVID-19 patients[20,21]. Another study held in Turkey pointed out that DM, HT, and CAD were the most frequent comorbidities among COVID-19 patients [22]. Our findings showed a correlation with their statements. The most common comorbid disease was recorded as HT (50.47%), which is followed by DM (28.04%), and CAD (23.36%) (Table 1). Therefore, detailed medical history should be taken and preventive measures for DRPs should be underlined by the clinical pharmacist.

A retrospective cohort study held by Imam et al. pointed out that older age and increased number of comorbidities were associated with mortality [21]. Among older patients (>60 years) (OR:3.66, 95% CI: 2.57–5.20) and increased number of comorbidities> 3 (OR: 4.11, 95% CI: 3.00–5.62) were independent predictors for mortality [21]. Similarly, our investigation pointed out that an increased number of comorbidities (OR = 1.952; 95% CI: 1.07–3.54, p<0.05) were associated with the increased number of the DRPs. The increased number of comorbidities were linked with DRP. However, in comparison of age, there was not statistically difference between the groups (Table 5). Many patients have multiple comorbidities especially elders. Cognitive service of pharmacist should be implemented into practice to improve healthcare services for COVID-19 patients. A detailed medication review process might be useful to detect and prevent DRPs. Hence, clinical pharmacists could provide pharmaceutical care for COVID-19 patients in the hospital setting [7,23].

Previous studies held in either in community pharmacy settings or hospital setting detected different number of DRPs per patient [7,24,25]. In our study, the mean number of DRP per patient was recorded as 1.93±1.91/patient. Our results were similar with Stafford et al. and Rhalimi et al. study. On the other hand, Wang et al., recorded the higher number of DRPs per patients than our findings. This difference could be explained by the settings of different studies. For instance, Stafford et al. study and our data obtained from hospital settings. However Wang et al and Rahlimi et al.'s studies were conducted in a community pharmacy settings [7,24,25].

Multivariate analysis showed that the number of medication used was associated as independent risk factors for the number of DRPs, which was consistent with previous studies [7,26–28]. Polypharmacy is a strong risk factor for DRPs. As a results, the number of used medications increased number of DRPs increased simultaneously. The presented finding extended the understanding that a higher number of medications is also an important predictors of DRP for COVID-19 patients (OR = 1.344; 95% CI: 1.12-1.61, p<0.001), that has not been studied extensively in the literature before [27,28]. Multiple medication use is inevitable with comorbidities. However, many of the DRPs may be prevented with well-planned pharmaceutical care services.

Another significant finding of our study is that serum potassium level was associated with DRPs. Compromised kidney functions is directly related with potassium levels. Many of our participants were suffered hypertension and diabetes which both may compromise the kidney functions. Patient with kidney diseases is more prone to drug related problems [29,30]. On the other hand, one of the most used hypertension drugs is diuretics which they could either spare potassium or prevent potassium secretion in kidneys. Also, hypokalemia or hyperkalemia may be directly related with the pharmacokinetic parameters of drugs. As in our finding level of serum potassium were related with DRPs which were consistent with literature [29,30]. Pharmacists should take into consideration that fluctuation of serum potassium level may be resulted as adverse events.

Limitations of the Study

This study had some limitations such as the generalizability of the results is limited as the sample was taken from only one center. In the future multicentered and wider studies are required to investigate the pharmaceutical care needs of COVID-19 patients. The number of patients was rather small. Finally, the

Table 2. Features Drug Related Problems (DRP) in COVID-19 patients

	Total	Median	[Min-Max]
Total No. of DRP,	201	2	[0-8]
Drug Interactions	140	1	[1-7]
Improper Drug Selection	40	1	[1-3]
Overdosage	21	1	[1-4]
Untreated Indications	-	-	
Adverse Reactions	-	-	
Failure to Receive Drugs	-	-	
Subtherapeutic Dosage	-	-	
Drug Use Without Indication.		-	

Table 3. Baseline Vital Signs of Patients

n=107	Median	[IQR]
Body Temperature, oC	37	[36.4-37.5]
Heartbeat (HBM)	87	[78-96.5]
Oxygen Saturation (spO2)	93	[88-95]
Systolic Blood Pressure (mmHg)	131	[119-145]
Diastolic Blood Pressure (mmHg)	76	[65-82]
Respiratory Rate (BPM)	20	[16-22]

HPM: Heartbeat per Minute, Breath per Minute

lack of a control group was a limitation of the present study, which was worth noting.

Conclusion

To the best of our knowledge, our study was the first to investigate the incidence, type, and related factor of DRPs detected by clinical pharmacists in COVID-19 patients' hospital settings. This study showed that a considerable proportion of patients with DRPs was high, and the most common category was the drug-drug interactions. In the multivariate model, the number of medications, number of comorbidities, serum potassium levels and lymphocytes ratio were significant related factors to the number of DRPs.

COVID-19 pandemic is still an important healthcare problem all around the world. Pharmacist involvement and pharmacist-led cognitive services would detect, prevent, and decrease unfavorable drug-related events. To improve healthcare services pharmacist should take responsibility and should become an indispensable component of the COVID-19 healthcare team.

Table 4. Baseline Biochemical values of participants

n=107	Reference Range	Median	[IQR, 25-75]
Acute Phase Reactants			
CRP mg/dL	0-5	63	[97.3, 24.7-122]
Procalcitonin ng/mL	0-0.5	0.157	[0.318, 0.02-0.34]
Ferritin ng/mL	21-274	369	[649, 142-791]
D-Dimer ng/mL	0-300	253	[391, 187-578]
Albumin g/dL	3.2-4.6	3.60	[0.50, 3.30-3.80]
Renal Function Parameters			
Urea (mg/dL)	17-49	41	[32.5,28.5-61]
Blood Urea Nitrogen, BUN (mg/dL)	8-23	19.2	[15.2, 13.3-28.5]
Creatinine (mg/dL(	0.7-1.3	0.88	[0.46, 0.74-1.15]
GFR (mL/min/1.73)	>90	78	[36, 60-96]
Hepatic Function Parameter			
Lactate dehydrogenase, LDH (U/L)	125-220	316	[169, 260-429]
Aspartate Aminotransferase, AST (U/L)	5-34	29	[19.5, 24-43.6]
Alanine Aminotransferase, ALT (U/L)	0-55	24	[24.5, 14.5-39]
Alkalen Phosphatase ALP (U/L)	40-150	55	[36.5, 39.3-75.8]
Gamma-Glutamyl Transferase, GGT (U/L)	12-64	31.5	[18.3, 24-42.3]
Total Bilirubin (mg/dL)	0.3-1.2	0.48	[0.31, 0.31-0.62]
Direct Bilirubin (mg/dL)	0-0.5	0.23	[0.15, 0.15-0.30]
Amylase (U/L)	28-100	36	[31.2, 30-60]
Lipase (U/L)	8-78	25	[17.5, 19-36.5]
Electrolytes			
Sodium mmol/L	135-145	137	[5, 135-140]
Potassium mmol/L	3.5-5.1	4.25	[0.795, 3.89-4.69]
Calcium mg/dL	8.4-10.6	8.60	[0.6, 8.3-8.9]
Complete Blood Count			
White Blood Cells, WBC (103/uL)	4.5-11	7.10	[5.69, 5.22-10.9]
Lymphocytes %	10-50	16.3	[16.3, 10.3-26.6]
Neutrophiles %	45-78	74.3	[16.3, 61.4-82.4]
Monocytes %	0-12	6.59	[4.91. 4.52-9.43]
Hemoglobulin (g/dL)	14.1-17.5	12.3	[4.52, 10.9-13.7]
Hematocrit %	40-52	36.6	[7.44, 32.6-40.1]
Mean Corpuscular Volume, MCV (fL)	80-97	85.6	[7.22, 82.4-89.6]
Prothrombin Time, PT (s)	11.4-16.2	14.5	[2.10, 13.7-158]
Activated Partial Thromboplastin Time, aPTT (s)	22-40	35.1	[7.25, 31.9-39.2]
International Normalized Ratio, INR	0.8-1.2	1.07	[0.215, 0.98-1.1]9

Table 5. Statistical analysis of factors associated with the number of drug-related problems

Variables	Univariate analysis			Multivariate analysis		
	OR	95% CI for Odds Ratio	p value	OR	95% CI for Odds Ratio	p value
Age, years	1.023	(0.99-1.05)	0.124			
Gender						
Male	0.88	(0.46-2.46)	0.880			
Female	Reference					
Hospital Stay (days)	1.051	(0.99-1.12)	0.113			
LDH U/L	1.00	(0.99-1.00)	0.889			
CRP mg/L	0.990	(099-1.00)	0.439			
Procalcitonin ng/mL	1.150	(0.71-1.77)	0.629			
Ferritin ng/mL	1.000	(1.00-1.00)	0.508			
D-Dimer ng/mL	1.000	(1.00-1.00)	0.881			
No of Comorbidities	2.097	(1.43-3.08)	**<0.0001**	1.952	(1.07-3.54)	**0.028**
No of Medication	1.32	(1.17-1.49)	**<0.0001**	1.344	(1.12-1.61)	**0.001**
Urea mg/dL	1.035	(1.01-1.06)	**0.006**	0.001	(0.00-10.34)	0.129
BUN mg/dL	1.000	(1.00-1.00)	**0.006**	1.000	(1.00-1.00)	0.128
Creatine mg/dL	2.225	(0.71-7.02)	0.172			
Sodium mmol/L	1.066	(0.96-1.18)	0.215			
Potassium mmol/L	2.409	(1.16-5.00)	**0.018**	5.252	(1.57-17.56)	**0.007**
WBC 103/µL	0.985	(0.945-1.028)	0.486			
Lymphocyte %	0.967	(0.94-1.00)	**0.050**	0.953	(0.91-0.99)	**0.041**
Quick COVID severity Index	1.169	(1.01-1.35)	**0.037**	1.245	(0.98-1.58)	0.070
LACE+ Index	1.233	(1.07-1.42)	**0.003**	0.798	(0.61-1.04)	0.093

Conflict of Interest

None

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